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The Encyclopedia of

Schizophrenia and Other Psychotic Disorders

THIRD EDITION

RICHARD NOLL, PH.D.

FOREWORD BY
LEONARD GEORGE, PH.D., R. PSYCH.

THE ENCYCLOPEDIA OF

SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS

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For Wolfgang Noll,
My beautiful boy of seven summers,
Sol invictus

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FOREWORD: THE HAUNTED ANIMAL

Our species is haunted by madness. One in every 100 of us will fall prey to it at some time in our lives, and of those, one in 10 will be driven by misery or confusion to take their own lives. Not only the afflicted suffer, of course. As Aristotle famously noted, we are social animals, profoundly linked with each other, and derangements of the psyche (the technical term is *psychoses*) strain the social web, burdening family, friends, communities, and economies. Directly or indirectly, madness touches us all.

Has it always been so? Experts disagree as to whether some forms of psychosis, such as schizophrenia, may have arisen over the last few centuries. But people showing the common mark of the psychotic disorders—disturbed contact with physical and social reality, leading to mental anguish and inability to live well—can be found in every culture on earth today and were likely among our ancestors at prehistory's dawn.

Throughout history, madness has been a terrible scourge and, also, a mirror. Beliefs about psychosis reflect the framework with which societies define reality. Traditional cultures going back to the Old Stone Age did not draw a line between animate and nonliving as we do today. Rather, the cosmos and everything in it was ensouled. In dreams and visions, a person's soul could wander in the invisible lands of the spirits. A soul's distress implied trouble in the spirit realm. Perhaps the soul had been kidnapped by a sorcerer or lost its way in the otherworld. Maybe the body had been invaded by some dark ghost. Or the person might have skewed the balance of the world by breaking a taboo laid down by spirits. A shaman may have been called in to divine the problem and heal the deranged person, by finding the wayward soul or extracting the invader—often literally by sucking it out of the body through a tube of bone or bark—or cutting a deal with the peeved sprite whose taboo had been slighted. Shamans lived on the cusp between seen and unseen worlds and partook of the weirdness of that liminal space, so their actions were often inscrutable. Ironically, many modern scholars who studied preliterate healing practices confused the patient's state with that of the doctor, seeing symptoms of psychosis in the odd behavior of shamans. The present work's author, Dr. Richard Noll, exposed the fallacy of the "schizophrenia metaphor" of shamanism in one of his earliest research papers.

The notion that madness can be caused by spiritual forces endured into the worldviews of the early civilizations—indeed, it has survived to the present. With the Vatican's blessing, a Roman college still offers courses in the study of demonic possession and exorcism, training priests to discern the signs of the devil's hand in severely disturbed behavior and the right techniques of "sucking out" the pest—no longer with a shaman's bone, but with sprays of holy water and chants of scripture. Dr. Noll's published collection of psychiatric case reports of the "possession syndrome" is the most important study of this topic in many decades.

In ancient Greece, all sorts of mental and physical maladies were taken to be the mischief of the *kakodaimones,* personifications of malign forces in one's character or environment, or else the result

of the gods' displeasure. Sufferers might make a pilgrimage to a temple-complex of the healing deity Asklepios. There, they would ease their souls by strolling through gardens and groves and attending the theater. At the climax of the therapy, they spent the night in the temple, where they prayed for a visit from the divine healer. Asklepios's favorite animal was the snake (which still curls around Asklepios's wand in the symbol of the medical profession)—feeling it slither over one's body in the darkened temple was a sure sign of good prognosis.

Hippocrates founded a medical tradition that sought natural causes for ailments. The cosmos was an interplay of four elements (air, fire, earth, and water), and the human being, as a *mikrokosmos* (small replica of the cosmos), featured the circulation of airy blood, fiery yellow bile, earthy black bile, and watery phlegm. If the balanced flow of these four humors was upset, illness of body or mind could ensue. Too much yellow bile could trigger bouts of mania, while an excess of black bile (*melan choler* in Greek) could lead to a deep melancholy. Either extreme could fray the sufferer's contact with reality for a while. The Hippocratic doctor would advise a moderate lifestyle—neither too much nor too little sleep, food, exercise, socializing. He might also try to bleed the excess humor from the body. Hippocratic medicine, as reformulated by Galen in the second century A.D., remained vital for classifying and treating madness well into the Enlightenment.

Christian authorities through the ages viewed madness in many ways. Christ's call to compassion for the sick drew Christian doctors to treat psychotic sufferers as patients who needed medical help, often of the Hippocratic/Galenic variety. Christianity cast the world as a battle between the Lord and Lucifer over the fate of souls, so it is no surprise that hurt psyches would be seen as casualties of that spiritual war. Folk healers peddled charms to keep Satan's spawn at bay or drive them out or offered to cut open the scalp of the mad person and remove the "folly stone" that had sprouted in the brain. With a little sleight of hand, they could give the plucked stone to the patient's grateful family as a keepsake—and then leave town as fast as possible.

By the later Middle Ages, the Catholic project of a universal church was in dire straits. The grip of Islam on Africa and the Middle East was not seriously loosened by the Crusades. Within western Europe itself, heresies like Catharism and Waldensianism threatened the Catholic monopoly of faith. The Black Death's ravages were strangely unresponsive to prayer, raising further doubts. Clearly, Christendom was under sustained attack by a potent foe. It could only be the devil, aided by a "fifth column" of perverse humans. This conclusion was drawn not by the ignorant masses but by the leading intellectual lights of the church, setting the foundation for the Great Witch Hunt. Deviant behaviors that were taken as signs of humoral imbalance in the past now marked a person as either a demonic victim or collaborator. The prescription for psychosis was often exorcism. As well as the pronouncement of holy mutterings, torturing the bewitched person was encouraged to discomfit the resident demon. The "witches" accused of sending the demons got even worse treatment. Tens of thousands confessed under torture. But some eagerly shared their tales of flying through the air at night on a goat or broom to the witches' sabbaths, where in Satan's honor they would kiss a giant cat beneath the tail, feast on babies' flesh, and plot spells to blight crops and abort good Christian fetuses. These delusional souls were freed from their psychoses by the stake or the noose.

There never were any witches. But the witch-hunters' fantasies surfaced again in the late 20th century as a wave of "ritual Satanic abuse" reports spread around the world. Investigators found no credible evidence for the alleged global conspiracy of devil-worshippers. Dr. Noll's timely writings on this topic helped eventually to stem the irrational tide.

In the 1400s, as the Witch Hunt was unleashed, the Renaissance bloomed in Italy. A brighter conception of humanity and nature gradually spread. No longer was the world the chessboard of God and devil, but a wondrous creation to be explored by the miracle that is humanity, "noble in reason, infinite in faculty," as Shakespeare put it. This rebirth of a proud and ingenious curiosity led to the rise of modern science. Mad people were no longer thought soiled by Satan's touch but somehow diseased. In the absence of useful treatments,

they were locked in "insane asylums" or "madhouses" in the care of a new breed of medical specialist, the "mad-doctor." Patients' disruptive acts had to be managed in these settings, leading to an era of inventive restraints. And the mad-doctors devised many clever means to try to shock or stress patients out of their psychoses. These methods were often not so different from those of the witch interrogators, but with much kinder motive.

The humanistic wisdom of the Renaissance bore fruit in the rise of democratic governments and legally enshrined human rights in Europe and the Americas. Seen with humanists' eyes, the denizens of the madhouses looked to be unfortunate kin, not only saddled with mental illness, but stripped of dignity and jailed in dungeons. Such was the view of the great reformers like Pinel, Rush, and Tuke, who began the process (which is not yet complete in some parts of the world) of unchaining the mad and treating them decently. But there were still no viable theories to explain the cause of psychosis or guide its treatment. Other areas of medicine were starting to see breakthroughs—scientists found the cause of many diseases to be microorganisms, and soon were creating vaccines. Medicine's trend was to focus on biology and neglect psychological and social factors in illness and health.

The imprint of this split between body and psyche has been clear in the disciplines of psychiatry and psychology since their inception in the 19th century. Camps of specialists framed the puzzle of psychosis as either biological or psychosocial. Their research produced a series of dead ends instead of insights. Each view had its turn dominating academic and popular culture. More harm than good came of these fractured perspectives. The reign of psychoanalysis for several decades was notably unhelpful. Dr. Noll's archival research, published in several articles and books, has shed much-needed light on this complex era.

The madness that haunts us still evades our grasp. Millions around the world succumb, and few recover fully. But there is good news. A revolution is taking place in our conceptions of health, illness, and recovery. Researchers have found that the most useful approach to health problems is to weigh the full range of biological and psychosocial influences. We suffer not just as ill bodies or as ill minds but as ill persons. In broad strokes, this "biopsychosocial" model is like the holistic vision of the ancients, but now confirmed, revised, and empowered by the tools of modern science. And it seems that psychosis is finally yielding some of its secrets to this approach. Let us hope that more and more effective therapies will be the result.

The study of psychosis is one of the fastest changing areas in health science. And its long history holds deep lessons that must never be lost. How are we to embrace this vast topic? We can have no better guide in the world than Dr. Richard Noll. The first two editions of the present book established it as the best single-volume resource for anyone wishing to learn about the history and current science of psychotic disorders. This, the third edition, is a masterpiece of erudition and clarity. Experts will find nuggets of knowledge that they missed in decades of study; nonspecialists will be introduced to the landscape of psychosis in straightforward language that is grounded in rock-solid scholarship. The best way to use this book—indeed, the best way for us to advance in our struggle with psychosis—may be to follow the advice of the alchemists of old: "*Ora, lege, lege, lege, relege, labora, et invenies*"—"Pray, read, read, read, reread, work, and you will find!" If we do so diligently, one day humankind may no longer be the haunted animal.

—Leonard George, Ph.D., R.Psych.
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PREFACE TO THE THIRD EDITION

This third edition of *The Encyclopedia of Schizophrenia and Other Psychotic Disorders* is a completely revised and updated reference to all the medical, scientific, and historical aspects of these ancient afflictions. The entries in this book have been carefully selected for their usefulness in the years to come.

This volume points both forward and backward in time. In addition to providing entries that summarize all the current theories, findings, and treatments for schizophrenia since the second edition was completed in the summer of 1999, this book has been thoroughly revised to place the science of schizophrenia into its historical context. Thus, this book combines the latest scholarly research in the history of medicine and psychiatry with the vast scientific research literature on the diagnosis, etiology, pathophysiology, course, outcome, and treatment of schizophrenia. There is no other reference work that combines these two perspectives in such depth.

For this edition, many entries have been combined into larger, more comprehensive essays. This change is most evident in the entries for two of the most rapidly changing areas of research in schizophrenia: antipsychotic drugs and genetics studies. The latest scientific information for all entries is distilled and explained in plain language, thoroughly embedded in the new historical scholarship on those topics. Extensive reviews of the latest findings on endocrine and immune system alterations, brain abnormalities, and blood vessel alterations in schizophrenia likewise combine historical and scientific perspectives. New research findings regarding the course and outcome of schizophrenia and possible new environmental risk factors are discussed in entries for those topics.

Since the last edition, an explosion of new scholarship on the history of psychiatry has broadened our understanding of the historical trajectory of the evolution of dementia praecox (1893) into schizophrenia (1908). Extensive, entirely new entries for these disorders appear in this edition, as well as for related psychotic disorders such as manic-depressive illness (1899) and bipolar disorder (1980). Disorders that may be biologically related to schizophrenia, such as schizotypal personality disorder, also received thorough updating. So have entries for psychotic disorders that appear to be distinct from schizophrenia and manic-depressive illness, such as paranoia, chronic delusional states in French psychiatry, and the atypical psychotic disorders. The history of treatments for schizophrenia and other psychotic disorders is covered in depth in new or significantly revised entries on psychosurgery, insulin coma therapy, metrazol shock therapy, and electroconvulsive therapy.

Throughout this book, there will be many references to the *Diagnostic and Statistical Manual of Mental Disorders, 4th ed., text revision,* or *DSM-IV-TR* (2000), produced by the American Psychiatric Association, and *The International Classification of Diseases, 10th ed.,* or *ICD-10* (1992), created by the World Health Organization. They are the two most often used diagnostic manuals for mental disorders throughout the world. The diagnostic criteria for schizophrenia

from these two volumes are included in appendixes in this volume.

Rather than including a huge bibliography at the end of the book and in order to prevent all the flipping of pages back and forth as the reader attempts to locate a particular reference, full citations of references are included after each entry. Publications in English, German, and French—the three primary languages in the history of psychiatry—are provided for scholars and for European readers of this volume. Those reference sources have been chosen carefully according to three criteria: (1) the source is recommended as the best review of the relevant research in a particular area, (2) the source represents the first mention of an important theory or research finding in print, and (3) the source refers directly to a passage quoted in the entry or cites a major representative work of the person listed in a biographical entry. The users of this book are encouraged to read further, and it is hoped that the extensive references provided with the entries will encourage further exploration in the spirit of the proverb that was a favorite among the ancient alchemists, *liber librum aperit* ("one book opens another").

There are many long citations from rare psychiatric texts and especially from autobiographical accounts. Our best feeling for what life must have been like for patients, their family members, and physicians alike over the past two centuries comes from such vivid reports. Many of these quotations are from volumes that are so obscure that they can only be found in the rare book collections of *some* specialized libraries, and care has been taken to select those passages that particularly make the history of psychiatry "come alive" for the reader.

No other book like this presently exists for understanding schizophrenia and the other psychotic disorders. It is hoped that the reader will find it of value when trying to come to grips with a subject that has mystified humankind for centuries.

—Richard Noll, Ph.D.
Allentown, Pennsylvania

MADNESS, PSYCHOSIS, SCHIZOPHRENIA: A BRIEF HISTORY

The history of schizophrenia is the history of psychiatry. The earliest clear description of this disease dates to only 1809—at about the time that the very first psychiatric textbooks were being written by dedicated physicians who worked in "madhouses" and "asylums" with the "insane." They collected their observations of lunatics, devised classifications for them, speculated as to the causes of their afflictions, and even performed crude autopsies on their bodies to see if they could discover the secret of madness. The profession of psychiatry grew out of the efforts of these physicians to understand and cure diseases of the mind, particularly those tragic, chronic mental illnesses that condemned thousands to debilitated lives in institutions. Therefore, the psychotic disorders, and schizophrenia in particular, have always been at the very heart of the concerns of the psychiatric profession and are in fact responsible for its existence.

As we enter the 21st century hardly a month goes by in which some new discovery in genetics is not announced, and the mission to explore the genetics of schizophrenia will no doubt occupy a prominent position in the research of the next decade. But our late 20th-century cultural persona of schizophrenia as primarily a "genetically transmitted disease" forces us to reexamine certain historical problems related to schizophrenia. Specifically, what is its ever-changing story over the centuries? What other masks has it worn on the various stages of human history? What guesses have been made as to its possible etiology? What have been the fads and fashions in its research?

The many individual entries in this encyclopedia provide detailed synopses of these topics, but below is a brief summary of the highlights of the history of this disease.

Did Schizophrenia Exist in Antiquity?

If schizophrenia is truly a brain disease that has a strong basis in genetics, then there should be evidence that this severe mental disorder has afflicted people for hundreds, if not thousands, of years. "Madness" has been reported in every society on record, no matter how ancient or how primitive, and descriptions of hallucinations, delusions, and bizarre behavior are often reported in association with "madness." For example, in an attempt to trace schizophrenia back to ancient Babylonian accounts (3000 B.C.) or to early Sanskrit texts from India, translation of descriptions of mental illness from these cultures have been collected in articles published in 1985 by D. V. Jeste and his colleagues and in 1984 by C. V. Haldipur. But it is still not clear from this historical evidence that schizophrenia—as we know it, as a disease with a particular course that begins in adolescence or early adulthood, with characteristic signs and symptoms, and a chronic deteriorating course (at least in the type of schizophrenia that seems to be the most "genetic")—existed in the ancient eras. This point (and the larger ramifications of this entire issue) has been eloquently argued and documented by psychiatrist E. Fuller Torrey in his book *Schizophrenia and Civilization* (1980).

There are many reasons for this doubt. First, ancient descriptions of madness that involved delusional, hallucinating, or confused individuals could be accounts of any number of physical or mental disorders. The same argument holds true for 19th- and 20th-century anthropological descriptions of "schizophrenia" or "psychosis" in preliterate (formerly called "primitive") societies. For example, these same symptoms could be

produced by head trauma, brain infections, injury due to birth complications, strokes, or by any number of other known organic mental disorders. Or they could be descriptions of the other psychotic disorders, such as bipolar disorder (manic-depressive psychosis) or any of the atypical psychotic disorders. What is missing in these accounts are descriptions of the full course of the disease process over time.

Another issue regarding "schizophrenia" in so-called primitive societies should also be addressed. In the 20th century there has been a long tradition among some anthropologists (usually psychoanalytically oriented) and certain psychiatrists and psychologists who are "armchair anthropologists" that the magico-religious healers and diviners known as shamans have perhaps been persons who would otherwise be labeled schizophrenic or certainly psychotic in our culture. The theory goes: since their bizarre behavior is accepted (visions, ecstatic trances, etc.) and since prominent social roles have been created for them, they seem to adapt just fine without any further deterioration. This absurd ethnocentric notion has unfortunately persisted with some very prominent proponents, often with those who have little or no true expertise in the study of shamanism, schizophrenia, or both. The "schizophrenia metaphor" of shamanism is unfounded.

Psychosis in Europe up to 1600

Since antiquity, persons with psychotic disorders and other forms of mental illness have been left to themselves, sent off in "ships of fools," locked in cages, "flogged into reason," chained, or simply killed, in some instances. Until the 1500s, the care of the insane in Europe—what little was offered—had been the responsibility of monks and nuns. For example, the oldest institution for the insane in England, the Bethlem Royal Hospital ("Bedlam"), was first established in 1247 as a priory, and by 1329 it functioned as a hospital. The patients were serviced by a 13th-century religious order known as the Bethlehemites, and on their habits they wore the special insignia of a red star with a dark blue center. The city of London took control of the place in 1346, and in 1547 it was made into a royal institution, headed by physicians, and the name was changed to St. Mary of Bethlehem. This was later changed to its present name, the Bethlehem Royal Hospital.

The reigning theory of madness was based on the antiphlogistic or humoral theory of disease. This theory had been in vogue since the time of Hippocrates (460–377 B.C.) and was elaborated upon by Galen (A.D. 129–199). Both mental and physical disorders were considered by Galen to be caused by an excess (*plethora*) of one of the four humors: black bile, yellow bile, blood, and phlegm. The cure was to remove the excess by bleeding the patient or by using purgatives or laxatives. Remnants of the humoral theory formed the basis of asylum treatment for persons with schizophrenia and the other psychotic disorders until well into the 19th century and are graphically described by the fathers of psychiatry in the earliest psychiatric textbooks.

The "New Philosophy" and Madness—the 1600s

Many social and historical changes converged in the 17th century (especially in England) to change this dark state of affairs for people with mental disorders. First, societies began to incarcerate mentally ill people in central institutions (jails, hospitals) where many of them could be observed together for long periods of time. Second, physicians (crude as their art may have been at the time, an era that medical historian Guy Williams has dubbed the Age of Agony) began to be put in charge of the care of the mentally ill in these institutions. The institution of private madhouses for the care of the insane (at a profit) also began in this era and also involved physicians. And third, with the influence of Francis Bacon's "new philosophy," which sparked science as we know it, the concept of "disease" began to take on new meaning. This was largely due to the influence of the English physician Thomas Sydenham (1624–89), often referred to as the "English Hippocrates," who emphasized the direct observation of illnesses and suggested their classification according to syndromes, or groups of symptoms. This differed from the centuries-old identification of diseases usually

by a single symptom, such as was the case with the ancient mental disorder known as "fury."

The 1700s: Madness Is Classified

Throughout the 1700s, physicians who doctored to the mentally ill in madhouses (both public and private) began to be recognized for their medical specialty and were called mad-doctors or lunatic-doctors in England and its colonies. The more scientifically minded mad-doctors began to study the symptoms of mental illness for the first time in terms of syndromes, and many of them contributed treatises and classifications of their insane patients. In this endeavor, the British led the way, and such figures as William Battle of St. Luke's Hospital in London, John Haslam of "Bedlam" in London, and William Cullen of Edinburgh became world-famous authorities through their written observations on madness. Daringly, Haslam even reported on his autopsies of corpses of Bedlam patients, in an age where such practices were discouraged by British laws, and "bodysnatchers" supplied medical students and professors with such commodities. Each author devised his own unique classification system for mental disorders, often borrowing concepts used for centuries, as well as coining new terms and phrases. It is certain that many cases of what we would now call schizophrenia were probably classified under one or more of these early attempts to devise a more scientific method of understanding mental illness.

The 1800s: Psychiatry (and Schizophrenia) Begins

Following the early lead of the British, after 1801 it was the French who dominated the medical study of the mentally ill until mid-century, when the Germans began their domination of this field. Indeed, the devotion of the early French *aliénistes* (Pinel, Esquirol, and the members of the "Esquirol Circle") to the study and classification of mental disorders directly led to the development of a distinct medical specialty for mental illness, which is now universally known as "psychiatry." The French were the first to include lectures on mental illness in their medical schools, and the British followed suit by the 1820s.

In 1801 French physician Philippe Pinel published his famous treatise on insanity (*l'aliénation mentale,* or "mental alienation," which led physicians who specialized in the care of the mentally ill to be called "alienists" in England). The first edition of Pinel's *Traité médico-philosophique sur l'aliénation mentale, ou la manie* established him as the world's leading authority on mental illness and helped to persuade the world that the mentally ill could be treated in a more humane manner through his philosophy of "moral treatment." When Pinel was put in charge of the large institution for insane men in Paris following the French Revolution, he became famous for freeing 53 patients from their chains—without any disastrous consequences. Indeed, one of them, a former French soldier named Chevigné, became his bodyguard. The legend of Pinel unshackling the insane fit well with the revolutionary and democratic spirit of the times, and it helped to free the psychological chains in the minds of caretakers of the mentally ill, that their charges were nothing more than beasts and should be treated as such. Variations of the "moral treatment" were already being developed in England by William Tuke at the York Retreat and by Vincenzo Chiarugi, often referred to as "the Pinel of Italy." This more humane treatment philosophy was not widely adopted in Europe until the mid-1800s, and even in England, it took the reformist physician John Conolly's "nonrestraint movement" in the 1840s to bring lasting changes finally in the asylums in that country.

In the young United States, Philadelphia physician Benjamin Rush of the Pennsylvania Hospital began to study the insane patients within his institution and published a book on the subject, his *Medical Inquiries and Observations upon the Diseases of the Mind* of 1812, the only major American textbook of psychiatry to appear until the 1880s. Thus, American physicians played almost no role in the scientific description and classification of mental disorders until the 20th century.

Schizophrenia now enters the picture. In 1809 the very first clinical descriptions of schizophrenia as we know it appeared in print in two separate works. Working independently in their respective

countries, John Haslam of the Bethlem Royal Hospital in London and Philippe Pinel of the Salpêtrière asylum in Paris both produced expanded second editions of books on mental illness that had been published previously; they contain the first complete reports of what we now know as schizophrenia in its "chronic" (or "Type II") form. The expanded second edition of 1809 of Pinel's original 1801 treatise has never been translated into English (a translation of the first edition appeared as early as 1806). Pinel's description of *démence* in the first edition strongly resembles the thought disorder of schizophrenia, and this concept was apparently illustrated with case material in the second edition that seemed to confirm this connection. However, the following case history reproduced here from Haslam's 1809 *Observations on Madness and Melancholy* may be the first valid historical evidence in the English language for schizophrenia:

> There is a form of insanity which occurs in young persons; and, as far as these cases have been the subject of my observation, they have been more frequently noticed in females. Those whom I have seen, have been distinguished by prompt capacity and lively disposition; and in general have become the favorites of parents and tutors, by their faculty in acquiring knowledge, and by a prematurity of attainment. This disorder commences, about or shortly after, the period of menstruation, and in many instances has been unconnected with hereditary taint; as far as could be ascertained by minute enquiry. The attack is almost imperceptible; some months usually elapse before it becomes the subject of particular notice; and fond relatives are frequently deceived by the hope that it is only an abatement of excessive vivacity, conducing to a prudent reserve, and steadiness of character. A degree of apparent thoughtfulness and inactivity precede, together with the diminution of the ordinary curiosity, concerning that which is passing before them; and they therefore neglect those objects and pursuits which formerly proved sources of delight and instruction. The sensibility appears to be considerably blunted; they do not bear the same affection towards their parents and relations; they become unfeeling to kindness, and careless of reproof. To their companions they show a cold civility, but take no interest whatever in their concerns. If they read a book they are unable to give any account of its contents; sometimes, with steadfast eyes, they will dwell for an hour on one page, and then turn over a number in a few minutes. It is very difficult to persuade them to write, which most readily develops their state of mind; much time is consumed and little is produced. The subject is reportedly begun, but they seldom advance beyond a sentence or two; the orthography becomes puzzling, and by endeavoring to adjust the spelling the subject vanishes. As their apathy increases they are negligent of their dress, and inattentive to personal cleanliness. Frequently they seem to experience transient impulses of passion, but these have no source in sentiment; the tears, which trickle down at one time, are as unmeaning as the loud laugh which succeeds them; and it often happens that a momentary gust of anger, with its attendant invectives, ceases before the threat can be concluded. As the disorder increases, the urine and feces are passed without restraint, and from the indolence which accompanies it, they generally become corpulent. Thus in the interval between puberty and manhood, I have painfully witnessed this hopeless and degrading change, which in a short time has transformed the most promising and vigorous intellect into a slavering and bloated idiot.

Haslam is describing what 20th-century British psychiatrist Timothy J. Crow has named "Type II schizophrenia" or the "Pinel-Haslam syndrome"; insidious onset, negative symptoms (attention deficits, problems in information processing, apathy, poverty of speech, loss of curiosity in people and activities), and gradual cognitive deterioration.

The cognitive deterioration described by Haslam, or *démence*, as Pinel termed it, was later elaborated upon by French *aliéniste* Benedict Augustin Morel in his descriptions of mental "degeneration," for which he coined the term *démence précoce* in 1853. Whereas the concept of degeneration probably referred to cases that we would label schizophrenia today, it also referred to cases of one of the most frequently encountered psychotic disorders of the 19th and early 20th century, the "general paralysis

of the insane," which was later found to be caused by tertiary syphilis.

After Morel's introduction of degeneration theory in the 1850s, and Jules Baillarger's very first description of the "double-formed insanity" (what we now call bipolar disorder) in 1854, the French alienists subsided in importance, and it was the Germans, led by Wilhelm Griesinger, who began to dominate psychiatry until well into the 20th century (except, perhaps, for Charcot's contributions in Paris in the 1880s to the understanding of hysteria and the use of hypnosis). Griesinger's 1861 textbook, *Die Pathologie und Therapie der Psychische Krankheiten (The Pathology and Therapy of Mental Disorders)*, provided a detailed classification of mental disorders that was based on the notion that they were organically based, indeed, that they were all largely diseases of the brain. Although not a new notion, the work of Griesinger and later German psychiatrists and neurologists helped to establish the biological approach in psychiatry. Because of the contributions of the Germans, the biological approach is the central research strategy in the study of schizophrenia and the psychotic disorders today.

The 1840s was the pivotal decade in the history of the profession of psychiatry. By this time the actual word *psychiatry* was in use in both Germany and England, and the very first professional associations of such physicians were formed in Germany, England, France, and in the United States. In 1844, 13 superintendents of state asylums from across America met together in Philadelphia and formed the organization that is now known as the American Psychiatric Association. In the 1870s, following the study of wounded veterans of the American Civil War, the first professional society for the medical specialty of neurology was founded. Thus the study of mental disorders now had two branches of medicine with two very different philosophies, which remained at odds with one another until well into the 20th century.

With the Germans taking the lead, psychiatry began to resemble its present form. Indeed, by the end of the 19th century our present notion of psychosis as a disorder involving a gross impairment in reality testing (a "break with reality") and the creation of a new reality had taken shape. Even today psychosis encompasses phenomena that were labeled "insanity," "alienation," and "dementia" or degeneration in the 19th century.

The "Clinical Method" of Psychopathology

In 1863 Karl Kahlbaum of Prussia published his Habilitation (the equivalent of a second doctoral dissertation in Germany, necessary for becoming a university professor), *Die Gruppirung der psychischen Krankheiten (The Classification of Psychiatric Diseases)*. In this book, Kahlbaum described a class of progressively degenerating psychotic disorders that he grouped under the term "Vesania typical" (typical insanity). In 1866 Kahlbaum became the director of a private psychiatric clinic in Görlitz, Prussia, a small town near Dresden. He was accompanied by his younger assistant, Ewald Hecker, and together they conducted a series of research studies on young psychotic patients that would eventuate in a major influence on the development of modern psychiatry. Together Kahlbaum and Hecker were the first to describe and name such syndromes as dysthymia, cyclothymia, paranoia, catatonia, and hebephrenia. These are just the diagnostic labels that survived into history. In an attempt to overthrow the confusion of the past, including the inclination of physicians since pagan antiquity to group all mental disorders as forms of either "mania" or "melancholia" (terms that were not distilled down to their present meaning until the period between 1850 and 1900), Kahlbaum made the mistake of coining new names for just about every syndrome. Though acknowledged as a major psychiatric thinker in the 19th century, perhaps second only to Emil Kraepelin, his classification system was too novel and idiosyncratic to be widely adopted, and thus Kahlbaum receded into the shadows of history.

Perhaps their most lasting contribution to psychiatry was the introduction of the "clinical method" from medicine to the study of mental diseases, a method which is now known as psychopathology. Other than Morel's claims about his degeneration theory, the element of time had largely been missing from definitions of mental disorders. Psychiatrists made pronouncements about prognosis that

were *not* based on careful observations of the changing symptoms of patients over time. Mad-doctors, alienists, and other physicians who wrote about the insane arbitrarily invented names for insanities and described their characteristic signs and symptoms based on a short-term, cross-sectional observation period of their lunatic patients. When the element of time was added to the concept of diagnosis, a diagnosis became more than just a description of a collection of symptoms: diagnosis now also defined prognosis (course and outcome). An additional feature of the clinical method was that the characteristic symptoms that define syndromes should be described without any prior assumption of brain pathology (although such links could be made later as scientific knowledge progressed). Karl Kahlbaum first made his appeal for the adoption of the clinical method in psychiatry in his 1874 book on catatonia. Without Kahlbaum and Hecker there would be no dementia praecox.

Dementia Praecox (1893)

In 1891 Emil Kraepelin left his position at the university in Dorpat (now Tartu, Estonia) to become a professor and director of the psychiatric clinic at the university in Heidelberg, Germany. Convinced of the value of Kahlbaum's suggestions for a more exact qualitative clinical method in psychiatry, Kraeplin realized that by adding a quantitative component to such a research program (which Kahlbaum never did), he could place psychiatry on a more scientific foundation. Quantification helped to eliminate any subjective biases on the part of the researcher. He began the first such research program of this nature in the history of psychiatry at Heidelberg in 1891, collecting data about every new patient that was admitted to the clinic (and not just "interesting cases," as had been the case in the past) and summarizing them on specially prepared index cards, his famous *Zahlkarten.* He had been keeping data on such cards since at least 1887. In his posthumously published *Memoirs* (which was first published in German 61 years after his death), Kraepelin described his method:

> . . . after the first thorough examination of a new patient, each of us had to throw in a note [in a "diagnosis box"] with his diagnosis written on it. After a while, the notes were taken out of the box, the diagnoses were listed, and the case was closed, the final interpretation of the disease was added to the original diagnosis. In this way, we were able to see what kind of mistakes had been made and were able to follow-up the reasons for the wrong original diagnosis (p. 61).

Kraepelin was obsessed with finding patterns in the data on these cards, taking them home with him or on vacation at times. In 1893, two years after starting his more rigorous research program in Heidelberg, the fourth edition of Kraepelin's textbook, *Psychiatrie,* reflected some preliminary impressions derived from the analysis of his cards. Diagnosis of clinical syndromes according to signs and symptoms, the traditional approach, was now augmented by indications of course and outcome (prognosis). In that edition he introduced a class of psychotic disorders he called "psychic degenerative processes." Three of these came directly from the work of Kahlbaum and Hecker: dementia paranoides (a sudden-onset, degenerative form of Kahlbaum's paranoia); catatonia (directly from Kahlbaum's 1874 monograph on the subject); and dementia praecox, which was essentially Hecker's hebephrenia (as described in 1871). Dementia praecox was hebephrenia and would remain so in Kraepelin's thinking for six more years.

In March 1896 the fifth edition of Kraepelin's textbook appeared. In it Kraepelin stated that he was confident of the value of his clinical method of using qualitative and quantitative data collected over a long period of observation of patients as a way of developing a diagnosis that included prognosis (course and outcome):

> What convinced me of the superiority of the clinical method of diagnosis (followed here) over the traditional one, was the *certainty with which we could predict (in conjunction with our new concept of disease) the future course of events.* Thanks to it the student can now find his way more easily in the difficult subject of psychiatry.

In the 1896 fifth edition, dementia praecox (still essentially hebephrenia), dementia paranoides, and

catatonia are separate psychotic disorders included among "metabolic disorders leading to dementia." In the sixth edition of *Psychiatrie* of 1899, Kraepelin reordered the psychiatric cosmos for the next century by grouping most of the insanities into two large categories, dementia praecox and manic-depressive illness. They were distinguished by the following characteristics: (1) dementia praecox was primarily a disorder of intellectual functioning, whereas manic-depressive illness was primarily a disorder of affects or mood, (2) dementia praecox had a uniformly deteriorating course and a poor prognosis, whereas manic-depressive insanity had a course of acute exacerbations followed by complete remissions with no lasting deterioration of intellectual functioning, and (3) there were no recoveries from dementia praecox, whereas in manic-depressive illness there were many complete recoveries. In 1899 dementia praecox took its now familiar form as a heterogenous class of psychotic disorders comprised of hebephrenic, catatonic, and paranoid forms. These forms have persisted until today, through Eugen Bleuler's 1908 description of schizophrenia (to which he added a fourth form, dementia simplex, or simple schizophrenia) to the main types of schizophrenia in *DSM-IV-TR* (the paranoid, catatonic, and disorganized types, with the latter retaining its historical designation as the hebephrenic type in *ICD-10* [1992]).

But what caused this terrible disease of rapid intellectual (cognitive) deterioration (dementia), mainly in the young (between 15 and 25 years old), and mainly in males? Kraepelin believed that heredity predisposed persons with dementia praecox to develop abnormalities in the metabolic functioning of the sex glands (gonads) after puberty, leading to an autointoxication (self-poisoning) process that eventually affected the brain. Autointoxication theories of various diseases, physical and mental, were highly influential from the 1890s to the 1920s in psychiatry.

Schizophrenia (1908)

Not everyone agreed with Kraepelin's emphasis on classification by prognosis. Indeed one Swiss psychiatrist, Eugen Bleuler, began to question the notion, observing that there were many different courses to the disorder, and that some persons with dementia praecox would plateau at a particular level of deficit and stay at that level for the rest of their lives, without degenerating any further. In 1908 Bleuler published a paper challenging Kraepelin's views, and suggested that the disorder be renamed *schizophrenia* (from two Greek words meaning "to split" and "mind") to remove the emphasis on prognosis suggested by the term *dementia praecox.* Bleuler had been using the term schizophrenia in lectures to his medical staff at the Burghölzli Hospital in Zurich, Switzerland, prior to this time. In 1911 Bleuler published his classic monograph, *Dementia Praecox oder die Gruppe der Schizophrenien.* His description of schizophrenia (to which he added a fourth subtype, Otto Diem's "simple schizophrenia") was hailed as a major contribution, and the ideas in Bleuler's 1911 book are still largely reflected in the classification systems in use today. No one has ever matched Bleuler's insightful description of this disease.

Bleuler had believed he was further developing Kraepelin's concepts of dementia praecox rather than inventing an entirely new disorder. Bleuler's objections to Kraepelin's dementia praecox were many, however. He objected (as many others did, particularly British psychiatrists) that there was no "dementia" in the classical, organic sense of the term (for example, as in today's Alzheimer's disease), but instead an intellectual deterioration that may or may not end up looking like dementia. He noted the deterioration was not progressive, with episodes of partial remission or complete recovery occurring in some cases. The term *praecox* was also objectionable to Bleuler, since he had encountered cases of schizophrenia that occurred during midlife (currently named late-onset schizophrenia). There were also cases of "latent schizophrenia," according to Bleuler, in which the psychotic disorder was not triggered by an endogenous disease process but by personal experiences, such as trauma. Bleuler went so far as to believe that cases of latent schizophrenia were more common than cases of manifest schizophrenia. Bleuer also noted the existence of people with paranoid personality disorders who resembled cases of dementia praecox. Bleuler widened Kraepelin's concept of dementia praecox by arguing that these cases, too, should be considered

part of the disease (an idea that has taken hold in our current notions of schizophrenia spectrum disorders, especially schizotypal personality disorder). Influenced by his associate Carl Gustav Jung and by Sigmund Freud and the psychoanalytic movement, Bleuler believed in the possibility of psychogenic or reactive triggers for schizophrenia, which Kraepelin did not allow.

In sum, Bleuler greatly widened the circumference of persons whom he considered should be diagnosed with dementia praecox. He also left open the possibilities for various courses and outcomes, and better prognoses, than Kraepelin did. He emphasized the heterogeneous nature of schizophrenia, with the possibility that multiple disease processes may underlie it, whereas Kraepelin held to the conviction that dementia praecox was one disease with at least three forms. It was therefore Bleuler's wider concept of schizophrenia that took hold, especially in America, and dominated psychiatry until 1980. In that year, the narrower diagnostic criteria and pessimistic prognosis for schizophrenia became the official diagnosis of this disorder in *DSM-III.* This narrower, "neo-Kraepelinian" definition of schizophrenia persists today.

The "Mind Twist Men" versus the "Brain Spot Men"

In the late 1800s and early 1900s a great battle erupted in American medicine that was to have a profound influence on the practice of psychiatry and on attitudes toward dementia praecox and schizophrenia.

The conflict raged between those traditional physicians who preferred the knowledge derived from the practice of medicine as an art and those who argued for the greater role of knowledge gained from laboratory studies to make the practice of medicine a science. Until the late 19th century, medical training had followed the master-apprentice model. One learned medical practice by observing one's mentor, and then by doing it oneself. Clinical lore and personal anecdotes were the only "evidence" to be trusted—especially in such a backward discipline of medicine as psychiatry, which was held in very low esteem by the rest of the medical profession. Such had been the basis of medical training for thousands of years, dating back to the Hippocratic literature of the ancient Greeks.

By the late 1860s, claims for the clinical relevance of basic science conducted in laboratories were being vigorously voiced by physicians in the United States. These physicians argued that personal anecdotes and clinical folklore were a bad way to conduct medical practice. Instead, new studies in anatomy, chemistry, and other scientific disciplines should be relied upon to make medical practice more scientific. Of course, as we enter the 21st century, we now know that these medical discontents prevailed. However, circa 1900, this victory was not apparent, and the psychiatry of the 20th century remained the only major subdiscipline of American medicine to reject laboratory science and its evidence that mental diseases may have biological causes.

Why did psychiatry remain in such a primitive state throughout most of the 20th century? The responsibility for this tragedy lies in the influence of two prominent American schools of psychiatry that were suspicious of laboratory science and rejected the claims of Kraepelin and his followers that dementia praecox or schizophrenia was caused by heredity (genetics) or other biological causes. The first of these schools, Adolf Meyer's "biosocial reaction" school, had an early influence from circa 1910 to the 1950s. The second of these schools, Sigmund Freud's psychoanalysis, had a profound and devastating influence on American psychiatry and retarded its development as a scientific branch of medicine from the 1920s to the 1970s.

The Meyerians. While acknowledging the potential value of laboratory research in psychiatry, prominent psychiatrists in America such as the Swiss émigrés Adolf Meyer and August Hoch preferred to rely upon the ability of the trained clinician to analyze the biosocial factors in the life of the "whole person" that contributed to the psychological and behavioral "reactions" that constituted all known mental disorders, including dementia praecox. The literature of Meyer and his supporters is laced throughout with polemics against the "failed" or "outdated" practice of psychiatrists who modeled their thinking and their fatalistic diagnostic and prognostic pronouncements on the medical pathologists. Most mental disorders, they

argued, were viewed by these older psychiatrists to be as irreversible as nervous tissue damage, or as irrefutable as the fateful hand dealt by heredity. Furthermore, the Meyerians pointed out—and with some truth—that the neuropathological, biochemical, and serological laboratory studies and the statistical studies of heredity had not proven themselves to be of any real relevance to the diagnosis and treatment of patients. Because the "can do" philosophy of the Meyerians blended so well with similar American cultural values of pragmatism and functionalism, personified in the figure of William James (1842–1910), in the first two decades of this century, they paved the way for the resounding acceptance of psychoanalytic theory by the 1920s in American psychiatry.

The Psychoanalysts. Psychoanalysis, like the Meyerian philosophy, rejected "pessimistic" hereditarian views and argued that patients could actually be understood and changed through the application of this new method. By World War I, even neurologically trained physicians such as James Jackson Putnam, Smith Ely Jelliffe, and William Alanson White had converted to the more optimistic worldview of Freudian psychoanalysis.

The Kraepelinians. The "old"—or perhaps more aptly put "Old World"—psychiatric perspective castigated by Adolf Meyer was primarily the 19th-century French (B. A. Morel, Valentin Magnan) and particularly German emphasis on hereditary degeneration theory, and in particular its avocation by the German psychiatrist Emil Kraepelin. One disorder in particular, dementia praecox, was often the focus of the heated charges and countercharges hurled between the Kraepelinians, the Meyerians, and the psychoanalysts. The biological and hereditarian etiology of dementia praecox (the disorder described and named by Kraepelin in the sixth edition of his *Psychiatrie* in 1899 as composed of the psychotic disorders paranoia, catatonia, and hebephrenia) indicated in his opinion an extremely poor prognosis for any patient that manifested the symptoms. Manic-depressive insanity, the nondeteriorating and sometimes remitting form of serious psychotic disturbance, was described by Kraepelin in the sixth edition of his *Psychiatrie* in 1899 and met with far greater acceptance among the Meyerians and psychoanalysts. Yet, Kraepelin insisted that it, too, had a firm etiologic basis in biological processes and that therefore both dementia praecox and manic-depressive insanity could be investigated through laboratory methods. The growth in laboratory studies of these illnesses are reflected in the bulkiness of volume III of the eighth edition of *Psychiatrie,* published in 1913, which is primarily concerned with dementia praecox and manic-depressive insanity.

While Kraepelin's diagnostic terms *dementia praecox* and *manic-depressive insanity* were adopted by American psychiatrists in the first quarter of this century, the etiologic and prognostic ideas of Kraepelin underwent considerable revisioning. This new—or perhaps more aptly put "New World"—dynamic or functional interpretation of dementia praecox was forged by the hands of Adolf Meyer, Smith Ely Jelliffe, and August Hoch, who coauthored a seminal monograph in 1911 containing their revisionist perspectives.

There was a small group of American physicians who believed that Kraepelin's theories about dementia praecox and schizophrenia were correct. They, too, viewed this devastating disorder as first and foremost a brain disease. They, too, knew that heredity (genetics) played a strong role in the cause and development of this disease. This group was led by Bayard Taylor Holmes (1852–1924) of Chicago and Elmer Ernest Southard (1876–1920) of Harvard Medical School in Boston.

Bayard Taylor Holmes was the editor of *Dementia Praecox Studies,* the first scientific or medical journal in any language to be named after a psychiatric disorder. During its short life (1918–22), *Dementia Praecox Studies* not only provided extensive bibliographic essays and reviews of published laboratory reports from several nations but also provided translations of selected experimental studies of unpublished doctoral theses from the original German or French. Perhaps most important, *Dementia Praecox Studies* served as the primary place of publication for the experimental reports of the Research Laboratory of the Psychopathic Hospital of Cook County (Illinois) and for the editorials of its director, Holmes. Bayard Taylor Holmes was also a noted Chicago surgeon and, in 1895, the unsuccessful Socialist candidate for mayor of Chicago.

Dementia Praecox Studies was the only journal ever produced by the handful of Kraepelinian physicians in the United States. Like Emil Kraepelin, they believed that mental disorders were first and foremost brain diseases with neuropathological, biochemical, infectious, and genetic causes. But from the 1910s until the late 1960s American psychiatry was dominated by the followers of Adolf Meyer's "psychosocial reaction" theory and Sigmund Freud's pseudoscience of psychoanalysis. These traditions of "mind twist men" (see below) were suspicious of laboratory science and rejected biological and genetic causes for mental disorders. The premature death from pneumonia of pathologist Elmer Ernest Southard left the "brain spot men" without a prominent spokesman. The death of Bayard Holmes in 1924 essentially ended the Kraepelinian movement in America for decades.

The opening pages of the January 1918 edition of *Dementia Praecox Studies* contain the following invitation from Herman Campbell Stevens for the submission of laboratory research reports: "The purpose of this publication is to arouse interest in the subject of dementia praecox. . . . How little is known about the disease is apparent from a reading of the standard treatises on psychiatry and from the current literature. It is the purpose of this journal to serve as a clearinghouse for scientifically established facts with regard to dementia praecox. Any competent and contentious study of a morphological, biochemical, or psychiatric nature will be accepted. It is the aim of the editors to encourage research in the hope that a rational therapy and prophylaxis will result." Bayard Holmes unabashedly expressed his "faith" in the hypothesis that "disease of the mind is the result of organic disease of the body," and as "in spite of the magnitude of this problem there is a great scarcity of books and monographs dealing with the physical, chemical and biologic conditions of the unfortunate victims of this disease," he urges "the publication of a journal devoted exclusively to the study from the organic point of view, of one part of the field of mental disease, viz., dementia praecox."

The most prominent bearer of the torch for Kraepelin in America was the neuropathologist—and arch-critic of Adolf Meyer—E. E. Southard. Southard was the first to describe (in 1915) cortical atrophy as a clear pathology in the brains of persons with dementia praecox. But when Southard died prematurely, so, too, did the only promise of a serious American program of neuropathological research on dementia praecox and manic-depressive insanity. Southard, with his characteristic humor, referred to the Meyerians and the psychoanalysts as "mind twist men" and Kraepelinians (such as himself) as "brain spot men," monikers as apt as any others applied since.

American Psychiatry and the Tragic Years of Psychoanalysis

Although laboratory research on the neurological, biochemical, and genetic causes and associated pathologies of schizophrenia continued in Munich at Kraepelin's Deutsche Forschungsanstalt fuer Psychiatrie (German Research Institute for Psychiatry) from 1917 until World War II, in America such research was the exception and not the rule. After the deaths of Southard and Holmes, Henry Cotton, N. D. C. Lewis, George Kirby, Seymour Kety (after the war), and a handful of others continued to look for biological evidence of the cause and characteristic disease processes in schizophrenia but failed miserably. This failure emboldened American, French, and British psychiatrists who had come under the influence of the ideas of psychoanalysts such as Sigmund Freud, Carl Gustav Jung, and Alfred Adler. Unfortunately, psychoanalytically oriented psychiatrists drew the wrong conclusion from the failure of laboratory science, and thousands of persons with schizophrenia and their family members suffered for it.

From the 1920s until the 1970s, psychoanalysis dominated American psychiatry, diverting the search for new drug treatments and basic biological research into a blind alley. Psychoanalysis was a covert ideology with absolutely no scientific evidence to support it. Psychoanalytic organizations maintained a cultlike, secret society social structure, which only added to its apparent mystery and allure to the "uninitiated" lay public. However, because so many prominent physicians converted to it, psychoanalysis and figures such as Sigmund Freud and Carl Jung enjoyed a legitimacy that was not deserved. Throughout the 20th century psy-

choanalysts blamed the victim—or the victim's mother—as the "cause" of schizophrenia (or other psychiatric illnesses). Just imagine the pain caused by such a theory! And yet, the "refrigerator mothers" and "schizophrenogenic mothers" seemed like real villains to psychiatrists. Medical students were trained to view the mothers of schizophrenics as "pathogens," as if they were viruses. This same tragedy of blaming the afflicted person or a family member for the "cause" of schizophrenia was additionally promoted in the various "family interaction theories" of the 1950s to 1970s that became so beloved of psychiatric social workers in particular. Family interaction theorists blamed unhealthy communication patterns within the entire family—thus making everyone share the blame for causing schizophrenia.

It took major advances in medical technology, specifically the computer revolution and the rise of new techniques in neuroimaging, genetics research, and psychopharmacology to swing the pendulum back to Kraepelin's search for the biological causes of the psychotic disorders.

Historians of science now regard psychoanalysis as a pseudoscience that inexplicably dominated a subdiscipline of medicine—psychiatry—and unnecessarily maintained a 19th-century attitude toward the causes and treatment of mental disorders. Psychoanalysis was the dominant medical pseudoscience of the 20th century, as phrenology was in the 19th century and animal magnetism was in the 18th century.

The 1970s: Schizophrenia Becomes a Physical Disease Once Again

Advances in the technology to study biochemistry, brain function and structure, genetics, and the development of brain imaging techniques (e.g., the CT scan) all converged to stimulate a biological renaissance in the study of schizophrenia and the psychotic disorders in the 1970s. Suddenly it was appropriate to speak of schizophrenia as a "brain disease," and psychoanalytic and family interaction models largely began to be ignored as legitimate causes of this disease (although it was found that psychosocial factors can have an effect on relapse rates in persons with schizophrenia). Genetic transmission was now estimated to be responsible for about 80 percent of the cause of schizophrenia, with other unknown environmental factors comprising the other 20 percent. Viral theories of the cause of schizophrenia were also resurrected after first being mentioned by Kraepelin and Bleuler almost a century before. Perinatal factors in the development of schizophrenia again began to be studied in earnest. Cross-cultural studies of the prevalence rates of schizophrenia were initiated by the World Health Organization. Twins studies and adoption studies conducted in the 1960s helped to form new and complex theories of the genetic transmission of schizophrenia in the 1970s and 1980s. After decades of disappointment and neglect, the search for the causes of schizophrenia once again was viewed as a promising endeavor.

The 1980s, 1990s, and Beyond

The last two decades of the 20th century brought more scientific progress than the last 100 years combined in the understanding and treatment of schizophrenia and other psychotic disorders.

We now know for a fact that genetics plays a key role in the cause and development of schizophrenia and bipolar disorder. Several candidates for the locus of the genes that cause schizophrenia are the subject of intense scrutiny. The mode of genetic transmission remains a mystery; however, the National Institute of Mental Health Schizophrenia Genetics Initiative that began in 1989 is collecting and analyzing the DNA of persons with schizophrenia and their entire families in order to find a solution. Environmental factors still play an important role, too, in the development of the psychotic disorders, but no one knows what they are or how they interact with genes.

Unfortunately, at the dawn of the 21st century most of the evidence concerning the "causes" of schizophrenia comes from epidemiological studies and not from the identification of a characteristic process of cellular pathology (as is the case in other diseases, including Alzheimer's disease). As two editorials that appeared in 1999 in *The New England Journal of Medicine* and *Nature Neuroscience* remind us, no one knows what causes schizophrenia.

Advances in brain imaging technology, neurochemistry, and neuropathology have produced sophisticated new models of schizophrenia based on the notion of disconnection between certain neural circuits or pathways in the brain. The prefrontal region of the frontal lobe and the temporal lobe are the two cortical regions most affected in schizophrenia. Subcortical structures such as the thalamus, a major relay center for messages traveling throughout the brain, and the hippocampus and cerebellum also have been implicated in schizophrenia.

With the push to make psychiatry a true medical science, the traditional schizophrenia subtypes of Kraepelin and Bleuler have been called into question by quantitative studies of the symptoms of schizophrenia. Although Timothy Crow offered the first major reconceptualization of schizophrenia with his Type I/Type II concept of syndromes characterized by positive and negative symptoms, respectively, others have used the statistical technique of factor analysis to come up with new "dimensions" of schizophrenia. Prominent schizophrenia researchers such as Peter F. Liddle and Nancy Andreasen have posited three syndromes for schizophrenia, and Mark Lenzenweger has argued for four. All of these dimensional models of schizophrenia claim that neuroimaging, neuropathological, and neuropsychological data provide a better "fit" with these new dimensions than the old, traditional clinical subtypes of Kraepelin and Bleuler.

The introduction of clozapine as the first of the new class of antipsychotic medications was the first major innovation in the treatment of psychosis to appear in 30 years. Pharmaceutical companies have a variety of new antipsychotics in the pipeline, and as more is understood about the interaction of the more than 100 different neurotransmitters in the brain, more effective drugs will continue to be designed and brought to market.

As we enter the 21st century the dominant explanatory paradigm in schizophrenia research is the neurodevelopmental model. First proposed by R. H. Murray in 1985 and D. R. Weinberger in 1986, the neurodevelopmental model claims that the causes of schizophrenia originate in subtle abnormalities that occur sometime during the early development of the nervous system of the fetus. This approach has sparked new research into a wide variety of old topics of schizophrenia research, such as childhood-onset schizophrenia. Whether neurodevelopmental schizophrenia turns out to be the main illness or is found to be only one of several subtypes of schizophrenia remains to be seen. Still, no one can dispute the fact that schizophrenia research will be one of the most fascinating areas of science as the new century unfolds.

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ENTRIES A–Z

A

abaissement du niveau mental Literally, a "lowering of the level (or threshold) of consciousness." Today, this idea is usually expressed by the term ALTERED STATE OF CONSCIOUSNESS.

French psychiatrist Pierre JANET (1859–1947) coined this term to refer to the apparent weakening of volitional control of consciousness and the subsequent DISSOCIATION (or "splitting") of consciousness into autonomous parts that may not even be aware of one another. Although Janet noted that this *abaissement* was common in forms of psychological automatisms such as found in multiple personalities, hysterics, the trance behavior of mediums, and in automatic writing, the term was adopted and used extensively by Swiss psychiatrist C. G. JUNG (1875–1961) in his famous 1907 monograph, *Über die Psychologie der Dementia Praecox: Ein Versuch* (The psychology of dementia praecox) to describe DEMENTIA PRAECOX (later "SCHIZOPHRENIA"). Jung felt that the *abaissement* was the "primary condition" and "the root of the schizophrenic disorder." He thought it resulted from both psychological and physiological causes. In dementia praecox, Jung argued that the *abaissement* caused the following effects commonly observed in schizophrenics: (1) the loss of whole regions of normally controlled contents of consciousness, (2) split-off fragments of the personality, (3) the prevention of normal trains of thought from being consistently carried through and completed, (4) a decrease in the responsibility and proper reaction of the ego, (5) constriction and distortion of thoughts and feelings, and (6) a lowering of the threshold of consciousness (as in an altered state), thereby allowing normally inhibited content of the unconscious to enter consciousness in the form of autonomous invasions.

Jung was briefly (in 1902) a student of Janet's in Paris and was greatly influenced by him. *Abaissement du niveau mental* was a term used frequently by C. G. Jung in his later writings.

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abilify See ANTIPSYCHOTIC DRUGS.

ablation studies In the late 19th and early 20th centuries, the modern neurosciences (then called the "brain sciences") were coming into being, just as the clinical syndromes of DEMENTIA PRAECOX and manic-depressive PSYCHOSIS were simultaneously being identified and described by Emil KRAEPELIN (1856–1926). It was natural that the investigative techniques of gross anatomy and neuropathology of the new "brain sciences" would be applied to the study of the brains of deceased patients that had suffered from these MENTAL DISORDERS. The many ablation studies of the brains of schizophrenics and manic-depressives involved the removal and systematic destruction of the brain tissue in order to look for structural abnormalities. Brain tissue was commonly ablated slice by slice, with careful records kept to document unusual formations. Not surprisingly, most of these studies were inconclusive due to the imprecision of this gross procedure. Modern brain imaging techniques and biochemical and genetic strategies of investigation have been more successful in detecting the subtle physiological abnormalities in the brains of people suffering from SCHIZOPHRENIA or manic-depressive psychosis.

See also BRAIN ABNORMALITIES IN SCHIZOPHRENIA; BRAIN IMAGING STUDIES IN SCHIZOPHRENIA.

aboulia In 19th-century psychiatry, aboulia was a "disorder of the will" or "a form of insanity characterized by an inability to exert the will." Before the rise of PSYCHOANALYSIS and behaviorism in the 20th century, many psychiatrists considered aboulia as the central characteristic of most MENTAL DISORDERS. Hence, much of what we would now call psychotherapy was actually "will-training," that is, training people to concentrate better, to focus their attention on tasks better, and to control their impulses.

DEMENTIA PRAECOX and SCHIZOPHRENIA were considered primarily disorders of the will by many psychiatrists. According to Emil KRAEPELIN, the essence of dementia praecox/schizophrenia was "that destruction of conscious volition . . . which is manifest in the loss of energy and drive, in disjointed volitional behavior. This rudderless state leads to impulsive instinctual activity: there is no planned reflection which suppresses impulses as they arise or directs them into proper channels."

Aboulia is again being considered in contemporary schizophrenia research because so many researchers have implicated the abnormal functioning of the frontal lobe—the seat of inhibition and "executive functioning" or "supervisory mental processes." Frontal lobe dysfunctions result in a disorder of volition or will, a symptom sometimes also called "AVOLITION."

See also BRAIN ABNORMALITIES IN SCHIZOPHRENIA.

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abuse of psychiatric patients The mentally ill have been ridiculed and scorned throughout human history. Although the efforts to humanize the treatment of the mentally ill through the "moral medicine" movement of the early 19th century resulted in many reforms in some asylums for the insane, reports have continued until present times of periodic abuses—both psychological and physiological—in psychiatric facilities throughout the world. It is often thought that the tremendous power that the staff of such institutions wields over the (usually) involuntarily committed, mentally ill patient can sometimes corrupt even the most empathetic and well-intentioned caregiver at stressful times.

Through the centuries, a massive and disturbing literature of first-person accounts has been created that documents such abuses. A small book published anonymously in London in 1752, entitled *Low-Life, Or One Half of the World Knows Not How the Other Half Lives,* describes the torturous conditions of the chained patients at the BETHLEM ROYAL HOSPITAL ("BEDLAM"), in which the author reports observing the nurses stealing for themselves the best portions of food that were originally intended for the patients. Sadly, even today such abuses by staff are frequently reported in large psychiatric institutions, and not only food but also property and even money often mysteriously disappear from patients who, when they complain, are told they are either confused, delusional, or lying. In *The New York World* newspaper in 1887, a serialized story entitled "Ten Days in a Mad House" described similar abuses. It was written by journalist-celebrity Elizabeth Seaman (née Cochrane), who, under the pseudonym Nellie BLY, faked mental illness and gained admission to the New York City Lunatic Asylum on Blackwell's Island (briefly named "Welfare Island" in the 1940s but now changed to "Roosevelt Island"). This account was published in book form in 1888.

Perhaps the most famous—and influential—autobiographical account was Clifford BEERS's *A Mind That Found Itself* (1908). Beers, a businessman who underwent a brief psychotic episode, was first put in a private sanitarium and then a state hospital. He described the repeated abuses of patients by attendants and how kindly new staff members were soon transformed into sadists through peer pressure. Beers writes:

> I soon observed that the only patients who were not likely to be subjected to abuse were the very

> ones least in need of care and treatment . . . The patient too weak, physically or mentally, to attend to his own wants was frequently abused because of that very helplessness which made it necessary for attendants to wait upon him.

He also relates the following anecdote, still familiar to those who work in today's psychiatric institutions:

> One attendant, on the very day he had been discharged for choking a patient into an insensibility so profound that it had been necessary to call a physician to restore him, said to me, "They are getting pretty damned strict these days, discharging a man for simply *choking* a patient." This illustrates the attitude of many attendants.

Beers eventually improved, wrote his autobiography, and founded the MENTAL HYGIENE MOVEMENT in the United States. His early efforts are still bearing fruit with the many mental patients' advocacy groups, especially the National Alliance for the Mentally Ill.

As much as we may prefer not to believe it, abuses are still a part of the world of almost any institution that serves an inpatient population of people who have chronic mental illnesses. A short autobiographical account by Leopold Bellak, a prominent psychiatrist, SCHIZOPHRENIA researcher, and professor at the Albert Einstein College of Medicine in New York City, includes a story that almost anyone today who has ever worked in such facilities will find familiar. These are the sort of events that go on *sub rosa* in the culture of the psychiatric hospital but that no one will openly admit to, especially administrators, who often do not want either to hear of such cases or believe them when reported. This leaves the honest witness to suffer the brunt of the negative consequences for his or her accusations, with the actual abuser often remaining unaffected. Bellak describes his first clinical experiences as a psychiatric aide on a chronic psychotic ward in 1938 and 1939:

> The utter sense of hopelessness fostered in institutions run in very poor and dictatorial fashion by an ill-trained staff was often hardly better than that described in *One Flew Over the Cuckoo's Nest.* Acts of sadism were tolerated, if not encouraged. On my first day as a psychiatric aide in a high-class sanitarium, I was put under the tutelage of an experienced psychiatric aide. Among his first words of wisdom to me were that if I should find it necessary to hit a patient, I should hit him in the abdomen in order to leave no telltale marks. Seeing a patient put into wet packs was the closest thing I could imagine to a rape.

In many countries today, political prisoners are sometimes incarcerated and abused in psychiatric institutions, a practice that led to the withdrawal of the Soviet Union from the WORLD PSYCHIATRIC ASSOCIATION in 1983, when it became clear that the USSR was likely to be expelled. As a result of the glasnost of the Gorbachev era, an official delegation of 26 Americans (including 14 psychiatrists and 2 lawyers) selected by the NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH) visited four Soviet psychiatric hospitals in February and March 1989 to investigate such reports. In July 1989 the investigative team released its report, claiming that many of the patients they examined had no discernible MENTAL DISORDERS and that the maximum security prisons in the Soviet Union still had the characteristics of "psychiatric prisons." They found that many patients had been incarcerated for "anti-Soviet thoughts" or undesirable political behavior. Drugs were used for "punitive rather than therapeutic purposes," and patients were denied most rights, especially the right to have a say in their treatment. Based on these grim findings, the delegation recommended that the Soviet Union not be readmitted to the World Psychiatric Association. However, due to the political climate of openness and optimism toward the changes in Soviet society, on October 18, 1989, the World Psychiatric Association voted to readmit the Soviet All-Union Society of Psychiatrists and Narcologists, but with the stipulation that it would be subject to suspension if the Soviets did not end their misuse of psychiatry against political dissidents. Despite the negative report and recommendations of the NIMH, the AMERICAN PSYCHIATRIC ASSOCIATION voted in favor of readmission.

The abuse of persons suffering from mental disorders, particularly those inpatients residing

in institutions, has also occurred for centuries in the form of involuntary participation in medical experiments aimed at preventing, treating, or curing mental disorders. In the given historical context of their respective eras, radical procedures were introduced as "rational treatments" that followed logically from a (then) current medical theory of the cause (etiology) or the disease process (pathophysiology) of mental disorders. Because of the severity of deterioration in functioning that occurs over time, persons with schizophrenia have been disproportionately abused in such experiments. Perhaps the best documented example of such abuse is that perpetuated by psychiatrist Henry A. COTTON and his associates at the New Jersey State Hospital at Trenton between 1918 and 1932. Like many prominent physicians in his day, Cotton believed that infections in various parts of the body (the teeth, gums, colon, stomach, cervix, testicles, and so on) could be transmitted to the brain via the blood and cause severe mental disorders such as DEMENTIA PRAECOX (schizophrenia) and manic-depressive insanity (BIPOLAR DISORDER). Unlike the majority of those physicians, Cotton chose to use his authority as superintendent and medical director of his state hospital to immediately remove most or all the teeth of recent admissions and to perform radical surgeries to eliminate the sources of focal infection. Hundreds of thousands of teeth were removed and more than 2,000 major surgical procedures were performed, resulting in the deaths of hundred of people. His own early statistics indicated a mortality rate of about 30 percent, and he was well aware of this fact, as historian Andrew Scull has documented. Although Cotton was recognized for his humane innovations at Trenton after taking control in 1907, eliminating many forms of physical restraint and replacing abusive hospital staff, and although his surgical treatments were indeed congruent with current medical theory, his continued use of such procedures even when an outside evaluator was able to show they did not eliminate mental illness, is horrifying. A similar story of abuse, PSYCHOSURGERY, also began with a seemingly rational treatment for mental illness but led to the disabling or death of an estimated 40,000 to 50,000 persons from the 1930s to the 1960s.

See also BEERS, CLIFFORD W.; CHEMICAL RESTRAINT; MECHANICAL RESTRAINT.

Beers, Clifford. *A Mind That Found Itself: An Autobiography.* New York: Longmans, Green, 1908.

Bellak, L. "An Idiosyncratic Overview." In *Disorders of the Schizophrenic Syndrome,* edited by L. Bellak. New York: Basic Books, 1979.

Peterson, D., ed. *A Mad People's History of Madness.* Pittsburgh, Pa.: University of Pittsburgh Press, 1982.

Pressman, Jack. *Last Resort: Psychosurgery and the Limits of Medicine.* Cambridge: Cambridge University Press, 1998.

Scull, Andrew. *Madhouse: A Tragic Tale of Megalomania and Modern Medicine.* New Haven, Conn.: Yale University Press, 2005.

accessory symptoms The name given by Eugen BLEULER in his 1911 classic, *Dementia Praecox, Or the Group of Schizophrenias,* to the symptoms of SCHIZOPHRENIA that may also appear in other types of mental illness. This is in contrast to the "fundamental symptoms" that uniquely characterize schizophrenia. Among the most easily recognizable of the accessory symptoms are HALLUCINATIONS and DELUSIONS. Bleuler emphasizes what an important role these accessory symptoms play in the life of the afflicted individual when he writes:

> It is not often that the fundamental symptoms are so markedly exhibited as to cause the patient to be hospitalized in a mental institution. It is primarily the accessory phenomena which makes his retention at home impossible, or it is they which make the psychosis manifest and give occasion to require psychiatric help. These accessory symptoms may be present throughout the whole course of this disease, or only in entirely arbitrary periods of illness.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenia.* Translated by Joseph Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

acedia Also spelled "accidia," it is a word that originated in the Middle Ages to refer to the apa-

thetic self-neglect or uncaring behavior of those who are melancholic (depressed) or otherwise mentally ill. In medieval Europe, the church designated Accidia (or sloth) as the fourth of the Seven Cardinal (Deadly) Sins. Acedia also described an impoverishment of mental energy, which, it was felt, could be reversed in an individual through an experience of "conversion," in which lost faith is recovered and psychological revitalization occurs. Thus, acedia was related to "MELANCHOLIA" or "DEPRESSION." This term was used in the 19th century but is now considered obsolete.

Jackson, S. W. *Melancholia and Depression: From Hippocratic Times to Modern Times.* New Haven, Conn.: Yale University Press, 1986.

acromania A diagnostic term used in the 18th and 19th centuries to label a "confirmed" or "incurable madness."

acting-out A common bit of jargon in the day-to-day conversation of mental health professionals today; it refers to the expression of socially inappropriate sexual and aggressive behaviors. It has its origins in psychoanalytic theory, in that sexual and aggressive instinctual impulses, which we normally repress, inhibit, or sublimate, are not held back (either unconsciously or in fantasy) and are instead "acted-out" in behavior. More often than not it refers to violent behavior, and if a psychiatric patient is engaged in acting-out behavior it is said that he or she is "going-off" (i.e., like the firing of a rocket or an explosion).

active phase of schizophrenia The period of time that the characteristic symptoms of SCHIZOPHRENIA are present. According to *DSM-IV-TR* (2000), two or more of the five characteristic symptoms must be "present for a significant portion of time during a one-month period (or less if successfully treated)." These five characteristic symptoms are:

(1) DELUSIONS
(2) HALLUCINATIONS
(3) disorganized speech (e.g., frequent derailment or incoherence)
(4) grossly disorganized or catatonic behavior
(5) negative symptoms, i.e., affective flattening, ALOGIA, or AVOLITION.

Returning to a method of diagnosing schizophrenia based on only one symptom that had been proposed in the past (see FIRST-RANK SYMPTOMS), *DSM-IV-TR* states that the identification of the active phase of schizophrenia may be identified by only one characteristic symptom if "delusions are bizarre" or "hallucinations consist of a voice keeping up a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other."

Although to receive a *DSM-IV-TR* diagnosis of schizophrenia, these symptoms of the active phase must be in evidence for at least one month (or less if successfully treated); attenuated forms of two or more of these active phase symptoms (such as odd beliefs or unusual experiences) or the presence of NEGATIVE SYMPTOMS must also be in evidence for a period of six months as either part of a PRODROMAL PHASE or a RESIDUAL PHASE. To receive a diagnosis of schizophrenia in *ICD-10* (1992), the characteristic symptoms of the active phase must be in evidence for more than one month, and although a prodromal phase is acknowledged, since such a syndrome cannot be identified reliably as belonging specifically to schizophrenia and not to any other MENTAL DISORDER, it is not included in this one-month duration.

The European definition of the active phase in *ICD-10* has a strict one-month minimum to be met before "an acute schizophrenia-like psychotic disorder" can be diagnosed as schizophrenia. However, the range of characteristic symptoms is wider in Europe than in North America.

The North American psychiatric definition of what constitutes an active phase of schizophrenia changed between 1987 and 1994. *DSM-IV*'s inclusion of negative symptoms as part of the active phase of schizophrenia and the lengthening of the time frame for the active phase are the two most significant departures from *DSM-III-R* of 1987.

acute In reference to diseases, *acute* refers to those that are sudden in onset and generally rather short-lived. However, acute phases of a disease are those periods when symptoms that are generally dormant can flare up.

acute and transient psychotic disorders One of the five types of ATYPICAL PSYCHOTIC DISORDERS found in *ICD-10* (1992) that cannot be readily classified as SCHIZOPHRENIA or as a mood disorder with psychotic features. The others in this category are persistent delusional disorders, induced DELUSIONAL DISORDER, SCHIZOAFFECTIVE DISORDER, and schizotypal disorder. Acute and transient psychotic disorders fall into two categories determined by the amount of time it took for the disorder to change from a nonpsychotic to a clearly psychotic state: abrupt onset (onset within 48 hours) or acute onset (onset in more than 48 hours but less than two weeks). If the onset is acute, *ICD-10* indicates it must be specified if it is associated with acute stress two weeks or less before the start of psychotic symptoms. These disorders are also subdivided according to whether POLYMORPHIC PSYCHOTIC SYMPTOMS are present or whether those typical of schizophrenia are present. If the symptoms are similar to those of schizophrenia, and if they last at least one month, the diagnosis is changed to schizophrenia. If the symptoms are polymorphic and nonschizophrenic, the diagnosis need not be changed after one month. However, after three months it may be changed to that of a persistent delusional disorder. DELUSIONS, HALLUCINATIONS, and incomprehensible or incoherent speech, or any combination of these, are the psychotic symptoms that are most often present in these disorders.

acute-chronic distinction The criterion in SCHIZOPHRENIA research that traditionally explores cognitive, perceptual, and behavioral differences in schizophrenics based on the amount of time they have been diagnosed with the disorder and have been hospitalized. Generally, ACUTE schizophrenics are those who have not been institutionalized for more than 3.5 years, and chronic schizophrenics are those whose total time spent in institutions has been six years or more. Acute schizophrenics have been found to differ from chronic schizophrenics across many neurophysiological and neuropsychological variables.

Studying schizophrenia by dividing persons into acute and chronic subgroups has virtually disappeared since the 1990s. Instead, a great deal of attention has been paid to trying to identify and understand the PRODROMAL PHASE of schizophrenia, which predates the "first episode" or first acute or active phase of characteristic psychotic symptoms. Additionally, the many cognitive and physical changes that occur as the illness persists over the years (in decades past simply lumped together as aspects of "chronic schizophrenia") are being identified and studied in detail.

See also ACUTE SCHIZOPHRENIA; CHRONIC SCHIZOPHRENIA; PRODROMAL PHASE.

acute delirius mania A late 19th-century term for the acute forms of CATATONIC EXCITEMENT. The syndrome was often described as an acute MENTAL DISORDER with a rapid onset and course, resembling DELIRIUM caused by fever, during which the patient would experience a rise in temperature, rapidly reach exhaustion, and then possibly death. Other names for this syndrome were Bell's syndrome or disease, typhomania, *Délire aigu,* delirius mania, acute delirium, delirium grave, mania gravis, and delirium acutum.

Fürstner, C. "Über delirium acutum," *Archiv für Psychiatrie* 11 (1881): 517–538.

acute recoverable psychosis Limited psychotic episode for which complete remission can occur. Acute recoverable psychoses (ARPs) is a generic term proposed for the psychotic disorders that generally last only from two weeks up to six months. These disorders may be predominantly affective, confusional (resembling organic mental disorders), or SCHIZOPHRENIA-like (usually distinguished by paranoid and nonparanoid varieties). It has been suggested that the shared core symptoms and characteristic natural history of the schizophrenia-like

ARPs indicate they are variants of the same underlying disorder, despite the many diagnostic labels.

See also ATYPICAL PSYCHOTIC DISORDERS.

Munro, A. "Schizophrenia-like Illnesses." In *New Perspectives in Schizophrenia,* edited by M. N. Menuck and M. V. Seeman. New York: Macmillan, 1985.

acute schizophrenia The ACUTE phase of SCHIZOPHRENIA is when the symptoms first flare up into a full PSYCHOSIS. However, "acute" can also refer to the length of time that active schizophrenic symptoms are evident or refer to a hypothesized variant of schizophrenia that has a better prognosis than CHRONIC SCHIZOPHRENIA. The ACUTE-CHRONIC DISTINCTION in studies of schizophrenia refers to the amount of time that has elapsed since the clear diagnosis of schizophrenia has been made. Many studies have shown psychological and behavioral differences between those patients in the early or acute stages of the illness versus those in the later or chronic stages of schizophrenia. For research purposes, acute schizophrenics are those who have had less than a total of 3.5 years' hospitalization. Studies have shown that chronic schizophrenics have more severe thought disorder and other cognitive deficits than acute schizophrenics, but many have argued that this deterioration may be due to the debilitating effects of institutionalization rather than being a result of the illness itself. Acute schizophrenia is often conceptually confused with REACTIVE SCHIZOPHRENIA, the type of schizophrenia in which patients are found to have a better pre-breakdown history and eventually improve, versus those who follow a lifelong chronic course.

Schizophrenia researchers no longer design studies along the lines of the acute-chronic distinction. The arbitrary criterion that a certain number of years or less of hospitalization defines acute schizophrenia is no longer used in contemporary schizophrenia research. Nor is the criterion provided in *DSM-III* (1980) and *DSM-III-R* (1987) that "chronic schizophrenia" is defined by an illness that has been in evidence for at least two years. Instead, research is focused more narrowly on groups identified as manifesting "first-episode schizophrenia" or "recent-onset schizophrenia" in which the active symptoms have been apparent for only days, weeks, or months. These terms have almost entirely replaced the old notion of acute schizophrenia.

ADD psychosis The acronym for "attention deficit disorder," a clinical diagnostic entity proposed by Leopold Bellak in 1985. Bellak claims that many cases of SCHIZOPHRENIA (perhaps as many as 10 percent) are misdiagnosed and are instead examples of "ADD PSYCHOSIS." ADD psychosis is organic in origin, and it is thought to constitute the end result of a particular neurological deficit (attention deficit disorder) on personality organization. Attention deficit disorder (a common childhood diagnosis given to children who are hyperactive and dyslexic, among other attributes) was formerly called "minimal brain dysfunction," and the concept of ADD psychosis is the lifelong extension of these neurological deficits into adulthood. Many of Bellak's proposed symptoms (primarily NEGATIVE SYMPTOMS) and associated neurological findings for ADD psychosis seem to be similar to Crow's Type II schizophrenia and Carpenter's "deficit syndrome."

See also CROW'S HYPOTHESIS; DEFICIT SYMPTOMS/SYNDROME.

Bellak, L. "ADD Psychosis as a Separate Entity," *Schizophrenia Bulletin* 11 (1985): 523–527.

adolescent insanity A term coined in 1873 by Thomas Clouston, a Scottish psychiatrist and lecturer in psychiatry at the University of Edinburgh. He sometimes also called this syndrome "developmental insanity." Clouston identified adolescent insanity as a psychotic syndrome with an AGE AT ONSET between 18 and 24 years. Clouston said males were predominantly affected and that 30 percent of the cases developed into a more serious "secondary DEMENTIA." A family history of such psychosis was noticed in 65 percent of his cases when compared with 25 percent of cases of insanity with other diagnoses. Clouston's concept of adolescent insanity never became popular and was forgotten after Emil KRAEPELIN elaborated his concept of DEMENTIA PRAECOX in 1896. Clous-

ton was not at all pleased by being ignored for his contribution, and in a 1904 textbook on psychiatry he wrote: "Since I first used the term in 1873 and described its general characteristics it has become generally accepted by writers in psychiatry. Lately, however, Kraepelin has taken the term Dementia Praecox and applied it to practically my whole group of adolescent cases, making it cover the curable and incurable. I strongly object. . . ." Clouston's syndrome is now regarded as one of the precursors to the NEURODEVELOPMENTAL MODEL OF SCHIZOPHRENIA that has become the overarching paradigm at the end of the 20th century.

Clouston, T. S. *Clinical Lectures on Mental Diseases, Sixth Edition.* London: Churchill, 1904.

O'Connell, P., et al. "Developmental Insanity or Dementia Praecox: Was the Wrong Concept Adopted?" *Schizophrenia Research* 23 (1997): 97–106.

adoption method and studies One of the research strategies to resolve the "nature versus nurture" controversy in the investigation of the causes of MENTAL DISORDERS. Adoption studies have tended to strongly support the argument for the genetic basis for many psychiatric disorders, including SCHIZOPHRENIA, BIPOLAR DISORDER (manic-depressive disorder), and even alcoholism.

Adoption studies have been carried out in two ways: in the first method, children separated at birth from parents with a psychiatric disorder, and then raised by adoptive parents, are located. If these offspring show a prevalence for, say, schizophrenia that is the same as might be expected if they had been raised at home by their schizophrenic parent(s), then the argument is supported that genetics rather than environment is the primary cause of schizophrenia. A second method used in adoption studies is to look at all children who have been adopted, matching those in a group who develop schizophrenia (or another mental disorder), and then matching other adoptees in a control group who have not developed schizophrenia. Research is then conducted on both the biological and adoptive relatives of these individuals in these two groups. If the schizophrenia adoptees show a higher prevalence of schizophrenia in their biological relatives but not their adoptive ones, then the genetic explanation for schizophrenia is supported.

The very first published study using these adoptive methods in schizophrenia research was reported by L. L. Heston in the *British Journal of Psychiatry* in 1966. In the late 1960s, a famous series of adoption studies using these two methods was conducted in Denmark by David Rosenthal and Seymour Kety. All of these studies have consistently shown that adopted children who develop schizophrenia are many times more likely to have biological relatives who have developed schizophrenia rather than adoptive relatives who have done so. In the 1980s Rosenthal and Kety and their associates published reviews of clinical studies using the adoptive methods that support this genetic hypothesis in AFFECTIVE DISORDERS (such as bipolar disorder) as well.

In the 1990s the Danish data underwent further analyses and was supplemented by an ongoing Finnish Adoptive Family Study of Schizophrenia. The Danish study found that biological relatives of schizophrenic adoptees are more likely to have typical "narrowly defined" schizophrenia but also have more "latent" nonpsychotic forms of the illness. In the initial 1971 published report of the Danish study, Rosenthal and his colleagues termed these latent, nonpsychotic forms of the disorder "SCHIZOPHRENIA SPECTRUM DISORDERS (SSD)" to indicate a potential underlying biological commonality between schizophrenia and other mental disorders. The results of the Finnish study, first published in 1991, are consistent with previous studies of adoptees, finding a lifetime prevalence rate of 9.4 percent in the adopted-away children of schizophrenic parents and a lifetime prevalence in a control group of adoptees of 1.2 percent. Therefore, adopted-away children of mothers suffering from schizophrenia bear a four-times greater risk of developing schizophrenia later in life than those adopted-away children whose mothers did not have schizophrenia. The Finnish study of Tienari and colleagues provided support for both strong genetic and strong environmental main effects as well as gene-environment interaction effects. People who develop schizophrenia are "genetically sensitive" to their environments.

See also GENETICS STUDIES.

Heston, L. L. "Psychiatric Disorders in Foster Home Reared Children of Schizophrenic Mothers," *British Journal of Psychiatry* 112 (1966): 819–825.

Tienari, P. J., and L. C. Wynne. "Adoption Studies of Schizophrenia," *Annals of Medicine* 26 (1994): 233–237.

Wahlberg, K. E., L. C. Wynne, et al. "Gene-Environment Interaction in Vulnerability to Schizophrenia: Findings from the Finnish Adoptive Family Study of Schizophrenia," *American Journal of Psychiatry* 154 (1997): 355–362.

Wender, P. H., S. S. Kety, D. Rosenthal, et al. "Psychiatric Disorders in the Biological and Adoptive Families of Adopted Individuals with Affective Disorders," *Archives of General Psychiatry* 43 (1986): 923–929.

affect The behavioral expression of what is interpreted by others as an inner, subjective emotion or mood. For centuries, the term *affect* has often been used interchangeably with *mood*. Affect, emotion, and mood are now three distinct concepts in psychiatry, with emotion referring to an immediate inner state of feeling that is fluid and changeable, and mood referring to a general emotional state that grips a person for a long period of time (such as DEPRESSION or MANIA). Facial expressions, tone of voice, body language, content of speech, and observable actions can all be interpreted as affects corresponding to privately experienced emotions or moods. However, outwardly expressed affect can be incongruent or totally contradictory with what a person is truly feeling inside. Additionally, the affect expressed by a person can conflict with social norms in social interactions. The clinical term *inappropriate affect* is often used to refer to these examples. Persons with SCHIZOPHRENIA have long been observed to display inappropriate affect, and these behaviors are social cues to others of psychological disturbance.

See also AFFECTIVE DISORDERS.

Owens, H., and J. S. Maxmen. "Mood and Affect: A Semantic Confusion," *American Journal of Psychiatry* 136 (1979): 97–99.

affective disorders Throughout history, the word *affective* has been related to terms such as mood, emotion, passion, feeling, sentiment, euphoria, dysphoria, euthymia, dysthymia, cyclothymia, and so on. All these terms have been used to describe inner, subjective states of experience that are difficult to put into words. Since the time of the ancient Greeks, the two main broad categories for dozens of mental illnesses caused by a disorder of affect have been MELANCHOLIA and MANIA. By the latter half of the 19th century, concepts of melancholia and mania that had taken on a variety of meanings since antiquity were redefined in modern clinical forms as DEPRESSION and mania.

The affective disorders were renamed MOOD DISORDERS in 1987 with the publication of *DSM-III-R*, and remain so in *DSM-IV-TR* (2000). These are a group of MENTAL DISORDERS in which there is a disturbance of mood, accompanied by a full or partial manic or depressive syndrome, which is not due to any other physical or mental disorder. The Mood Disorders (Depressive Disorders, BIPOLAR DISORDERS, Mood Disorder Due to a General Medical Condition, Substance-Induced Mood Disorder) are characterized by "mood episodes" (Major Depressive Episode, Manic Episode, Mixed Episode, and Hypomanis Episode). Like SCHIZOPHRENIA, there is evidence that the development of the various mood disorders is influenced, in part, by genetics.

For centuries it had been noticed that alterations of mania and melancholia could afflict the same person at various times, but it was only in 1850 that a French ALIENIST, Jean-Pierre FALRET, proposed at a lecture to the Paris Psychiatric Society that this might be evidence of a single underlying disorder, a CIRCULAR INSANITY (*la folie circulaire*). In 1854 he and another French alienist, Jules-Gabriel-Francois BAILLARGER, published papers at almost the same time making this assertion (Baillarger called it the "double-formed insanity"). After 1899, when Emil KRAEPELIN essentially grouped all the AFFECTIVE DISORDERS under the broad diagnostic category of "manic-depressive illness" (*das manisch-depressive Irrsein*) and distinguished it from DEMENTIA PRAECOX (schizophrenia), all persons manifesting an affective or mood disorder were regarded as manic-depressive or potentially manic-depressive. In 1957, based on longitudinal studies of families with members who suffered from affective disorders, German psychiatrist Karl Leonhard

(1904–88) presented evidence that "monopolar" depression or mania were distinct illnesses from "bipolar" illness. However, the official separation of MANIC-DEPRESSIVE ILLNESS from major depression as distinct disorders did not occur until 1980, when *DSM-III* introduced the term *bipolar disorder* to replace Kraepelin's term. German psychiatrist Karl Kleist (1879–1960) had originally coined the term *bipolar* in 1953.

The relationship between schizophrenia and mood disorders, particularly the bipolar disorders, is the subject of much ongoing debate and research. Although Kraepelin distinctly separated dementia praecox from manic-depressive illness as the two main forms of insanity, it is still not clear among prominent psychiatrists and researchers if they are separate diseases or two ends of the spectrum of the same underlying disease. For example, in clinical situations, a person suffering from bipolar disorder with psychotic features (DELUSIONS and HALLUCINATIONS), particularly the sort of PARANOIA that accompanies manic episodes, can be indistinguishable from someone suffering from PARANOID SCHIZOPHRENIA.

Causes of Affective Disorders

Like schizophrenia, affective disorders are thought to be characterized by ETIOLOGIC HETEROGENEITY. Multiple causes—experiential (e.g., psychological trauma), social, genetic, biochemical (neurotransmitter dysfunction), endocrine dysfunction (particularly the thyroid gland and the hypothalamic-pituitary-adrenal glands axis), immune system dysfunction, biorhythm dysfunction, brain structure abnormalities, viral infection—have been proposed. A clear summary of the evidence and issues in the causes of affective disorders can be found in the chapter on "Causes" in E. Fuller Torry and Michael Knable's 2002 book, *Surviving Manic Depression: A Manual on Bipolar Disorder for Patients, Families and Providers.*

See also ANTIDEPRESSANT DRUGS; MANIC-DEPRESSIVE ILLNESS; SCHIZOAFFECTIVE DISORDER.

Berrios, G. E. "Mood Disorders: Clinical Section." In *A History of Clinical Psychiatry,* edited by G. E. Berrios and R. Porter. London: Athlone Press, 1995.

Taylor, A. M. "Are Schizophrenia and Affective Disorder Related? A Selected Literature Review," *American Journal of Psychiatry* 149 (1992): 22–32.

Torrey, E. F., and M. B. Knable. "Are Schizophrenia and Bipolar Disorder One Disease or Two? Introduction to the Symposium," *Schizophrenia Research* 39 (1999): 93–94.

Torrey, E. F., and M. B. Knable. *Surviving Manic Depression: A Manual on Bipolar Disorder for Patients, Families and Providers.* New York: Basic Books, 2002.

affective disturbances One of the "Four A's" (AUTISM, AFFECTIVE DISTURBANCES, ASSOCIATION DISTURBANCES, AMBIVALENCE) that Eugen BLEULER proposed as the fundamental symptoms of SCHIZOPHRENIA. Since then, this disturbance in the ability of schizophrenics to feel and/or express the full range of human emotions has been included in most definitions of schizophrenia. In *Dementia Praecox, Or the Group of Schizophrenias* (1911), Bleuler writes:

> Patients with schizophrenia react differently to their affective disturbances. The majority are not aware of them and consider their reaction as normal. The more intelligent, however, may reason about it quite acutely. At the beginning they sense the emotional emptiness as rather painful, so that they may be easily mistaken for melancholics. One of our catatonics considered himself as "insensitized"; one of Jung's patients could not pray any more because of "hardening of her feelings." Later, they tend to displace the changes in themselves to the outer world which itself becomes hollow, empty, strange, because of these affective changes. Often the element of strangeness has a touch of the uncanny and the hostile.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenias,* trans. Joseph Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

Africa Many studies have been done in Africa since the 1930s to determine how prevalent SCHIZOPHRENIA is on this continent. The majority of impressions from around Africa is that the prevalence of schizophrenia is quite low. Most of the disorders described in these reports resemble an ACUTE RECOVERABLE PSYCHOSIS rather than schizo-

phrenia. Unfortunately, there is as yet no conclusive study that can give a reasonable estimate of the prevalence of schizophrenia in Africa.

after-care movement The original name for the organized efforts of mental health professionals in Europe (and later the United States) to provide support services for deinstitutionalized mental patients so that they will not relapse and require readmission. A physician by the name of Lindpainter initiated this movement in Nassau, Germany, in 1829. It became so popular that it was advocated by psychiatrist Jean FALRET in France in 1841 and instituted in England in 1871, by an organization called the Guild of Friends of the Infirm in Mind.

The first outpatient clinic devoted to the prevention of mental disorders was founded at the Pennsylvania Hospital in Philadelphia in 1885, and other organized efforts to provide financial and social assistance to discharged mental patients were started in America at around this time. Forms of HYDROTHERAPY, various emetics, and some pharmacological substances were administered. Due to the excessive amount of psychiatric patients "deinstitutionalized" in the United States in the 1950s (estimated to be about 200,000 between 1955 and 1967), the United States government began to provide federal funds for Community Mental Health Centers (CMHCs) in 1963 to provide after-care for these people. However, studies have shown that only a small percentage of discharged psychiatric patients have received consistent care from the CMHCs. The lack of a major effort to provide housing for these individuals led to the phenomenon in the United States of the tens (and perhaps hundreds) of thousands of "mentally ill homeless" on American streets by the late 1980s.

age at onset The general age range at which a particular disorder is thought to begin. Some disorders can begin to afflict a person at any age, but most have particular critical periods in the life cycle during which they are more likely to appear. However, the insidious nature of many psychiatric symptoms often makes it difficult to pinpoint exactly when a particular mental disorder is thought to begin.

In SCHIZOPHRENIA, it has been commonly observed that the first major signs of this psychotic disorder occur during adolescence or early adulthood, usually between age 15 and 25. However, cases of LATE-ONSET SCHIZOPHRENIA occurring after the age of 45 have been reported in the literature. Early-onset schizophrenia is more characteristic of males than females, with 1980s studies of late-onset schizophrenia indicating a high female-to-male ratio and a predominance of paranoid symptoms. The average age of onset for BIPOLAR DISORDERS has been found to be about 30 (average range, ages 20 to 40), with occurrences of brief manic or HYPOMANIC EPISODES in early adulthood leading up to the development of a psychotic disorder at about this time.

It has long been known that many physical illnesses (such as multiple sclerosis or Alzheimer's disease) have typical age ranges of onset, and the establishment of similar patterns in many MENTAL DISORDERS supports the belief that they are essentially biological in nature and not caused by supernatural forces or psychoanalytic demons such as "unresolved conflicts" or "SCHIZOPHRENOGENIC MOTHERS." Schizophrenia and bipolar disorder are thought to be disorders characterized by incomplete age-dependent penetrance, which is a term in genetics research that refers to the likelihood that someone with a particular genetic predisposition will develop a corresponding disorder at a particular time in the life cycle.

See also INCOMPLETE PENETRANCE.

Hafner, H., et al. "Causes and Consequences of the Gender Difference in Age at Onset of Schizophrenia," *Schizophrenia Bulletin* 24 (1998): 87–98.

Keith, S. J., and S. M. Matthews. "The Diagnosis of Schizophrenia: A Review of Onset and Duration Issues," *Schizophrenia Bulletin* 17 (1991): 51–67.

AIDS and psychiatric patients Although no studies of the incidence and prevalence of Acquired Immune Deficiency Syndrome (AIDS) in psychiatric patients have been conducted (as of early

1989), the institutionalized populations and deinstitutionalized "street people" are at high risk for contracting this disorder. This will no doubt be an important issue in the future. As many institutionalized patients contract and develop AIDS, the need will arise for special psychiatric inpatient units designed for those that need to be placed on body fluid precautions. State hospitals in particular are believed to be fertile breeding ground for the spread of this disorder; several high-risk populations (IV drug abusers, prisoners, promiscuous patients with impulse control disorders) are combined in the wards of these institutions and freely engage in high-risk sexual behaviors. Male wards in psychiatric hospitals—as in prisons—are known for their promotion of homosexual practices, and sometimes these same patients engage in sexual activities with members of the opposite sex when given free hours on the grounds during the day.

Recognizing this danger, and the ethical problems AIDS poses for psychiatrists, the AMERICAN PSYCHIATRIC ASSOCIATION's Ad Hoc Committee on AIDS Policy issued AIDS policy guidelines, which were published in full in the *American Journal of Psychiatry* in April 1988. The APA's "Guidelines for Inpatient Psychiatric Units" recommends to psychiatrists that, "Regardless of HIV serologic status, all inpatients should be considered potentially at risk for transmitting or receiving HIV infection."

During the early years of the AIDS epidemic, there was some concern that the confusion and other signs of mental deterioration documented in AIDS patients might be misdiagnosed as signs of SCHIZOPHRENIA or other MENTAL DISORDERS. But a major study released by the WORLD HEALTH ORGANIZATION in 1988 indicates that mental deterioration is evident only in the later, more serious stages of the illness, when the diagnosis of AIDS has already become evident through the detectable presence of human immunodeficiency virus (HIV) antibodies in the blood.

American Psychiatric Association. "AIDS Policy: Guidelines for Inpatient Psychiatric Units," *American Journal of Psychiatry* 145 (1988): 4.

Woody, G. E., et al. "Psychiatric Symptoms, Risky Behavior, and HIV Infection," *NIDA Research Monographs* 172 (1997): 156–170.

AIDS and schizophrenia See HIV AND SCHIZOPHRENIA.

AIDS dementia complex Since 1981, when AIDS was first observed to occur in the United States in homosexual males, there has been an intense effort to identify the signs and symptoms of the disorder. One of the features that has been observed in many persons who have developed AIDS is a marked mental deterioration. It is now known that HIV-positive persons also develop symptoms of an ORGANIC MENTAL DISORDER—namely, DEMENTIA—which is due to the direct infection of the brain by HIV (human immunodeficiency virus). In fact, the syndrome that was first described in a 1986 publication by researcher B. A. Navia and colleagues as the "AIDS dementia complex" has been found to be the initial clinical presentation of AIDS in as many as one-fourth of all patients. Based on this work, the diagnostic criteria for AIDS formed by the Centers for Disease Control in the United States has modified the criteria to allow the diagnosis of AIDS solely on the basis of dementia in a seropositive (that is, tested positive for HIV in the blood) individual without any other evidence of an opportunistic infection or Karposi's sarcoma. Besides the usual signs of dementia—forgetfulness, poor concentration, confusion, slowed thinking—there are movement problems (loss of balance, leg weakness) and more serious psychiatric symptoms, such as DEPRESSION, apathy, and even the thought disorder or mania of PSYCHOSIS. The later stages of the disorder are marked by the most severe forms of these symptoms.

There has been some concern that the early stages of AIDS dementia complex may be misdiagnosed as SCHIZOPHRENIA, although a routine HIV test should help to clear up the issue. Research on the retroviruses stimulated by AIDS may lead to a better understanding of the causes of the psychotic disorders. VIRAL THEORIES OF SCHIZOPHRENIA have long been suggested.

Jones, G. H. "HIV and the Onset of Schizophrenia," *The Lancet* 1 (1987): 982.

Navia, B. A., et al. "The AIDS Dementia Complex. I. Clinical Features," *Annals of Neurology* 19 (1986): 517–524.

———. "AIDS Dementia Complex as the Presenting Sole Manifestation of HIV Infection," *Annals of Neurology* 44 (1987): 65–69.

akathisia A symptom found in many psychiatric patients treated with ANTIPSYCHOTIC DRUGS. The term was coined in a 1901 article in the French journal *Review neurologique* by a neurologist from Prague, Ladislav Haskovec (1866–1944), and is derived from Greek word for "the inability to sit down." It is usually defined as the compulsion to be in motion. Patients with akathisia report feeling restless, uncomfortable with remaining still, and needing to pace or fidget continually. The neurological mechanism for this behavior is not well understood. Akathisia seems to be a symptom that appears in patients who are treated with high-potency conventional antipsychotic drugs. Sometimes this symptom can be alleviated by lowering the dosage, switching to a lower-potency drug, or by administering a contra-active drug such as the ones used to treat acute dystonic reactions (namely, anticholinergic and antiparkinsonian agents, antihistamines, and benzodiazepines). When the side effects are refractory, psychiatric experts often suggest adding propranolol as an adjunct treatment.

Akathisia is a classic early sign of Parkinson's disease. The fact that antipsychotic drugs may produce serious Parkinsonian side effects has been known since the first clinical trials of CHLORPROMAZINE (THORAZINE), a PHENOTHIAZINE, in France in 1952. Akathisia and other Parkinsonian side effects may have been known to have been associated with the use of phenothiazine-type drugs as early as 1947. Akathisia is a side effect that occurs in up to 20 to 25 percent of persons taking antipsychotic medication. It is also a lesser side effect of selective-serotonin reuptake inhibitor (SSRI) drugs such as Prozac used in the treatment of depression and anxiety. *DSM-IV* (1994) suggested that a new syndrome called "neuroleptic-induced acute akathisia" may possibly be added as a diagnostic category in future editions.

akinesia See BRADYKINESIA.

Akineton See ANTIPARKINSONIAN DRUGS.

alcohol amnestic disorder See KORSAKOV'S PSYCHOSIS.

alienation mentale See MENTAL ALIENATION.

alienism An obsolete 19th-century term for the study and treatment of mental diseases. In France this medical discipline was referred to as *MÉDICINE MENTALE*. It predates "PSYCHIATRY" as a conventional label for this profession. The word *psychiatry* was first used in English to describe this profession in 1846, following the reintroduction of the word *psychiatrics* by FEUCHTERSLEBEN in 1845. From about the mid-1800s this profession was also called "medical psychology" or "mental science."

alienist An archaic, obsolete term for a psychiatrist that was commonly used in the 1800s. The French term for this professional was *aliéniste*. Other commonly used terms for psychiatrists, especially in England, were "mental pathologist" and "psychiater" (from the German word of the same spelling). "Lunatic doctor" and "MAD-DOCTOR" were terms more commonly employed in the 17th and 18th centuries. These men frequently worked in "mad-houses" and later "lunatic asylums." MENTAL ALIENATION—first used in the 15th century as a term for mental illness—became the standard term for mental illness in the late 18th and early 19th centuries, hence the derivation of the label for this type of professional. "Alienists" also referred to those psychiatric experts who were requested to make legal competency determinations in court, especially at LUNACY TRIALS.

allele One of several alternative forms of a GENE. Alleles always occupy the same place ("locus") on a CHROMOSOME.

almshouses Houses founded by private charities for the reception and support of the (usually) poor. These are the famous "poor houses" that provided "indoor relief." Mentally ill individuals were frequently guests at almshouses. The word dates back

to medieval times, when it referred to the house where the alms of the monastery were dispensed to the needy. Many such institutions were built in the United States during the Age of Reform from the 1820s to the 1840s, as were many penitentiaries and asylums for the mentally ill. In Pennsylvania, the famous Philadelphia Poorhouse was utilized by the many medical schools for the training of new physicians. Today's rough equivalent of almshouses are rescue missions and halfway houses. Perhaps the best historical description of these institutions can be found in the chapter entitled "The Almshouse Experience," in David J. Rothman's book on the rise of institutions in America.

Rothman, D. J. *The Discovery of the Asylum: Social Order and Disorder in the New Republic.* Boston: Little, Brown, 1971.

alogia One of the NEGATIVE SYMPTOMS of SCHIZOPHRENIA. Alogia is the term now used in place of "poverty of speech" to refer to the underproduction of speech, the abbreviation of speech, or the relative lack of any attempt to speak (mutism) that is often manifest in persons with schizophrenia.

altered state of consciousness Psychologist Charles Tart, who is commonly regarded as a leading authority on altered states of consciousness (ASCs), often defines an ASC as a "qualitative alteration in the overall patterning of mental functioning, such that the experiencer feels his consciousness is radically different from the way it functions ordinarily."

In an effort to understand the phenomenology of SCHIZOPHRENIA, the subjective reports of schizophrenic experience began to be collected in the 1960s and compared with other unusual ASCs—such as those reported in "mystical" experience or in the psychedelic experiences of those who have ingested hallucinogenic substances. A famous paper was published in 1966 by Malcom Bowers and D. X. Freedman, which suggested that some schizophrenics have "psychedelic experiences" during the onset of their psychosis. However, further phenomenological studies of the ASCs of schizophrenics in the 1970s and 1980s have not supported the contention that they are similar to mystical or drug-induced ASCs. In the early 1960s hallucinogens were called psychotomimetic or "psychosis-mimicking" drugs, but this term has fallen out of conventional usage.

In 1961 psychiatrists Humphrey Osmond (who coined the word *psychedelic*) and Abram Hoffer designed a diagnostic test for schizophrenia, the Hoffer-Osmond Diagnostic Test, the first to be based on the subjective reports of schizophrenic experiences of perceptual distortions. It was believed that this test distinguished schizophrenia from other psychiatric disorders based on the uniqueness of the phenomenology of the ASCs experienced by schizophrenics. A later scale whose items were also derived from autobiographical accounts of schizophrenics was devised in 1970 by Osmond and psychologist A. Moneim El-Meligi—the Experiential World Inventory. This self-report inventory of 400 items purported to measure subjective changes with scales for five major phenomenological categories: sensory perception, time perception, body perception, self perception, and perception of others. Neither of these phenomenologically based measures ever became popular, and they have not been used in research since the early 1970s.

Bowers, M., and D. X. Freedman. "Psychedelic Experiences in Acute Psychosis," *Archives of General Psychiatry* 15 (1966): 240–248.

El-Meligi, A. M., and H. Osmond. *EWI: Manual for the Clinical Use of the Experiential World Inventory*. New York: Mens Sana Press, 1970.

Alzheimer, Alois (1864–1915) German neurologist who is best remembered for identifying Alzheimer's disease (a form of presenile dementia) in 1906, but who also published research on SCHIZOPHRENIA and MANIC-DEPRESSIVE ILLNESS. Starting in 1903 he worked under Emil KRAEPELIN in the research laboratory at the University of Munich. Along with German neurologist Franz Nissl (1860–1919), these three men conducted research on the underlying disease processes in the nervous system that caused MENTAL DISORDERS

such as DEMENTIA PRAECOX; they made major contributions to the field of neuropathology. Earlier Nissl had invented new staining techniques that allowed for the study of nerve cells, and Alzheimer discovered the organic disease process in the ailment that is still known by his name. Alzheimer considered dementia praecox an essentially organic disease of the brain.

Alzheimer is credited for conducting the very first neurohistological study of schizophrenia (dementia praecox). In 1897 Alzheimer published a paper in which he described abnormal nerve cells in the cortex of young patients with psychotic disorders who did not have a known organic brain disease. Alzheimer believed that dementia praecox (schizophrenia), presenile dementia (later called Alzheimer's disease) and epilepsy were all organic brain diseases. However, he did not believe that hysteria or manic-depressive illness were organic brain diseases. Thus, in the early 20th century there were numerous published reports of neuropathological studies on dementia praecox (schizophrenia) and epilepsy, but none on the mood disorders. He held a professorship at Breslau University and taught there from 1912 until his death in 1915.

Alzheimer, A. "Beitrage zur pathologischen Anatomie der Hirnrinde und zur anatomischen Grundlagen der Psychosen," *Monatsschrift Psychiatrie und Neurologie* 2 (1897): 82–120.

amantadine See ANTIPARKINSONIAN DRUGS.

ambivalence The presence of two contradictory drives, tendencies, emotions, or thoughts that are aimed at the same person, object, or goal. These contradictory urges may be unconscious, conscious, or only partly conscious, but in SCHIZOPHRENIA they are a very common phenomenon that tends to paralyze the willful, volitional actions of the afflicted. For example, a commonly reported experience of people with schizophrenia is that, when they try to express a thought or feeling or attempt an action, their minds suddenly become flooded with many different and often contradictory choices, and they are unable to focus on only one. One of Eugen BLEULER's higher-functioning patients once told him that, "When one expresses a thought, one always sees the counter thought. This intensifies itself and becomes so rapid that one doesn't really know which was the first." Another of his patients expressed the ambivalence so characteristic of schizophrenia by telling Bleuler, "I am a human being like yourself, even though I am not a human being." Bleuler reports that example in his classic 1911 book, *Dementia Praecox, Or the Group of Schizophrenias,* in which "ambivalence" is described as one of the "fundamental symptoms" of schizophrenia. AMBIVALENCE is one of Bleuler's famous "Four A's" (AUTISM, ASSOCIATIONS DISTURBANCES, AFFECTIVE DISTURBANCES, ambivalence), which he felt were the central identifying symptoms of schizophrenia that differentiated it from other mental disorders. Bleuler identified three types of ambivalence in schizophrenia: affective ambivalence, ambivalence of will, and intellectual ambivalence. Modern theorists think that schizophrenic ambivalence may be due to disorders in attention that disable the individual's ability to focus attention on one goal or thought and screen out all other contradictory "noise" that might otherwise flood the mind.

See also ATTENTION, DISORDERS IN.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenias*, trans. Joseph Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

ambulatory schizophrenic This is a term for a person with SCHIZOPHRENIA whose level of functioning is high enough that inpatient care is not generally required. It is also applied to schizophrenic patients within psychiatric institutions who can be trusted to reside on open wards or be allowed frequent brief visits into the surrounding community. The term seems to be slowly falling out of conventional usage, with the synonym "high-functioning" replacing "ambulatory" as a label for these schizophrenics.

See also BORDERLINE SCHIZOPHRENIA.

amenomania In his 1812 psychiatric manual, *Medical Inquiries and Observations upon the Diseases*

of the Mind, American alienist Benjamin RUSH claimed that, "Amenomania is a common form of partial insanity." By the examples he gives, it seems that Rush used this term to describe what we might now call a DELUSIONAL DISORDER in people who may not be paralyzed by mental illness but who have fixed delusions or eccentric beliefs on certain topics that may be quite bizarre.

In particular, Rush believed this disorder was found "most frequently in the enthusiasts in religion," which explains his derivation of the word. The grandiose religious delusions that characterize amenomania, Rush claims, may also be indicative of what we now call BIPOLAR DISORDER or PARANOID SCHIZOPHRENIA, for people with amenomania believe they are "the peculiar favourites of heaven." They converse with angels and with spirits of the dead, they see visions, and they believe they are "exalted into beings of the highest order." Rush describes a familiar psychotic DELUSION still encountered in a few patients today when he reports, "I have seen two instances of persons, who believed themselves to be the Messiah."

Psychologist Milton Rokeach experimentally grouped three such schizophrenic patients together in the same environment and described the results in 1964 in his unique book, *The Three Christs of Ypsilanti.*

Rokeach, M. *The Three Christs of Ypsilanti.* New York: Alfred A. Knopf, 1964.

Rush, B. *Medical Inquiries and Observations on the Diseases of the Mind.* Philadelphia: Kimber & Richardson, 1812.

American Psychiatric Association The professional organization of physicians who specialize in the practice of PSYCHIATRY. The precursor to the APA was founded at a meeting in Philadelphia on October 16, 1844, by "the original thirteen" physicians: Francis T. Stribling, Samuel B. Woodward, Samuel White, Isaac RAY, Pliny EARLE, Thomas KIRKBRIDE, Aramiah BRIGHAM, Luther Bell, William AWL, John Galt, Nehemia Cuter, John Butler, and Charles H. Steadman. The original name decided upon by these men was the Association of Medical Superintendents of American Institutions for the Insane. Benjamin RUSH—the "father of American psychiatry"—was a physician at the Pennsylvania Hospital in Philadelphia in the early 1800s and his image appears on the modern logo for this organization. In that founding year the association also published the first English-language psychiatric journal, the *American Journal of Insanity,* which in 1921, under the urging of then-APA president William Alanson White, changed its name to the *American Journal of Psychiatry.* The association changed its name to the American Medico-Psychological Association in 1893 and then to its present title, the American Psychiatric Association, in 1921.

The American Psychiatric Association is responsible for the continually revised editions of the *Diagnostic and Statistical Manual of Mental Disorders,* which is the most widely accepted diagnostic manual used in North America. The most recent edition was *DSM-IV-TR,* published in 2000.

McGovern, C. M. *Masters of Madness: Social Origins of the American Psychiatric Profession.* Hanover and London: University Press of New England, 1985.

American Psychological Association The professional society of American psychologists. It was founded in July 1892 by G. Stanley Hall (1844–1924), a professor of psychology at Clark University in Worcester, Massachusetts.

amine The name for a type of organic compound that contains nitrogen. Amines function as NEUROTRANSMITTERS in the brain. CATECHOLAMINES are a type of amine.

See also DOPAMINE HYPOTHESIS.

amisulpride See ANTIPSYCHOTIC DRUGS.

amphetamine psychosis An obsolete diagnostic term for the psychotic episodes brought on in some people by the ingestion of amphetamine (usually in the form of the "street drug" methamphetamine, or "speed") or similarly acting substances. Irritability, paranoid delusions, and even violent behavior may be exhibited during these acute psychotic episodes.

The main pharmacological effect of amphetamine is believed to be the release of CATECHOLAMINES, one of which, dopamine, is hypothesized to cause schizophrenic symptoms when there is an excess of it. Amphetamine activates or worsens preexisting psychotic symptoms, and ANTIPSYCHOTIC DRUGS work as a potent antidote to the psychosis produced by extreme amphetamine intoxication. Thus, the biochemical properties and effects of amphetamine have been studied as a model for understanding the underlying biochemical processes in schizophrenia.

See also BIOCHEMICAL THEORIES OF SCHIZOPHRENIA; DOPAMINE HYPOTHESIS.

anhedonia The chronic inability to experience pleasure. It is often a sign of a MOOD DISORDER, such as a depressive episode, but can also be found in schizophrenics as a form of their AFFECTIVE DISTURBANCES.

animal models of schizophrenia Animals have long been used in a variety of experimental research studies in many areas of medicine. Animals are routinely used in neurobiological, neurochemical, neuroendocrine, genetics, and pharmacological research, for example, to test hypotheses that would be injurious, lethal, and therefore ethically forbidden if performed on human beings. Attempts to induce behaviors or physiological changes in animals that are similar to those found in persons with SCHIZOPHRENIA have a long history in psychiatric research. However, the development of reliable "models" of the etiology (cause) and pathophysiology of schizophrenia date to only the early 1970s. These animal models focused on pharmacologically manipulating the NEUROTRANSMITTER DOPAMINE and studying the resulting changes in pathophysiology and behavior. Such animal research led, in part, to the DOPAMINE HYPOTHESIS of schizophrenia, first posited by Solomon Snyder and his colleagues in 1976 in the *American Journal of Psychiatry.* The dopamine hypothesis of the cause of schizophrenia was subsequently rejected in its strict monocausal form, as other neurotransmitters were linked to the disorder. Animal models of schizophrenia based on direct manipulations of the dopaminergic system have outlived their usefulness and are no longer conducted in their classical form. However, dopamine is still implicated in the pathophysiology of schizophrenia, and dopamine receptors in the brain remain a target of ANTIPSYCHOTIC DRUGS.

The problem with animal models of schizophrenia is that they are most reliable when focusing on a single issue (e.g., the effects of manipulating the levels of dopamine in the nervous system) but not multiple factors. Since schizophrenia is characterized by a multiplicity of factors leading to its (unknown) cause and resulting in its (still largely unknown) pathophysiology, the development of a single animal model of schizophrenia is doubtful. However, two schizophrenia researchers at the NATIONAL INSTITUTE OF MENTAL HEALTH, the National Institutes of Health, in Bethesda, Maryland, Daniel Weinberger (chief of the Clinical Brain Disorders branch), and B. K. Lipska (chief of the Unit on Animal Models, Clinical Brain Disorders branch), propose that future animal models should focus on three emerging areas of schizophrenia research: (1) testing the NEURODEVELOPMENTAL MODEL OF SCHIZOPHRENIA by experimentally inducing disruption in the development of animal brain development at various stages of embryonic or fetal development through maternal malnutrition, the introduction of possible teratogens (such as viruses) that may disrupt the creation or maturation of nerve cells *in utero,* the creation of lesions in the brains of newly born animals, inducing "stress" in neonates, and so on, (2) the use of drugs to study the possible role that the neurotransmitter glutamate, particularly the "hypofunctioning" of the glutamatergic system of the brain, plays in the underlying pathophysiology of schizophrenia, and (3) genetics, particularly by inserting transgenic mutations in developing embryos or knocking out certain genes that are candidates for the development of schizophrenia in human beings.

The functioning of the immune system in schizophrenia is an additional area of research that lends itself to animal models. In a study published in *Neuroscience Biobehavior Review* in June 2005, a team of researchers in Zurich, Switzerland, investigated the long-known epidemiological

link between bacterial or viral infections in pregnant mothers and the later higher risk of the postpuberty development of schizophrenia in their children. Using pregnant mice in a series of different conditions, they argue this epidemiological link in schizophrenia is mediated by the prenatal activation of the fetal immune system in response to the elevation of the maternal cytokine level due to infection. This study combined assumptions from the neurodevelopmental model and theories of IMMUNE SYSTEM ALTERATIONS IN SCHIZOPHRENIA.

The National Institutes of Health provides the latest information of animal models used in genetics research on its Web site: www.nih.gov/science/models.

Lipska, B. K., and D. R. Weinberger. "Animal Models of Schizophrenia." In *Schizophrenia.* 2nd ed., edited by S. R. Hirsch and D. R. Weinberger. Oxford: Blackwell, 2003.

Meyer, U., et al. "Towards an Immuno-Precipitated Neurodevelopmental Animal of Schizophrenia," *Neuroscience Biobehavior Review* 15 (June 2005): 913–947.

animal spirits A prescientific concept used to explain the cause of MENTAL DISORDERS, particularly mania. A 17th-century treatise by Thomas Willis, *De anima brutorum* (1672), claims that "animal spirits" were distillations from the blood contained in the brain. Their production in the brain was thought to irritate the nervous system and stimulate intellectual functioning so severely that mania would be the result.

anticholinergic effects The effect of some drugs that act as antagonists to the actions of cholinergic nerve fibers, usually of the parasympathetic nervous system. Such cholinergic nerve cells or fibers are those that use acetylcholine as their NEUROTRANSMITTERS. Drugs that have anticholinergic effects block the transmission of this neurotransmitter, thus preventing the communication between nerve cells and thereby altering behavior.

Most psychoactive drugs have anticholinergic effects in both the central and the peripheral nervous systems. The types of drugs that have anticholinergic effects are heterocyclic antidepressants, antipsychotics, antihistamines, ANTIPARKINSONIAN DRUGS, and some hypnotics. If a patient is taking a combination of these drugs (such as an antipsychotic drug with an antidepressant—a common combination) or if an overdose of these drugs is taken, the additive anticholinergic effects can cause a crisis. The combination of signs and symptoms that indicate there is too much of an effect is called the "anticholinergic syndrome." At its worst, a patient suffering from an anticholinergic syndrome will have confusion, DELIRIUM with disorientation, agitation, visual and AUDITORY HALLUCINATIONS, anxiety, restlessness, pseudoseizures, and perhaps even thought disorder (e.g., delusions). Dry mouth, constipation, urinary retention, decreased sweating, increased body temperature, flushing, discoordination, and tachycardia are common but far less serious side effects due to anticholinergic syndrome. The treatment for the anticholinergic syndrome is anticholinesterase drug therapy.

anticipation (genetic) A phenomenon observed over time in some genetic diseases in which each successive generation develops the disease at a progressively earlier age and with a course that is more severe. This phenomenon was noted in the 19th century and was cited as evidence for the medical theory of hereditary DEGENERATION. A useful historical survey of the survival of this idea was provided by German psychiatric researcher Manfred Spitzer in the journal *Nervenarzt* in 1995.

The term *anticipation* was first used in the context of degeneration theory (and with reference to DEMENTIA PRAECOX) in the published text of an invited Huxley Lecture by F. W. Mott, delivered at the Charing Cross Hospital Medical School in London in 1910. Mott was a physician at Charing Cross Hospital as well as a pathologist for the London County Asylums and Fullerian Professor of Physiology at the Royal Institution. Presenting charts of various pedigrees as evidence for the heredity basis of nervous and mental diseases, Mott noted that, "almost invariably in the case of insane parents and offspring, the offspring is affected earlier than the parent." He proposed a name for this phenomenon: "the law of anticipation." Mott did

place limits on this process of intergenerational degeneration, stating that "the general tendency is for insanity not to proceed beyond three generations. . . . Not infrequently the stock dies out by the inborn tendency to insanity manifesting itself in the form of congenital imbecility or insanity of adolescence—dementia praecox." This is a good thing, according to Mott: "thus rotten twigs are continually breaking off the tree of life."

In an important paper published in 1992, R. I. Richards and G. R. Sutherland were the first to propose the possible underlying molecular mechanism for the phenomenon of anticipation: the repeating of a three nucleotide sequence (e.g., CAG or CTG). These three-letter repeats (triplet repeats) enlarge further in the genomes of each successive generation, and longer repeats are correlated with more severe disease. Because of this proliferation of the three-letter repeats in succeeding generations, they also are called trinucleotide expansions. Triplet repeats are known to cause at least 13 different neurodegenerative disorders, making them an attractive focus of research on SCHIZOPHRENIA. However, there is a fundamental difference between schizophrenia and these other disorders. These neurodegenerative disorders are caused by single genes and follow classic patterns of Mendelian inheritance, whereas schizophrenia is thought to be a disorder caused, in part, by many genes and follows confusing NON-MENDELIAN PATTERNS OF TRANSMISSION. The possibility that genetic anticipation caused by triplet repeats is part of the schizophrenia disease process was first proposed by Anne Bassett and W. G. Honer in an article published in the *American Journal of Human Genetics* in 1994.

Anticipation is currently of great interest in GENETICS STUDIES of schizophrenia, particularly those involving genetic association studies. Anticipation is also of great interest to researchers studying CHILDHOOD-ONSET SCHIZOPHRENIA. No candidate trinucleotide repeat has yet been conclusively linked to schizophrenia. Promising trinucleotide expansions in schizophrenia such as CAG and CTG have not been reliably confirmed in replication studies—a familiar and frustrating pattern in almost all areas of biological research on schizophrenia.

Since so many genetic diseases manifest anticipation, a central public-access online database of known trinucleotide sequences called Satellog was established in June 2005 to assist geneticists in their research. The name of this database refers to the fact that trinucleotide repeats are also known as satellite repeats. However, methodological problems with identifying anticipation in diseases and psychiatric disorders such as schizophrenia were identified as early as 1945 by Lionel S. Penrose (1898–1972), then the Galton Professor of Eugenics at University College London in England: "This finding, which in one form or another, is characteristic of mental hospital data, has in the past been attributed to a tendency for progressive degeneration or anticipation of diseases in succeeding generations. Such an explanation, which is not in accordance with the concepts of modern genetics, is unnecessary, because the more likely explanations are close at hand." He further developed his warning about possible "ascertainment bias" in documenting anticipation in a 1948 article published in the *Annals of Eugenics.*

Whether the proposed mechanism of trinucleotide repeats can fully explain the phenomenon of anticipation is doubtful, and even if a definitive genetic pattern of nucleotide repeats is found in some forms of schizophrenia, the phenomenon of anticipation in this disease—for which there is some suggestive evidence—may have to be accounted for by factors as yet unknown.

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antidepressant drugs The class of psychoactive drugs that alleviate the symptoms of depression. The term *antidepressant* was coined by Max Lurie in 1952 but did not come into common usage until the 1960s. The first drugs used specifically for depression were amphetamines. The first designer drug marketed as a treatment for "mild depression" (in 1942) was Benzedrine (racemic amphetamine sulfate), the first of the amphetamine drugs developed and introduced by the pharmaceutical company Smith Kline and French in 1936. Two years later, it was being recommended as a treatment for obesity, and for at least the next 30 years amphetamines were prescribed as "diet pills" by physicians. Dexadrine (dextroamphetamine sulfate) appeared in 1946, followed by a drug that combined Dexadrine with a barbiturate, amobarbital (Amytal).

The second generation of antidepressants involved two separate categories of drugs. Monoamine oxidase inhibitors (MAO inhibitors) included drugs such as iproniazid (Marsilid), developed in 1952 for tuberculosis but first used in PSYCHIATRY in 1957. It was discovered by Nathan Kline. Tricyclic antidepressants were first introduced in 1957 with imipramine (Tofranil) after its discovery by Roland Kuhn. In the decades after they were developed, researchers found that drugs of both these classes increased levels of serotonin and norepinephrine in the brain, giving rise to the idea—still unproven—that depression was caused by deficiencies of these NEUROTRANSMITTERS in the brain. It should be repeated in this age of Prozac that there is no evidence that depression is caused by a lack of serotonin or any other chemical in the brain.

The first two generations of antidepressants were designed in an era in which little was known about neurotransmitters (called neurohumors or neurohormones prior to the 1960s) in the brain, and indeed many neurotransmitters had still not been discovered yet. The third generation of designer drugs for the treatment of depression (and now anxiety as well) were created from theories of "reuptake inhibition" based on this new knowledge. These drugs inhibited the reuptake of monoamine neurotransmitters such as DOPAMINE, norepinepherine, and serotonin. In 1979 the drug mianserin appeared under the trade name Athymil in France and in the United Kingdom as Norval. Others were trazodone (Desyrel), released in the United States in 1982, and maprotiline (Ludiomil), first used in France in 1975 and in America in 1981. Other drugs of this generation, which are sometimes called "atypical antidepressants," are amoxapine (Ascendin), bupropion (Wellbutrin, Zyban), clomipramine (Anafranil), and venlafaxine (Effexor).

The fourth generation of antidepressant drugs are the SSRIs, or selective serotonin reuptake inhibitors. Since these drugs work selectively on serotonin in the brain, there are fewer anticholinergic or antihistaminic side effects, allowing for little or no sedation and little impairment of learning, memory, and cognition. The SSRIs are also used in the treatment of anxiety disorders and obsessive compulsive disorder. Prozac, introduced in the United States in 1988 (but approved by the FDA in December 1987), is arguably the most famous drug in the history of medicine. Other SSRIs that followed Prozac were sertraline, introduced as Zoloft in the United States in 1992; paroxetine, marketed as Paxil in 1992; fluvoxamine, trade name Luvox, 1995; citalopram, trade name Celexa, 1998; and escitalopram (Lexapro), introduced in the United States in 2002.

How they are thought to work (pharmacodynamics) The first promising modern biological (neurotransmitter) theory for the pathophysiology (and perhaps the cause) of a MENTAL DISORDER was the "catecholamine theory of depression," first proposed in a highly influential article by Harvard psychiatrist Joseph Schildkraut (1934–) published in 1965 in the *American Journal of Psychiatry.* It had long been suspected that the monoamines (CATECHOLAMINES and INDOLAMINES) were involved in

depression. Dopamine and norepinepherine are catecholamines, whereas serotonin is an indolamine. The role of catecholamines in the "causation" of depression was noted as early as 1959 by Canadian psychiatrist Abram Hoffer at a conference on depression at McGill University in Montreal, but his speculation had no effect on psychiatrists or psychopharmacologists. The catecholamine theory of depression resulted from investigations into how antidepressant drugs such as MAO inhibitors and the tricyclic antidepressants affected brain chemistry. Both types of antidepressants were found to act on the neurotransmitter norepinepherine. Schildkraut's theory that abnormally low levels of the catecholamine neurotransmitter norepinepherine was associated with depression dominated psychiatric thinking in the 1970s and early 1980s. In the 1980s, the role of norepinepherine as the sole factor in depression was discredited when another similar "neurotransmitter deficit" theory involving serotonin emerged, leading to the production of designer SSRIs such as Prozac. SSRIs work by keeping more serotonin at receptor sites. The 1968 discovery that the tricyclic antidepressant imipramine blocked the reuptake of serotonin led to the speculation by Swedish pharmacologist Arvid Carlsson (1923–) that this specific action might be a contributing source of its antidepressant effect. Carlsson and his colleagues Kjell Fuxe and Urban Ungerstedt published their discovery that year in the *Journal of Pharmacy and Pharmacology.* Research on the connection between blockade of serotonin reuptake and the alleviation of depression soon followed, resulting in the first SSRI to be marketed as an antidepressant, zimeldine (Zelmid), in Europe in 1982. It was withdrawn from the market in 1983 because it caused Guillan-Barré syndrome in some persons who took it.

Since the late 1980s, the dominant biological theory of DEPRESSION is the monocausal neurotransmitter theory that deficient levels of serotonin at receptor cites in the brain produce depression (expanded in the 21st century to anxiety, obsessional thoughts, and social phobias). Depression, however, is a highly complex syndrome involving not only neurotransmitters (of which there are more than 100, only a few of which have been studied in detail), but cognitive, emotional, social, experiential, and genetic factors as well in its production. The humoral metaphor of a dyscrasia, an imbalance in bodily fluids, as a cause of disease is still quite strong with regard to the presumed low levels of serotonin and depression.

The use of antidepressant drugs in schizophrenia Persons with schizophrenia do indeed experience depression. In a review of studies by S. G. Siris published in 1991, it was concluded that about 25 percent of persons with schizophrenia also suffer from depression. This is not surprising considering the countless disappointments and losses persons with schizophrenia experience in interpersonal relationships and occupational goals/achievements. Depression occurs throughout the course of schizophrenia, both prior to and after the onset of the active phase of symptoms. Depression is a common part of the RESIDUAL PHASE of schizophrenia following the storm of active psychotic symptoms. *ICD-10* includes a formal diagnostic category of postpsychotic depression for this, whereas *DSM-IV-TR* mentions postpsychotic depression in an appendix. Antidepressant medication is often prescribed along with antipsychotic medication, although treatment of depression in schizophrenia with antidepressant drugs but without also administering antipsychotic drugs is not recommended. In a major review of the double-blind, placebo-controlled studies of the use of antidepressant drugs along with first-generation ANTIPSYCHOTIC DRUGS in schizophrenia by S. G. Siris and C. Bench in 2003, the results were said to be mixed but generally favorable. There was some weak evidence that SSRIs and some tricyclics might alleviate some NEGATIVE SYMPTOMS in some persons with schizophrenia. The symptoms of severe depression (ANHEDONIA, AVOLITION, ALOGIA, AKATHISIA, AKINESIA, and so on) can often mimic negative symptoms, so the negative symptoms of schizophrenia may actually not have been alleviated. However, some antidepressants—particularly SSRIs such as Prozac and Paxil—have been linked to the onset of manic episodes and psychotic episodes. Several of the ATYPICAL ANTIPSYCHOTICS, such as olanzapine (Zyprexa), have been found to lessen depressive symptoms and are often used to treat bipolar disorder.

Side effects However, although the SSRIs are in widespread use, there are severe side effects. If too

much serotonin accumulates in the central nervous system through the use of SSRIs, the "serotonin syndrome" may occur. The serotonin syndrome is characterized by disorientation, confusion, hypomania, agitation, restlessness, fever, chills, sweating, diarrhea, hypertension, tachycardia, ataxia, increased reflexes, and myoclonus. Visual hallucinations have also been reported. The symptoms vanish 24 to 48 hours after drug use is discontinued. When use of SSRIs is halted, the "serotonin withdrawal syndrome" manifests in about 60 percent of people who have taken these drugs. Withdrawal symptoms include anxiety, agitation, crying spells, irritability, dizziness, vertigo, nausea, vomiting, diarrhea, fatigue, chills, sensations of electric shocks, insomnia, and vivid dreams.

Akathisia as a side effect of SSRI use has been increasingly linked to suicidal behavior, violence, and homicidal behavior.

Sexual dysfunction occurs in up to 80 percent of persons treated with SSRIs, although some more conservative estimates place it within the 30 to 40 percent range, reflecting a more restrictive definition of the range of what constitutes a sexual dysfunction. This fact was kept hidden by pharmaceutical companies for many years prior to the introduction of SSRIs to the market in the 1980s. Since the first SSRIs were marketed as antidepressants, and since the alleviation of depression was touted as its main effect, the fact that more sexual dysfunction occurs in persons taking these drugs than the alleviation of depressive symptoms has led critics of the pharmaceutical industry to question the very meaning of what a drug's main effect may be. From an iconoclastic point of view, if we are to categorize drugs by their main effect, then there may be better evidence that the SSRIs are "sexual-dysfunction-inducing drugs" rather than antidepressants.

See also DEPRESSION.

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antiparkinsonian drugs These are drugs that are administered to relieve PARKINSONISM, the side effects of antipsychotic drugs that will usually appear within weeks or a few months after beginning antipsychotic drug therapy. Patients who suffer from this side effect exhibit a triad of signs: tremors (usually in the hands but also in the wrists and elbows), rigidity (extreme tension in muscles that make the body actually feel rigid), and AKINESIA or BRADYKINESIA (an absence or a slowness of body or facial muscle motion). Common ANTIPARKINSONIAN DRUGS are amantadine (trade name Symmetrel), BENZTROPINE (Cogentin), biperiden (Akineton), and DIPHENHYDRAMINE (Benadryl). Parkinson's syndrome, which is induced by ANTIPSYCHOTIC DRUGS, should not be confused with Parkinson's disease, which is a progressive neurological disorder that is not reversible.

antipsychiatry See LAING, RONALD DAVID.

anti-psychosis A curative substance that the prescient Daniel H. Tuke hypothesized, in 1881, would one day be created to reverse the symptoms of mental disorders. His prophetic remarks were delivered on August 2 in London in his presidential address to the Medico-Psychological Association in which he lamented the special problems of "psychological" medicine as opposed to the more forthright "organic" medicine:

> It must be frankly granted that Psychological Medicine can boast, as yet, of no specifics, nor is it likely, perhaps, that such a boast will ever be made. It may be difficult to suppress the hope, but we cannot entertain the expectation that some future Sydenham will discover an *anti-psychosis* which will as safely and speedily cut short an attack of mania or melancholia as bark an attack of ague.

Today's ANTIPSYCHOTIC DRUGS are named, in part, as a memorial to Tuke's farsightedness.

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antipsychotic drugs The class of drugs that suppress or alleviate psychotic symptoms (primarily POSITIVE SYMPTOMS such as hallucinations and delusions). The term *antipsychotic drugs* was used for the first time to refer to these pharmacological agents by a German-Canadian psychiatrist, Heinz Lehmann of Montreal, in an article published in the *Canadian Medical Association Journal* in 1961. They are also commonly referred to as neuroleptics (coined by Jean Delay of France in 1955), antischizophrenic agents, and major tranquilizers (which is a misnomer). From 1955 to the 1990s, antipsychotic drugs were most often referred to as neuroleptics in Europe and major tranquilizers in the United States. Smith Kline and French introduced CHLORPROMAZINE (THORAZINE) in 1955 just months before another new drug that revolutionized outpatient psychiatry, the famous "minor" tranquilizer mebrobamate (Miltown), so in a marketing contrast to Miltown, Thorazine was soon sold to physicians by pharmaceutical companies as a "major tranquilizer." Antipsychotic drugs are the treatment of choice for SCHIZOPHRENIA and other psychotic disorders, but some—particularly those introduced since 1990—have been used effectively in the treatment of MANIC EPISODES (particularly "mixed" or dysphoric mania) and have an antidepressant effect as well.

Historical Background

Prior to 1952 there were only weakly effective drugs for treating persons suffering from schizophrenia or other psychotic disorders. Most of the drugs used by MAD-DOCTORS and ALIENISTS in asylums were used to sedate patients in order to reduce suffering, promote prolonged sleep, and thereby improve patient management by asylum staff. These drugs were widely in use from at least 1840 until the mid-20th century, and they include opiates, hyocine, digitalis, chloral (after 1869), bromides, barbiturates (after 1903), anticholinergic agents, and paraldehyde (a distinctly foul-smelling drug when exhaled by asylum patients that led to its characteristic odor permeating mental institutions prior to the introduction of chlorpromazine). These are the drugs that enjoyed a long life in the asylum, but in reality almost anything and everything was tried on asylum patients in a desperate effort to find effective treatment.

In 1931 two physicians from India, Ganneth Sen and Katrick Bose, published a report of their research using an extract from the roots of the Rauwolfia plant. Rauwolfia had been used for centuries in traditional Indian medicine for the treatment of mental illness because of its ability to calm excited persons. Sen and Bose recommended its use for high blood pressure as well as the treatment of psychiatric disorders. Three chemists working for the Ciba pharmaceutical company in Basel, Switzerland, isolated the sedative agent from the plant, the alkaloid reserpine. In April 1954 Nathan Kline published a report in the *Annals of the New York Academy of Sciences* on the effectiveness of reserpine and a preparation of its whole root (marketed as Raudixin for hypertension) on the inpatients at Rockland State Hospital in Orangeburg, New York. The following year, the effectiveness of RESERPINE for the treatment of anxiety and depression was confirmed in a randomized and controlled experiment conducted by David Lewis Davies and Michael Shepard of the Maudsley Hospital in England. They published their report in the British medical journal *Lancet,* but their results were largely overlooked due to the explosion of interest in chlorpromazine (Thorazine) at that time. Reserpine was used in psychiatric practice until 1961, when it was taken off the market due to adversive side effects.

In 1955 approximately 559,000 persons were residing in American psychiatric hospitals. In 1956, two years after the first antipsychotic drug chlorpromazine (Thorazine in the United States; Largactil in Europe) was approved for use in America (as an anti-emetic, not an antipsychotic), the number of inpatients began to drop steadily on a year-by-year basis. Patients who responded well to these drugs (not all, by any means, but a significant number) soon became well enough to be released back into the community. A similar pattern followed in the United Kingdom in the 1960s. If only the numbers are considered, from the perspective of local and national governments that funded psychiatric inpatient care, "deinstitutionalization" was a success. By 1983 fewer than

220,000 persons resided in psychiatric hospitals in the United States. By the 1990s most persons with schizophrenia were quickly stabilized on antipsycotic drugs and discharged somewhat rapidly. There is no question that antipsychotic drugs have had a profound effect on the practice of psychiatry and in the treatment of schizophrenia. However, the introduction of chlorpromazine and the PHENOTHIAZINES into psychiatric practice was perhaps only partly responsible for this emptying of the wards of psychiatric hospitals. Other factors are social and financial. In America, changing the care of persons with mental disorders from inpatient institutions to the community shifted the financial responsibility from the states to the federal government. In Japan, the introduction of phenothiazines was actually followed by an increase, not a decrease, in the population of psychiatric institutions.

The first of the phenothiazine antihistamine drugs, promethazine (synthesized in 1947), had been used by French naval surgeon Henri Laborit (1914–95) as an agent to deepen anesthesia and to relax patients prior to surgery. Working with the phenothiazine nucleus, in December 1950, French biochemist Paul Charpentier synthesized more potential pharmacological agents and developed the second phenothiazine, chlorpromazine. It was found to produce a calmness, disinterest, and detachment from external stimuli, and conscious sedation in patients who took it—a condition Laborit called an "artificial hibernation." Laborit believed there might be a therapeutic effect on psychosis. As he put it in his early 1952 article in *Presse Medicale:* "These findings allow one to anticipate certain indications for the use of this compound in psychiatry. . . ." At his suggestion, in 1952 chlorpromazine was tested in clinical trials on patients at the Val-de Grace military hospital in Paris by Pierre Hamon, Jean Paraire, and Jean Velluz. Shortly following this first psychiatric trial, at the Ste.-Anne Mental Hospital in Paris, Jean Delay and Pierre Deniker conducted a clinical trial on psychotic patients and found an alleviation of HALLUCINATIONS and DELUSIONS occurred without the patients being unduly sedated by the drug. After only three months of their chlorpromazine clinical trial, Delay and Deniker became the first to publish scientific claims of success in articles that appeared in the *Presse Medicale* and *Annales-Medico-Psychologiques* in 1952. Although none of these men—Laborit, Hamon, Paraire, Velluz, Delay, or Deniker—was ever awarded the Nobel Prize for the discovery of the antipsychotic properties of chlorpromazine, they fought bitterly with one another over who should be credited with priority in the discovery. This very public controversy probably led the Nobel committees to pass over them continually for the Nobel Prize in medicine.

Clinical trials followed in Lyons, France, and in 1953 in Basel, Switzerland, the United States, and Canada. A common—almost miraculous—observation in these trials was that some chronic patients who were noncommunicative for years suddenly "woke up" and became responsive to their environment. Many reported that the voices they heard were gone, and some were surprised at what year it was and how high prices had become. By the late 1950s many people believed that chlorpromazine had become a wonder drug along the lines of penicillin, a marvel of modern medical science.

The phenothiazines dominated the treatment of schizophrenia and other psychotic disorders for decades, and many are still in use. Following the approval of chlorpromazine (Thorazine) for use in the United States in March 1954, and the pharmaceutical company Smith Kline and French immediately experienced enormous profits, other phenothiazine "major tranquilizers" followed: prochlorperazine, 1957 (marketed as Compazine in 1956); perphenazine, patented in 1956, marketed as Trilafon in 1957; thioridazine, 1958 (Mellaril, 1959); trifluoperazine, 1959 (Stelazine, 1958); fluphenazine, 1960 (Prolixin, 1960). The next class of antipsychotic drugs, the butyrophenomes, was used in Europe from 1959 onward. However, the first of these drugs, haloperidol (Haldol), was not introduced in the United States until 1967. By the 1980s it became the most widely prescribed antipsychotic drug in the United States.

Antipsychotic drugs are now classified into three broad groups or "generations," the preferred terminology of the WORLD PSYCHIATRIC ASSOCIATION: conventional, typical, or first-generation antipsychotics (1954–75), which are grouped into three chemical classes: the phenothiazines, begin-

ning with chlorpromazine (Thorazine) in 1954; the butyrophenomes, beginning in 1959 with haloperidol (marketed as Haldol in America in 1967); the THIOXANTHENES, beginning with thiothixene (Navane); and miscellaneous or alternative agents to the phenothiazines, introduced first in the early 1970s, such as LOXAPINE (Loxitane), molindone (Moban), and pimozide (Orap); atypical or second-generation antipsychotics, beginning in 1990 (no new antipsychotic drugs were marketed in the United States between 1975 and 1990) with the introduction of clozapine (Clozaril), and followed by RISPERIDONE (RISPERDAL) in 1993, OLANZAPINE (Zyprexa) in 1996, sertinole (Serlect) in 1997, quetiapine (Seroquel) in 1999, ziprasidone (GEODON) in 2000, aripiprazole (Abilify) in 2003, and zotepine (not approved for use in North America but available in Europe and in many countries worldwide); and third-generation antipsychotics, beginning with amisulpride (Solian) in 2005. Amulsipride is considered to be the start of a new generation of drugs because, although it is often referred to as an atypical antipsychotic, it has a different effect on the NEUROTRANSMITTERS of the brain than the other atypical agents and, in low doses, is effective in the treatment of dysthymia and depression.

How they are thought to work (pharmacodynamics) First-generation antipsychotics work, in part, by blocking certain receptor sites for the neurotransmitter DOPAMINE, particularly the D_2 receptors. Until the 1990s, the blocking of D_2 receptors was thought to be the sole mechanism for reducing psychotic symptoms. Second-generation or atypical antipsychotic drugs also block, or are antagonists, at the same dopamine receptor sites, but they all have a second action, usually the antagonism of the serotonin $5HT_2$ receptors. In general, to be considered an "atypical" antipsychotic, the blocking of serotonin $5HT_2$ receptor must be greater, and occur at lower doses, than the D_2 receptor blockade. The serotonin psychedelic drug LSD (banned from production and distribution in the United States since 1966) is thought to produce its characteristic hallucinations and "psychosis-mimicking" state by being an agonist of $5HT_2$. Aripiprazole (Abilify) works differently by being a partial agonist at D_2 receptors and at serotonin $5HT_{1a}$ receptors, and an antagonist at serotonin $5HT_2$ receptors. The first third-generation drug, amisulpride (Solian), is the first atypical that does not block serotonin receptors, but instead blocks two different dopamine receptors, D_2 and D_3, in the limbic system of the brain but not the basal ganglia (the part of the brain that is primarily linked to producing the Parkinsonian side effects of antipsychotic medication).

Since there are more than 100 identifiable neurotransmitters and only a select few have been studied in depth, future generations of antipsychotic drugs will no doubt target other neurotransmitter systems. In particular, the neurotransmitter glutamate, which has been linked to schizophrenia since 1980, will be of particular interest to psychopharmacologists in the decades to come.

Pharmacogenetics It has long been observed by physicians and researchers that not everyone responds to a given medication in the same way. Some respond only to lower doses, some to higher, and some not at all. Ethnic differences, in particular, have been noted, and the underlying reasons for these differences in response to medication have been sought by identifying the genes that code for drug metabolizing enzymes (DMEs), which are known to be different between Caucasians, Asians, black Africans, and African Americans. With the rise of medical genomics—an entirely new approach to disease and health based on knowledge of genetic differences—pharmaceutical companies have been keen to apply this new knowledge to the development of new drugs. This field is known as pharmacogenetics, a term first used as early as 1959 by F. Vogel in an article in a German pediatric journal in reference to the speculation that adverse drug reactions might be due to genetic differences between people. Designer drugs which are based on slight differences in genes between people (single nucleotide polymorphisms, SNPs or "snips") and can target treatment-resistant patients with a variety of diseases are a long-term development goal of pharmaceutical companies. Such designer drugs might be developed for the treatment of schizophrenia, although currently no such pharmacogenomic drugs for schizophrenia yet exist.

Side effects It was noticed at least as early as 1953 that chlorpromazine (Thorazine) produced serious side effects (dyskinesias and AKATHISIA) in some patients. As early as 1956 there was a published

report that such side effects continued for months in some patients after being completely taken off phenothiazines. As the new era of phenothiazine use continued, severe and bizarre movement disorders (tremors, rigidity, eye-rolls, grimaces, excessive drooling) became increasingly apparent. By 1957 the syndrome later renamed (in 1964) TARDIVE DYSKINESIA (TD) had been described in an article by a German physician, Matthais Schoenecker, in *Der Nervenarzt.* The emergence of such severe side effects was an unwelcome surprise to those few psychiatrists in the 1950s and 1960s who connected them with the use of phenothiazines. This was especially true in America, a country where mental hospital staff and physicians were amazed as they saw patients "wake up" and regain their humanity on an almost daily basis. But considering the massive doses of these drugs patients were initially administered in the early days (particularly in the United States, where daily doses of 3,000 mg a day were routine as compared with the 150 mg a day given in Europe to patients), it is a wonder that more physicians, patients, and families did not sound the alarm earlier. Most preferred to attribute the side effects to "psychodynamic" (unconscious impulses) or other "spontaneous" biological causes and not to the new drugs. The turning point was the publication of a book in 1965, *The Action of Neuroleptic Drugs*, by Hans-Joachim Haase and Paul Janssen, which detailed the serious side effects of large doses and long-term use. Still, despite the fact that the authors were a prominent psychiatrist and a world-renowned psychopharmacologist, the idea that such serious side effects were caused by these psychiatric "wonder drugs" was met with strong initial resistance by American psychiatrists until a joint task force formed by the Food and Drug Administration and the American College of Neuropsychopharmacology published a convincing report documenting such side effects in 1973. As law professor and historian Sheldon Gelman put it in his 1999 book, *Medicating Schizophrenia: A History,* "Except to a few researchers, tardive dyskinesia remained invisible until the early 1970s. It was as if the disorder simply did not exist" (p. 88).

The adverse effects of antipsychotic drug use fall into several categories:

Central nervous system effects: we now know that these drugs cause acute EXTRAPYRAMIDAL SYNDROMES (EPS) as a serious side effect early in the course of treatment. EPS is characterized by a triad of symptoms: (a) dystonias (involuntary muscle spasms, sustained abnormal posturing of the face, tongue, limbs, trunk); (b) akathisia; and (c) PARKINSONISM (not to be confused with Parkinson's disease). Long-term use of the first-generation antipsychotics leads to brain damage and a chronic syndrome of the above triad of symptoms, TD. Unlike TD, the acute EPS side effects are usually completely reversible through lowering the dosage of ANTIPSYCHOTIC DRUGS or withdrawing them completely for a time (a "drug holiday"). Anticholinergic side effects are also quite common with the first-generation antipsychotics in particular: dry mouth, dilated pupils and blurred vision, increased heart rate, constipation, urinary retention, dizziness, and drying of lung secretions. Side effects can be reversed by giving the patient ANTIPARKINSONIAN DRUGS, anticholinergic drugs, or antiadrenergic drugs. Tardive dyskinesia is managed by these same drugs but is not reversible. Clozapine is the only effective drug for persons with TD. Atypical antipsychotics cause far fewer side effects and because of this are often preferred in the early years of treatment of schizophrenia. However, there are concerns specific to the long-term use of clozapine. Persons taking clozapine must have their blood cell counts monitored weekly to prevent agranulocytosis, a dangerous lowering of the white blood cell counts. Alterations in normal EEG patterns and, at times, seizures may occur. All antipsychotic drugs lower the seizure threshold, making them more likely.

Thermoregulatory adverse effects: The most severe is NEUROLEPTIC MALIGNANT SYNDROME (NMS), which can be fatal in 5 to 20 percent of cases if unnoticed and untreated. The syndrome resembles an older one known as lethal catatonia in the pre–antipsychotics era. *DSM-IV* criteria for NMS indicate that muscle rigidity and hyperthermia (a body temperature of 101–104 degrees Fahrenheit) must be present. The clinical picture of NMS is similar to CATATONIA. Both typical and atypical antipsychotic drugs can cause NMS, and it can happen at any point during treatment. Hyperthermia and hypothermia (a core body temperature below 95 degrees Fahrenheit) may also occur,

with hypothermia associated with sudden unexplained deaths that coincide with the administration of antipsychotic drugs.

Other miscellaneous adverse effects: Sedation is a problem in about 40 percent of persons taking clozapine, as is extreme weight gain. Weight gain is also a serious side effect of olanzapine, but the other atypical antipsychotics also cause weight gain to a greater or lesser degree. Several atypical agents also affect heart rhythms and blood pressure. Changes in the relative numbers of blood corpusules (blood dyscrasias) may also occur with the use of first-generation antipsychotics and with clozapine. Leukopenia (abnormally low white blood cell counts) is the most common, and agranulocytosis (granulocyte count below 500/mm) may be life threatening. There is also an increased risk of developing diabetes and hyperglycemia with these drugs. Excessive salivation (sialorrhea) happens to almost all patients who take clozapine. Dry mouth (xerostomia) is also common. Constipation can be a problem with first-generation antipsychotics and clozapine. Transient elevation of liver enzymes occurs with the use of all antipsychotics. Extended use of the phenothiazines (such as chlorpromazine) can lead to changes in the cornea, lens, and retinas of the eyes. Sexual dysfunctions are common. Treatment with phenothiazines can cause photosensitivity and lead to sunburns or rashes.

DSM-IV-TR (2000) includes a new category for "medication induced movement disorders." Specific diagnostic criteria are offered for the following syndromes: Neuroleptic-induced Parkinsonism; Neuroleptic Malignant Syndrome, Neuroleptic-induced Acute Dystonia, Neuroleptic-induced Acute Akathisia, Neuroleptic-induced Tardive Dyskinesia, Medication-induced Postural Tremor, and Medication-induced Movement Disorder Not Otherwise Specified. Thus, the treatment of standard mental disorders has led to side effects that have now created a whole new category of mental disorders to accompany, not replace, the earlier diagnoses.

Administration of drugs and compliance In 2004 the AMERICAN PSYCHIATRIC ASSOCIATION (APA) issued a revision of its practice guidelines for the psychopharmacological treatment of persons with schizophrenia. The guidelines offer treatment algorithms, or decision paths, for physicians to follow when treating newly psychotic individuals, when practicing maintence therapy as a follow-up, and for patients who are "treatment resistant" and for whom antipsychotic drugs do not seem to work. Atypical antipsychotics such as risperidol, which produce fewer acute EPS side effects and which, if used long-term, may prevent the development of tardive dyskinesia, are the first-line treatments for schizophrenia. The guidelines offer suggested combinations of drugs in such refractory cases and, if all else fails, ECT (electroconvulsive therapy) as a last resort. Suggestions are also given for how to manage acute side effects such as EPS and tardive dyskinesia in chronic patients.

It has long been known that persons with schizophrenia have a difficult time complying with medication treatment after they are released from inpatient settings. Forgetting to take medication, or consciously choosing not to, has been associated with higher rates of relapse and hospitalizations. It is estimated that noncompliance rates in persons with schizophrenia who are living in the community range between 24 percent and 63 percent. The avoidance of side effects is often cited as a reason persons with schizophrenia do not take their medications, but due to the problems many persons have in focusing their attention, many simply forget or are easily distracted by other events in their daily lives. Injectable forms of medications such as Prolixin have been developed to solve this problem. Depending on the medication or the dose, the effect of injectable forms of antipsychotic drugs can last weeks.

However, medication compliance is not just a problem with persons with schizophrenia who are patients. Psychiatrists who treat persons with schizophrenia have been studied in the United States by the Schizophrenia Patient Outcomes Research Team (PORT) and have been found to be lacking in adherence to evidenced-based treatment guidelines set by the American Psychiatric Association. Physician-conformance to APA guidelines was found to be "modest at best." A common problem was the tendency of psychiatrists to engage in "polypharmacy"—the administration of more than one antipsychotic drug, or combinations of antipsychotic drugs and other types of drugs—when there was no scientific evidence to recommend such combinations.

Subtype differences in treatment responsiveness Recent GENETICS STUDIES of schizophrenia have not, as yet, identified characteristic schizophrenia subtype profiles for each of the classic forms of schizophrenia (paranoid, hebephrenic [disorganized], catatonic types). The lack of firm underlying biological knowledge of possible differences in the causes (etiologies) and pathophysiologies of the different schizophrenia subtypes, researchers and pharmaceutical companies who manufacture antipsychotic drugs have increasingly tended to regard schizophrenia as a single heterogeneous disorder rather than several different disorders (the classic subtypes). Fewer studies examine subtype differences than a quarter century ago, and antipsychotic drugs are marketed for "schizophrenia"—not for "paranoid schizophrenia," "disorganized schizophrenia" (hebephrenia prior to 1994), or "catatonic schizophrenia." An additional subtype of schizophrenia, the "undifferentiated type," was added to *DSM-III* in 1980 to refer to patients who do not manifest dominant symptoms of the three classic subtypes and which may include a mixture of symptoms from each. The undifferentiated type category is among the most widely used today in psychiatric institutions and also adds to the perception that schizophrenia may be one disease because there are no treatment differences between the classic subtypes. The presence of positive and negative symptoms, not classic subtypes, guide treatment. However, some differences in the responsiveness of the classic schizophrenia subtypes to treatment have been documented in the literature of the past 40 years. Since antipsychotic drugs have always worked best to alleviate positive symptoms, persons with paranoid schizophrenia (a subtype characterized entirely by positive symptoms such as paranoid delusions and auditory hallucinations of voices) have generally responded quite well to these drugs. Persons with the disorganized type of schizophrenia (hebephrenia) and the catatonic type (catatonia) have traditionally been treatment-resistant. Although catatonia (a syndrome that is essential to the diagnosis of the catatonic subtype of schizophrenia but which may be a separate syndrome of its own) has long been thought to have virtually vanished since the introduction of antipsychotic drugs in 1952, since 1983 there have been reports that it has been mislabeled, or relabeled, as neuroleptic malignant syndrome. In the pre–antipsychotic era literature, catatonia was treated effectively with barbiturates and electroshock therapy. The potency of barbiturates in essentially curing catatonia through the induction of prolonged sleep was documented as early as 1930 by W. J. Bleckwenn in the *Archives of Neurology and Psychiatry.* In 1983 physicians Gregory Fricchione and Ned Cassem of the Massachusetts General Hospital in Boston reported in an article in the *Journal of Clinical Psychopharmacology* that lorazepam (Ativan), a benzodiazepine "minor tranquilizer," reversed neuroleptic malignant syndrome. Later at Stony Brook Hospital in New York, Fricchione and Max Fink found that barbiturates, lorazepam, and ECT all were 100 percent effective in curing NMS, thus adding weight to the evidence that NMS and "lethal catatonia" were perhaps one and the same syndrome (with NMS being an iatrogenic form of lethal catatonia caused by the use of antipsychotic drugs). Although electroconvulsive therapy (ECT) is effective in the treatment of core catatonic symptoms (mutism, stupor, akathisia, clouded consciousness), the evidence is less clear that ECT works to alleviate core psychotic symptoms such as delusions and hallucinations. Treatment of catatonia or suspected NMS with benzodiazepines or barbiturates is therefore recommended first before using ECT. Although the combination of ECT with antipsychotic drugs has been explored in some studies, indicating that ECT may work best in patients with acute exacerbations and short episode duration, there is not enough evidence upon which to base treatment recommendations for psychiatrists as to when ECT can be used in conjunction with antipsychotic drugs. HEBEPHRENIA, or the disorganized type of schizophrenia, continues to be the most treatment-resistant form of schizophrenia due to the presence of negative symptoms, which still do not respond well to any present antipsychotic drug. Still, the notion that "one treatment fits all" remains dominant in the current pharmacological response to schizophrenia.

Relapse, treatment-resistant schizophrenia, and the natural course of the disease Several studies have shown that, on average, if a group of persons with schizophrenia that is in remission (the residual type) is switched from treatment with an antipsy-

cotic drug to a placebo, approximately 65 to 85 percent of them will relapse within one year. A variety of studies estimate that 20 to 33 percent of persons with schizophrenia exhibit treatment refractoriness to antipsychotic drugs and that an additional number, about 15 percent, experience an alleviation of symptoms with placebo treatment alone in double-blind studies. Clozapine is recommended as the treatment of choice in chronic treatment-resistant schizophrenia, demonstrating a therapeutic effect in about 30 percent of such persons.

Antipsychotic drugs do not "cure" schizophrenia: their main function is to significantly lower the probability of total relapse into psychosis by reducing the positive symptoms (hallucinations and delusions). Based on interpretations of the various long-term follow-up studies of schizophrenia, antipsychotic drugs do not seem to slow or stop whatever natural disease process is at work in schizophrenia. Antipsychotic drugs do not have any demonstrable effect on the various patterns of the COURSE AND OUTCOME OF SCHIZOPHRENIA. One controversial literature review by the noted schizophrenia researcher Richard Jed Wyatt (1939–2002) disputed this conclusion. In his reanalysis of 22 studies, Wyatt argued that early intervention with antipsychotic drugs in persons undergoing their first episode of active symptoms increased the likelihood of lessening the severity the long-term course of the disease. He additionally suggested that perhaps even going so far as to identifying young persons at-risk for schizophrenia and giving them antipsychotic medication as a preventive measure before they suffer hallucinations and delusions may delay or prevent the first-episode onset of schizophrenia. In an even more controversial claim, Wyatt suggested such actions might prevent the "brain damage" the schizophrenia disease process produces. However, although the evidence is abundant that long-term treatment with antipsychotic drugs produces irreversible brain damage that results in the syndrome known as tardive dyskinesia, there is still no clear evidence that a psychotic episode leads directly to irreversible structural brain damage. Although the evidence for brain changes in schizophrenia is clear, it is not clear that active phases of the illness in which delusions and hallucinations are floridly present causes them or follows such changes as part of the progressing underlying disease process. Wyatt's argument that withholding the use of antipsychotic drugs leads to brain damage currently has no evidence to support it.

Summary

In essence, the effect of the usage of antipsychotic drugs in schizophrenia can be summed up in the following way: (a) antipsychotic drugs alleviate positive symptoms in most, but certainly not all, persons with schizophrenia, especially in the early years of the disease, with 20 to 33 percent of all persons with schizophrenia demonstrating little or no response to antipsychotic drugs, (2) the use of these drugs is correlated with, but is perhaps not the sole cause of, less overall hospitalization time and shorter stays in inpatient settings, (3) although the use of antipsychotic drugs, is beneficial in reversing acute exacerbations of psychosis, and help persons function better in daily life in the short term by eliminating hallucinations and delusions, there is as yet no evidence that the use of these drugs dramatically improves negative symptoms, or overall interpersonal functioning over the life span, (4) there is no evidence that antipsychotic drugs affect the natural disease course of schizophrenia, and (5) the history of psychiatry repeatedly has documented that, for at least 15 to 20 years after the introduction of new psychopharmacologic agents (such as antipsychotics or antidepressants), pharmaceutical companies and hopeful physicians tend to deny (consciously or unconsciously) the harmful side effects of these drugs and have highly biased positive views of their therapeutic power and potential.

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Delay, J., P. Deniker, and J.-M. Harl. "Utilisation en therapeutique psychiatrique d'une phenothiazine d'action centrale elective (4560 RP)," *Annales Medico-Psychologique* 110 (1952): 112–117.

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Lieberman, J. A., and R. M. Murray, eds. *Comprehensive Care of Schizophrenia: A Textbook of Clinical Management.* London: Martin Dunitz, 2001.

McGlashan, T. H. "Early Detection and Intervention in Schizophrenia Research," *Schizophrenia Bulletin* 22 (1996): 327–345.

Sen, G., and K. Bose. "*Rauwolfia Serpentina,* a New Indian Drug for Insanity and High Blood Pressure," *Indian Medical World* 61 (1931): 194–201.

Vogel, F. "Moderne Probleme der Humangenetik," *Ergebnisse innere Medizin und Kinderheilkunde* 12 (1959): 52–125.

antisocial behavior Behavior that is disrupting or harmful to society as a whole. Persons who are experiencing a psychotic disorder may, due to their lack of full contact with reality, commit antisocial acts against others or against property. Sometimes extreme violence—such as assaults or even homicides—have been known to result. If such persons are legally judged insane, then they are generally not considered responsible for the antisocial behavior committed while under the influence of the psychotic disorder. Particularly dangerous diagnostic categories include those afflicted with the psychotic hostility and delusional beliefs characteristic of some people with PARANOID SCHIZOPHRENIA or the manic episodes of BIPOLAR DISORDER.

anxiety A symptom of most MENTAL DISORDERS that is usually described as a feeling of uneasiness, apprehension, or dread. Anxiety can be a pervasive feeling that is not associated with any one person or thing in particular, which is generally how most definitions distinguish it from fear, which usually does have an object. Anxiety can be overwhelming in the ACUTE RECOVERABLE PSYCHOSES and in active phases of BIPOLAR DISORDER. Schizophrenics commonly report anxiety, especially during the PRODROMAL PHASE, when the awareness of frighteningly new psychotic symptoms causes anxiety, and during periods in chronic schizophrenia, when exacerbations of psychotic symptoms occur. From a psychoanalytic point of view, anxiety is a sign that the ego has not successfully been able to keep unpleasant or threatening thoughts or feelings entirely out of awareness, so that, even though the actual content of the threatening thought or feeling may be unconscious, the unpleasant effects are still experienced as anxiety.

APA nomenclature The terminology and diagnostic schemata devised and continually revised by the American Psychiatric Association in its continuing editions of the *Diagnostic and Statistical Manual of Mental Disorders.* This term is often used in contradistinction to ICD nomenclature, the diagnostic schemata for mental disorders found in the WORLD HEALTH ORGANIZATION's continuing revisions of the *International Classification of Diseases.*

apathy A symptom present in many mental disorders but especially in DEPRESSION, ORGANIC MENTAL DISORDERS (due to brain damage), and in SCHIZOPHRENIA. This symptom of "uncaring" or of "lack of interest in the self or in the world" is pervasive, like a MOOD DISORDER, and is indicative of the AFFECTIVE DISTURBANCES of schizophrenia.

Argentina The only prevalence study of SCHIZOPHRENIA conducted in Argentina found a low rate of 1.1 per 1,000.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

Arieti, Silvano (1914–1981) An American psychiatrist and psychoanalyst long recognized as a leading authority on SCHIZOPHRENIA. He was a professor of clinical psychiatry at the New York Medical College and was a training analyst and supervisor at the William Alanson White Institute for Psychoanalysis. For many years he was editor in chief of *The American Handbook of Psychiatry.* His most significant contribution to the study of schizophrenia was his comprehensive volume, *Interpretation of Schizophrenia,* which was hailed soon after the appearance of the first edition in 1955 as the most complete presentation on the disorder since Eugen BLEULER's in 1911. A significantly revised and expanded second edition appeared in 1974. His psychoanalytic orientation is evident throughout the volume, particularly in the sections concerning psychotherapy and schizophrenics.

Arieti, S. *Interpretation of Schizophrenia.* Rev. 2nd ed. New York: Basic Books, 1974.

aripiprazole See ANTIPSYCHOTIC DRUGS.

Aristotelian thinking A concept used by Silvano ARIETI to denote the usual rational, logical processes employed by "normal" human beings. In his book *Interpretation of Schizophrenia,* Arieti contrasts Aristotelian thinking in normals with the more "primitive" and irrational logic that he calls PALEOLOGIC THOUGHT and that, he argues, characterizes schizophrenics. This idea fit in well with psychoanalytic notions of SCHIZOPHRENIA being an expression of REGRESSION to a more primitive and infantile mode of reasoning and experiencing the world. Arieti writes in the 1974 revised edition of his classic volume: "The paleologic type of organization is archaic or incomplete in comparison to the Aristotelian. The schizophrenic patient, when he thinks in a typically schizophrenic way, uses non-Aristotelian cognitive organizations."

Arnold, Thomas (1742–1816) The author of *Observations on the Nature, Kinds, Causes, and Prevention of Insanity, Lunacy or Madness* (1782), an important achievement in the development of modern psychiatry. Arnold was an Edinburgh-trained English physician who had studied under William Cullen. After completing his medical training, he opened a private mad-house in Leicester, which provided him with the important observations on mental disorders that he then used to create the classification system outlined in his 1782 book. He classified MENTAL DISORDERS according to their symptom clusters, as it is still done today, and he divided them into two main classes: "ideal insanity," which referred to disorders of perception such as HALLUCINATIONS and illusions; and "notional insanity," those disorders characterized by DELUSIONS. This system influenced later authors of psychiatric works. Two other influential books by Arnold are *A Case of Hydrophobia Successfully Treated* (1793) and *Observations on the Management of the Insane* (1809).

art, schizophrenic The relationship between "madness" and "creativity" has been the subject of speculation for at least 2,000 years. Master artists such as Vincent Van Gogh (1853–90), who clearly suffered from a mental illness that led to his incarceration in an asylum and eventual suicide, or abstract expressionist Jackson Pollock (1912–1956), who was hospitalized for severe alcoholism in 1938 and whose psychotic-like drawings were later published by his analyst, have stimulated the argument over whether madmen and artists draw from the same unconscious well for their inspiration.

Psychiatrists and psychologists have studied the artwork of schizophrenics in particular for more than a century. The very first psychiatrist to study the artwork of mental patients was Max Simon, whose groundbreaking paper, *"L'Imagination dans la folie: Étude sur les dessins, plans, descriptions, et costumes des aliénés,"* was published in the French psychiatric journal *Annales Médico-Psychologiques* in 1876. Simon correlated five major classifications of artistic style with five different classes of MENTAL DISORDERS. As have most subsequent psychiatric commentators, Simon noted the similarities in style of psychotic art with the creations of small children and of people in primitive societies. In 1880 the famous Italian criminologist and psychopathologist Cesare

Lombroso (1836–1909) wrote a paper, "On the Art of the Insane," which was published as a chapter in his book *The Man of Genius* in 1888. In addition to reaffirming Simon's observations, Lombroso remarked on the prevalence of sexual symbolism in the artwork of psychotics. German psychiatrist Fritz Mohr constructed the first diagnostic test based on the drawings of mental patients in 1906.

Perhaps the most famous book on schizophrenic art was published in German in 1922 (and translated into English and published in 1972)—the classic work *Bildnerei der Geisteskranken (Artistry of the Mentally Ill)* by Hans Prinzhorn (1886–1933). Prinzhorn was a psychiatrist at the Heidelberg Psychiatric Clinic and amassed a unique collection of 5,000 pieces of artwork produced by psychiatric patients from institutions in Germany, Austria, Switzerland, Italy, and the Netherlands between 1890 and 1920. Prinzhorn detailed the case histories of "ten schizophrenic artists" along with reproductions of their artwork. His approach to schizophrenic art was essentially aesthetic, and he concluded that the content of the artwork had no value as a diagnostic tool. Prinzhorn made the interesting observation that HALLUCINATIONS were rarely depicted in the art of schizophrenics. He identified the "components" of the "schizophrenic configuration" that distinguish schizophrenic art from other styles (such as similar productions by children and "primitives") and argues that the "schizophrenic outlook" is most closely mirrored by the abstract art of the 20th century. Prinzhorn concludes: "Existing artistic abilities are therefore not necessarily destroyed by the schizophrenic process but can in fact maintain themselves unchanged over long periods. . . . We have also demonstrated that during the progress of schizophrenia, while the patient declines into a highly confused, unapproachable final state with all the typical symptoms in their greatest extremes, his superficial, craftsmanlike dexterity develops great configurative power which allows him to produce pictures of undoubted artistic quality."

Many psychoanalytic papers have been published on schizophrenic art since 1918, perhaps the most notable being Ernst Kris's paper, "Comments on Spontaneous Artistic Creations by Psychotics," which was included in his chapter on "The Art of the Insane" in his famous book, *Psychoanalytic Explorations in Art* (1952). Sexual and aggressive expressions of the id that characterize primitive and infantile PRIMARY PROCESS thinking are examined in the art of schizophrenics in these writings. The practical use of artistic creations as a tool in the psychotherapy of schizophrenics was described by Margaret Naumberg in 1950 in her book, *Schizophrenic Art: Its Meaning in Psychotherapy.* In the second edition (1974) of Silvano ARIETI's *Interpretation of Schizophrenia,* more examples of this form of art therapy with psychotics are provided, with a psychoanalytic interpretation of these productions.

The use of creative techniques in psychotherapy (such as drawing, painting, sculpture, dance) was pioneered by Swiss psychiatrist C. G. JUNG (1875–1961), who interpreted such material as if it gave a snapshot or X-ray of the patient's internal world. Although not technically schizophrenic, but apparently often on the brink of psychosis, artist Jackson Pollock spent several years in analysis with Jungian analyst Dr. Joseph Henderson, who eventually allowed the publication of many of the drawings that Pollock did during therapy in *Jackson Pollock: Psychoanalytic Drawings (1970).* In excerpts from a previously unpublished lecture on his former patient (but reproduced in the Pollock biography by B. H. Friedman, *Jackson Pollock: Energy Made Visible* [1972]), Henderson makes the following observations that are typical of many Jungian psychoanalytic interpretations: "Following a prolonged period of representing human figures and animals in an anguished, dismembered or lamed condition, there came a new development in the drawings Pollock made during therapy. This was not merely the dissociation of schizophrenia, though he was frequently close to it. It has seemed to me a parallel with similar states of mind ritually induced among tribal societies or in shamanistic trance states. In this light the patient appears to have been in a state similar to the novice in a tribal initiation rite during which he is ritually dismembered at the onset of an ordeal whose goal is to change him from a boy into a man." Similar Jungian interpretations of schizophrenic experience and art are found in the writings of the Jungian analyst John Weir Perry.

Honoring the long tradition of schizophrenic art, the quarterly research review publication of the NATIONAL INSTITUTE OF MENTAL HEALTH,

Schizophrenia Bulletin, continues to feature on its cover the artwork created by current and former mental patients, with a description of the piece by its author included in the "About the Cover" section following the table of contents.

Friedman, B. H. *Jackson Pollock: Energy Made Visible.* New York: McGraw-Hill, 1972.
Kris, E. *Psychoanalytic Explorations in Art.* New York: International Universities Press, 1952.
Lombroso, C. *The Man of Genius.* 1880. Reprint, London: Scott, 1895.
Naumberg, M. *Schizophrenic Art: Its Meaning in Psychotherapy.* New York: Grune & Stratton, 1950.
Prinzhorn, H. *Artistry of the Mentally Ill: A Contribution to the Psychology and Psychopathology of Configuration.* Translated by E. v. Brockdorff from the 2nd German edition. (1922). New York: Springer-Verlag, 1972.
Simon, M. "L'Imagination dans le folie: Étude sur les dessins, plans, descriptions, et costumes des aliénés," *Annales Médico-Psychologiques* 16 (1876): 358–390.
Wysuph, C. I. *Jackson Pollock: Psychoanalytic Drawings.* New York: Horizon Press, 1970.

"as-if" personality See BORDERLINE CASES; BORDERLINE SCHIZOPHRENIA.

Asperger's disorder See AUTISM, INFANTILE.

association disturbances One of THE "FOUR A's" (association disturbances, AFFECTIVE DISTURBANCES, AMBIVALENCE, AUTISM) that Eugen BLEULER identified as the "fundamental symptoms" that uniquely characterize SCHIZOPHRENIA. Bleuler devoted a large section of his 1911 classic, *Dementia Praecox, Or the Group of Schizophrenias,* to the description of these association disturbances in schizophrenia. In one paragraph he summarizes his basic observations on association disturbances in schizophrenia:

> In the normal thinking process, the numerous actual and latent images combine to determine each association. In schizophrenia, however, single images or whole combinations may be rendered ineffective, in an apparently haphazard fashion. Instead, thinking operates with ideas and concepts which have no, or a completely insufficient, connection with the main idea and should therefore be excluded from the thought-process. The result is that thinking becomes confused, bizarre, incorrect, abrupt. Sometimes, all the associative threads fail and the thought chain is totally interrupted; after such "blocking," ideas may emerge which have no recognizable connection with preceding ones.

Today this association disturbance in schizophrenia is referred to as a form of FORMAL THOUGHT DISORDER.

See also LOOSENING OF ASSOCIATIONS.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenias,* trans. Joseph Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

Association of Medical Officers of Asylums and Hospitals for the Insane The first and oldest professional psychiatric association in the world, it was founded in Great Britain in 1841. In 1865 its name was changed to the Medico-Psychological Association of Great Britain and Ireland. It became the Royal Medico-Psychological Association in 1926 and eventually changed to its present title, the Royal College of Psychiatrists, in 1971. The association began publication of a professional journal, *The Asylum Journal,* in 1842 but later changed its name to the *Journal of Mental Science.* It is now published by the Royal College of Psychiatrists as the *British Journal of Psychiatry.*

Association of Medical Superintendents of American Institutions for the Insane The initial name for the professional society of American psychiatrists, founded in 1844, that is known today as the AMERICAN PSYCHIATRIC ASSOCIATION.

Association Studies See GENETICS STUDIES.

asthenic type One of the types of physique that psychiatrist and neurologist Ernst Kretschmer

claimed to be representative of schizophrenics (*schizophrenes*) in his 1921 book, *Körperbau und Charakter* (Physique and character). Asthenic types were excessively thin and looked taller than they truly were. Other physical types, such as the ATHLETIC TYPE and the dysplastic type, were also thought by Kretschmer to be prevalent among schizophrenics. Kretschmer concludes: "There is a clear biological affinity between the psychic disposition of the schizophrenes and the bodily disposition characteristic of the asthenics, athletics, and certain dysplastics." Although Kretschmer's theory of how certain temperaments were related to specific types of physique has not been taken seriously for many decades, he nonetheless deserves credit as one of the pioneers in the search for the BIOLOGICAL MARKERS OF SCHIZOPHRENIA.

Kretschmer, E. *Physique and Character: An Investigation of the Nature of Constitution and of the Theory of Temperament.* 1921. Reprint, New York: The Humanities Press, 1951.

asylums A word that originally meant a place of sanctuary—such as a church or monastery—*asylum* later became the word of choice to designate institutions for the insane, particularly in the very late 18th and throughout the 19th centuries. Using the word *hospital* as the official name for institutions for the mentally disordered did not come into vogue in the United States until the State Care Act was passed into law in 1890, officially replacing the term *asylum* with *hospital* in the system of state mental hospitals that this legislation mandated. A similar official shift in terminology followed suit in Great Britain shortly thereafter.

For centuries the mentally ill were treated in general hospitals, but more often than not they were relegated to the streets, poor-houses, and prisons. Sometimes small houses or "one-man asylums" were built to contain particularly troublesome psychotics. In the 17th and 18th centuries, especially in England, hospitals and private "madhouses" were created to incarcerate the mentally ill, although the royal hospitals also treated the general medical problems of the community. With the humanistic movement toward the adoption of moral medicine in the early 1800s, much legislation in England (and subsequently the United States) was passed regulating the care of the mentally ill by setting up national programs of institutions and licensing the operators of private madhouses. Private psychiatric facilities presently refer to themselves as clinics or institutes. Now there is a trend, particularly in the United States, to change the names of public institutions for the mentally ill from hospitals to psychiatric centers.

The first institution in the United States built solely for the care of the insane was opened in Williamsburg, Virginia, in 1769. By 1830 only 13 hospitals and asylums existed in the United States, mostly in the Atlantic states but also as far west as Ohio and Kentucky. Generally their patient population was relatively small, no more than 50 or so for most of them, but a few had a capacity of 200 or more. However, in the 1830s and 1840s a definite shift in public opinion toward the "deviant and dependant" led to the notion that institutions should be built and utilized as places of first resort for intervention. Not only were asylums constructed in record numbers for the insane, but also penitentiaries for the criminal, orphan asylums for homeless children, ALMSHOUSES for the poor, and reformatories for delinquents. It was not that overwhelming new numbers of these people were suddenly appearing but simply that the general public and government's philosophy of dealing with these social problems changed. By 1860, of the 33 states then in existence, 28 had asylums for the insane. Incredibly, between 1840 and 1870 the number of people involuntarily committed to state-run institutions in the United States increased from 2,500 to more than 74,000—far higher than the rate of growth for the population of the United States in that period (only three and one half times). By 1955, just prior to the largest waves in the deinstitutionalization of psychiatric patients, that number had swollen to 559,000 patients in psychiatric hospitals.

See also COMMITMENT.

Deutsch, A. *The Mentally Ill in America: A History of Their Care and Treatment from Colonial Times.* 2nd ed. New York: Columbia University Press, 1949.

Rothman, D. J. *The Discovery of the Asylum: Social Order and Disorder in the New Republic.* Boston: Little, Brown, 1971.

asyndetic thinking A term coined by psychiatrist Norman Cameron to describe the apparent lack of causal linkage or connectedness between elements in the language of schizophrenics. Cameron contributed to the study of the unique structure of schizophrenic language in two noted papers written in the 1930s and listed below.

See also COGNITIVE STUDIES OF SCHIZOPHRENIA.

Cameron, N. "Deterioration and Regression in Schizophrenic Thinking," *Journal of Abnormal and Social Psychology* 34 (1939): 265.

———. "Reasoning, Regression and Communication in Schizophrenics," *Psychological Monographs* 50, no. 1 (1938).

athletic type One of the three main "types of physique" that Ernst Kretschmer proposed were characteristic of "schizophrenes" in his 1921 book *Körperbau und Charakter (Physique and Character).* The ASTHENIC TYPE was the most clearly associated with schizophrenics; also the dysplastic type was common. The athletic type, according to Kretschmer, "is recognized by the strong development of the skeleton, the musculature and also the skin." Kretschmer attempted to devise a taxonomic system of body types that correlated with particular psychological types, in particular those with the psychotic disorders of SCHIZOPHRENIA (whom he referred to as "schizophrenes") and manic-depressive psychosis (whom, following FALRET, he referred to as "circulars").

atropine intoxication therapy A little-used form of treatment for SCHIZOPHRENIA introduced by G. R. Forrer in the late 1940s in which a coma would be induced in patients through the toxic state produced by injections of atropine. Never very popular, this procedure was discontinued in light of the ostensible effectiveness of INSULIN COMA THERAPY.

See also COMA THERAPY; NITROGEN INHALATION THERAPY.

Forrer, G. R. "Atropine Toxicity in the Treatment of Schizophrenia," *Journal of the Michigan Medical Society* 49 (1950): 184–185.

attention, disorders in An almost universal characteristic of SCHIZOPHRENIA that has been observed since earliest times is the inability of an individual with the disorder to willfully focus his or her attention on a thought, feeling, object, or activity for any great length of time before it is disrupted. Since the late 1950s, this problem in functioning has been referred to as attentional deficits or disorders of attention.

Schizophrenics have been observed to have extreme difficulty in sustaining and selectively focusing their attention. This has been true not only in the earliest clinical descriptions of the disorder, but also in many experimental studies of schizophrenic cognition conducted since 1961. In the 1913 English translation of his papers on *Dementia Praecox and Paraphrenia,* Emil KRAEPELIN observed in his schizophrenic patients that "it is quite common for them to lose both inclination and ability on their own initiative to keep their attention fixed for any length of time." Oftentimes unsophisticated family members or other caretakers of schizophrenics tragically mistake these "gaps" in attention that disrupt activity as signs that the afflicted person is "lazy" or "being difficult." These short circuits in the willful activities of schizophrenics are instead almost universal characteristics of the disease, particularly in the nonparanoid subtypes of schizophrenia.

In 1961 Andrew McGhie and James Chapman published a classic paper on this topic that influenced the next several decades of the experimental study of schizophrenia. In their published report, the authors collected representative statements from schizophrenics about their own inner experiences and concluded that in schizophrenia "a primary disorder is that of a decrease in the selective and inhibitory functions of attention." In other words, McGhie and Chapman were arguing that the selective "filtering" mechanism that we all use to screen out unwanted ideas and feelings, when we are focusing our attention on something else, is not functioning properly in schizophrenics. They find it difficult to screen out all these unwanted stimuli from inside themselves and from the outside world, and this disrupts not only their ability to think and communicate, but it also distorts their perceptions and sensations.

Reports by McGhie and Chapman's patients illustrate the disorders in attention characteristic of schizophrenia:

> "It's as if I am too wide awake—very, very alert. I can't relax at all. Everything seems to go through me. I just can't shut things out."
>
> "My concentration is very poor. I jump from one thing to another. If I am talking to someone they only need to cross their legs or scratch their heads and I am distracted and I forget what I am saying."
>
> "I can't concentrate on television because I can't watch the screen and listen to what is being said at the same time. I can't seem to take in two things like this at the same time, especially when one of them means watching and the other means listening. On the other hand I always seem to be taking in too much at the one time and then I can't handle it and can't make sense of it."
>
> "Sometimes when people speak to me my head is overloaded. It's too much to hold at once. It goes out as quickly as it goes in. It makes you forget what you just heard because you can't get hearing it long enough. It's just words in the air unless you can figure it out from their faces."

Since McGhie and Chapman's paper was published, many experimental studies have been conducted to understand the disorders of attention in schizophrenia. This research has been a trend in COGNITIVE STUDIES OF SCHIZOPHRENIA, which use metaphors of the mind derived from the computer sciences to examine INFORMATION PROCESSING IN SCHIZOPHRENIA. Some of this research has attempted to correlate certain attention deficits with deficits in the specific information processing abilities of the two cerebral hemispheres of the brain.

In the search for childhood predictors of later adult schizophrenia, research has focused on disturbances in attention in children as one possible way to predict the later development of schizophrenia. In an ongoing LONGITUDINAL STUDY, psychologists Barbara A. Cornblatt and L. Erlenmeyer-Kimling of the New York State Psychiatric Institute are following a group of children evaluated for "global attention deficits" that may prove to be a "marker of risk" for schizophrenia. (See also HIGH-RISK STUDIES; NONPARANOID SCHIZOPHRENIA.)

In the late 1990s, the ability of persons with schizophrenia to screen out relevant from irrelevant sensations was studied under the new term SENSORIMOTOR GATING. Attempts to improve the ability of schizophrenics to focus their attention through "attention training" have produced only mild and temporary improvements.

Cornblatt, B. A., and J. G. Keilp. "Impaired Attention, Genetics, and Pathophysiology of Schizophrenia," *Schizophrenia Bulletin* 20 (1994): 31–46.

Cornblatt, B. A., and L. Erlenmeyer-Kimling. "Global Attentional Deviance as a Marker of Risk for Schizophrenia: Specificity and Predictive Validity," *Journal of Abnormal Psychology* (1985): 470–486.

McGhie, A., and J. Chapman. "Disorders of Attention and Perception in Early Schizophrenia," *British Journal of Medical Psychology* 34 (1961): 103–117.

Medalia, A., et al. "Effectiveness of Attention Training in Schizophrenia," *Schizophrenia Bulletin* 24 (1998): 147–152.

Swerdlow, N. R., et al. "Using an Animal Model of Deficient Sensorimotor Gating to Study the Pathophysiology and New Treatments of Schizophrenia," *Schizophrenia Bulletin* 24 (1998): 303–316.

attention-deficit hyperactivity disorder (ADHD) See HYPERKINESIA.

atypical antipsychotics See ANTIPSYCHOTIC DRUGS.

atypical psychotic disorders The generic term for psychotic disorders with a sudden onset, short duration, and complete or almost complete remission and return to normal functioning. More than 200 synonyms or partial synonyms for these disorders have been documented. These BRIEF PSYCHOTIC DISORDERS, as they are called in *DSM-IV-TR* (2000), or ACUTE AND TRANSIENT PSYCHOTIC DISORDERS, as they are grouped in *ICD-10* (1992), have historically been those that do not fall within the two great psychotic disorders described in 1899 by Emil KRAEPELIN, DEMENTIA PRAECOX (later,

SCHIZOPHRENIA) and MANIC-DEPRESSIVE ILLNESS. Since these disorders are periodic, cyclic, and have a good prognosis, Kraepelin tended to subsume them under his concept of manic-depressive illness as forms of MANIA. Today they are regarded as a large and little-understood group of psychotic disorders that do not easily fit the diagnostic categories of schizophrenia or of the AFFECTIVE DISORDERS and which are therefore regarded separately. The incidence of these disorders is believed to be greater in developing, or Third World, countries than in First World countries (such as the western European countries, the United Kingdom, the United States, and Japan). In First World (developed) countries they are generally split into two main types, depending on the length of time they are in evidence: (1) a group of chronic persistent delusional disorders, and (2) a group of acute and transient disorders with POLYMORPHIC PSYCHOTIC SYMPTOMS.

Cultural differences in diagnosis In North America, where *DSM-IV-TR* is most widely used, these disorders are now referred to as "brief psychotic disorders." Formerly they were referred to as "brief psychotic reactions" in *DSM-III* (1980) and *DSM-III-R* (1987), but the word *reaction* was dropped because it implied a particular cause of the psychotic disorder—a reaction to a stressful event or events—and this was not found in all cases. Although *ICD-10* (1992) is used worldwide and is promoted by the WORLD HEALTH ORGANIZATION as the standard diagnostic reference book, individual countries refuse to give up traditional terms that have a long history. For example, in France the term BOUFFÉE DELIRANTE has been used quite popularly since the 1890s for these disorders. In Germany, where Karl Kahlbaum first proposed the term DYSPHRENIA for these disorders in 1863, the term CYCLOID PSYCHOSES is still quite popular. In Scandinavian countries, the terms REACTIVE PSYCHOSES, psychogenic psychoses, and schizophreniform psychoses are still popular following a long history dating back to a 1916 book by Danish psychiatrist August Wimmer (1872–1937) on psychogenic forms of mental disease. In Japan, the term *atypical psychoses* has been the most popular term for these disorders since a 1941 publication by Japanese psychiatrist Hisatoshi Mitsuda that first described these disorders. In Japan the prognosis is usually presumed to be favorable, but in the 1980s and 1990s a residual "defect syndrome" has been found in a small proportion of these patients, launching a debate over the differential diagnosis between certain atypical psychoses and schizophrenia. In Japan these disorders are seen to have etiological (causal) links to genetics; epilepsy, with an increased risk of epilepsy found in relatives of patients with atypical psychoses; and endocrinological disorders such as luteal insufficiency and latent hypothyroidism.

Culture-bound syndromes There are some disorders that do not fit easily into Western diagnostic categories in psychiatry that are specific to particular populations or cultural areas of the world. These "culture-bound syndromes" (for example, *amok* among the Malay, or various forms of spirit possession) are considered separately from psychotic disorders in *ICD-10* because many of them more closely fit other diagnostic categories (such as personality disorders or dissociative disorders) rather than Western concepts of psychosis. *ICD-10* provides a list of these culture-specific syndromes and offers suggested Western psychiatric diagnoses that may be analogous to them.

The issue of misdiagnosis There are numerous medical conditions and medications that may cause symptoms of psychosis. Invariably these may present as atypical psychoses. A useful text that describes these conditions and offers suggestions for making the differential diagnosis between a medical disorder and a mental disorder is *Distinguishing Psychological from Organic Disorders* by Robert L. Taylor.

Marneros, A., and F. Pillman. *Brief Psychoses—The Acute and Transient Psychotic Disorders.* Cambridge: Cambridge University Press, 2003.

Pillman, F., and A. Marneros. "Brief and Acute Psychoses: The Development of Concepts," *History of Psychiatry* 14 (2003): 161–177.

Pull, C. B., J. M. Cloos, and N. V. Murthy. "Atypical Psychotic Disorders." In *Schizophrenia.* 2nd ed., edited by S. R. Hirsch and D. Weinberger. Cambridge: Blackwell, 2003.

Taylor, R. L. *Distinguishing Psychological from Organic Disorders: Screening for Psychological Masquerade.* London: Free Association Books, 2000.

auditory hallucinations Perhaps the most common type of HALLUCINATION found in the psychotic disorders. These are hallucinations of sound, and they are found across many diagnostic categories and are even experienced in rare instances by "normals" who do not exhibit signs of a MENTAL DISORDER. Strictly speaking, auditory hallucinations may indicate a psychotic disorder only when they are accompanied by gross impairment in REALITY TESTING.

Auditory verbal hallucinations (AVHs)—specifically the hearing of voices—is the most common type of hallucination experienced by person with SCHIZOPHRENIA. It is estimated that approximately 50 percent of all schizophrenics have experienced AVHs. The voices are usually identified as being male or female and do not usually belong to anyone known to the person experiencing them. The voices quiet if the experiencer is engaged in meaningful conversation, but they intensify if there is no background noise in the immediate environment or if the background noise has no meaning. *DSM-IV-TR* (2000) states that schizophrenia can be diagnosed if only one of the following characteristic symptoms has been in evidence for a significant portion of a one-month period (or less if successfully treated): AVHs of a voice keeping up a running commentary on the person's behavior or thoughts, or AVHs of two or more voices conversing with one another. AVHs are one of the most common POSITIVE SYMPTOMS of schizophrenia.

The hearing of "voices" is the most common type of auditory hallucination reported, but individuals have also reported hallucinations of "clicks," "rushing noises," and "music." A common misconception, which is no longer supported by recent research on the psychotic disorders, is that the hearing of "voices" is a definite sign of schizophrenia. Indeed, even in conventional clinical practice today one of the most common (and usually one of the first) questions asked of a patient upon admission to a psychiatric crisis center or a psychiatric hospital is, "Have you been hearing voices?" If the answer is "yes," then the patient is usually diagnosed as schizophrenic. To illustrate how clinicians place too much emphasis on "hearing voices" as a symptom of schizophrenia, Stanford University psychologist David L. Rosenham had normal volunteers go to psychiatric hospitals and report that they had been hearing voices for about three weeks. This was their only reported symptom. Not only were most of them admitted, but they were also given schizophrenic diagnoses. Rosenham's remarkable report of this experiment, "On Being Sane in Insane Places," was published in *Science* in 1973 and received much publicity.

In the 1919 English translation of the eighth edition of his famous textbook of psychiatry, *Dementia Praecox and Paraphrenia,* Emil KRAEPELIN observes that "the hearing of voices" was "the symptom peculiarly characteristic of dementia praecox." He noted that, as a rule, what the voices say is "unpleasant and disturbing." These voices tease, mock, threaten, and abuse the suffering patient. However, Kraepelin also reports that some of his patients heard "good voices" at times. A common characteristic of these auditory hallucinations is that, "Many of the voices make remarks about the thoughts and doings of the patient." Another quality that Kraepelin thought was specific to the auditory hallucinations of schizophrenics was that "the patient's own thoughts appear to them to be spoken aloud." One of Kraepelin's patients told him, "I have the feeling as if someone beside me said out loud what I think."

In *Dementia Praecox, Or the Group of Schizophrenias* (1911), Eugen BLEULER argued that hallucinations were one of the accessory symptoms of schizophrenia that could be found in other disorders (such as manic-depressive psychosis) as well. However, Bleuler thought that auditory hallucinations were more common in schizophrenia than in other disorders. "Almost every schizophrenic who is hospitalized hears 'voices,' occasionally or continually." Bleuler adds that,

> The most common auditory hallucination is that of speech. The "voices" of our patients embody all their strivings and fears, and their entire transformed relationship to the external world. . . . For the patient, as for his attendant, the "voices" become, above all, the representatives of the pathological or hostile powers. The voices not only speak to the patient, but they pass electricity through his body, beat him, paralyze him, take his thoughts away.

Different types of auditory hallucinations were among the 11 FIRST-RANK SYMPTOMS of schizophrenia proposed by the German psychiatrist Kurt Schneider in his phenomenologically based textbook, *Clinical Psychopathology* (1959). The presence of any one of these 11 symptoms was proposed as sufficient to make the diagnosis of schizophrenia. In this sense, it is said that each of these symptoms—including the auditory hallucinations of voices—is PATHOGNOMONIC of schizophrenia, at least according to Schneider.

The psychoanalytic interpretation of auditory hallucinations was only briefly discussed by Sigmund FREUD (1857–1939). In his essay "Metapsychological Supplement to the Theory of Dreams" (1916), Freud made reference to the "dream hallucination" and compared it to schizophrenic auditory hallucinations. Although he noted that both of these were examples of REGRESSION, he suggested that an additional factor in schizophrenia was a disturbance in "that institution of the ego" concerned with the "testing of reality." In his famous 1914 paper "On Narcissism," Freud makes it clear that the "voices" heard in schizophrenic auditory hallucinations do not represent the *superego* itself, as might be thought, given the critical, moralistic judgments and threats made by the voices, but instead Freud thought that these voices represent the regressive undoing or deterioration of the superego. Freud writes: "The voices as well as the indefinite number of speakers, are brought into the foreground again by the disease, and so the evolution of conscience is regressively reproduced."

Later psychoanalytic writers mostly agree with psychoanalyst Otto Fenichel, who, in his textbook *The Psychoanalytic Theory of the Neuroses* (1945), believes that schizophrenic auditory hallucinations serve as a defense: they are "substitutes for perception" after a break with reality. "Inner conflicts are projected and experienced as if they were external perceptions," Fenichel explains.

PSYCHOANALYSIS is now only a historical curiosity of the 20th century, like animal magnetism and phrenology in the 18th and 19th centuries. Although such speculations by Freud and his followers were highly influential on psychiatric thinking from the 1920s until the 1970s, advances in the brain sciences have refuted all the major claims of psychoanalysis. Psychoanalysis is now regarded as a pseudoscience and has no place in ethical psychiatric practice.

The invention of brain imaging technologies in the 1970s has allowed researchers to observe an active, living human brain hallucinating in real time. Increasingly more sophisticated techniques for observing or "capturing" the metabolic activity of the brain during auditory hallucinations have used such measures as regional cerebral blood flow (rCBF), positron emission tomography (PET scans), single photon emission computed tomography (SPECT), and functional magnetic resonance imaging (fMRI). Computer generated images of regional neuronal activity have given us pictures of the various parts of the brain that "light up" when someone is experiencing an auditory hallucination.

The first published study that showed the auditory hallucinations were not "imaginary" (or products of some vague Freudian "superego" or "defense mechanism") but due to the activity of a specific region of the brain was conducted by P. K. McGuire and colleagues. It appeared in the British medical journal *Lancet* in 1993. Using SPECT technology to study regional cerebral blood flow (blood rushes to a part of the brain when that part is being used), they found that auditory hallucinations were associated with increased rCBF in Broca's area of the brain (an area associated with language expression) and, to a lesser extent, in the medial frontal cortex and left medial temporal cortex.

Since 1993 numerous brain imaging studies have confirmed that auditory hallucinations are associated with activity in the parts of the brain that govern the hearing and speaking of words. These functional imaging studies have also confirmed that there is an abnormal interaction between areas of the brain known as the prefrontal area (where so-called executive control of the brain, mind, and body take place) and the auditory association areas in the temporal lobe of the brain (particularly Heschl's gyrus). When these areas are activated during auditory hallucinations, such hallucinations are "heard" as "real" by the person with schizophrenia.

Both conventional and atypical antipsychotics have been the treatment of choice for auditory hallucinations. However, in 25 to 30 percent of cases,

drugs do not stop the "voices." Numerous psychological techniques have been developed to help persons with schizophrenia cope with their hallucinations. Almost all these techniques produced some limited benefit to such persons by reducing their feeling of distress caused by the hallucinations, but none of the techniques effectively eliminated the frequency of the hallucinations. The strategies that have been tried are (1) distracting activities, such as listening to music, (2) behavioral activities, such as exercise, and (3) cognitive training to teach patients to ignore the voices in their heads.

The very few other clinical studies of auditory hallucinations have generally been in phenomenological research on the relationship of certain types of hallucinations with certain diagnostic categories. Auditory hallucinations have been found to occur across diagnostic categories, including in psychotic depressions and BIPOLAR DISORDER, but the auditory hallucination of "voices" may be most common in the paranoid subtype of schizophrenia.

Asaad, G., and B. Shapiro. "Hallucinations: Theoretical and Clinical Overview," *American Journal of Psychiatry* 143 (1986): 1,088–1,097.

David, A. S. "Auditory Hallucinations: Phenomenology, Neuropsychology, and Neuroimaging Update," *Acta Psychiatrica Scandinavica* 395 (1999): 95–104.

Dierks, T., et al. "Activation of Heschl's Gyrus during Auditory Hallucinations," *Neuron* 22 (1999): 615–621.

Frith, C. "The Role of the Prefrontal Cortex in Self-Consciousness: The Case of Auditory Hallucinations," *Philosophical Transactions of the Royal Society of London. B. Biological Sciences* 1346 (1996): 1,505–1,512.

Leudar, I., and P. Thomas. *Voices of Reason, Voices of Insanity: Studies of Verbal Hallucinations.* London: Routledge, 2000.

McGuire, P. K., G. M. S. Shah, and R. M. Murray. "Increased Blood Flow in Broca's Area during Auditory Hallucinations in Schizophrenia," *Lancet* 342 (1993): 70–796.

Shergill, S., R. M. Murray, and P. K. McGuire. "Auditory Hallucinations: A Review of Psychological Treatments," *Schizophrenia Research* 32 (1998): 137–150.

Australia Several studies have been done on the Australian aborigines to determine their prevalence rates for schizophrenia; two of the better ones both came up with a rate of 4.4 per 1,000. Schizophrenia prevalence rates for the rest of the continent as a whole still need to be determined.

Autenreith, Ferdinand (1772–1835) A German physician who believed in the curability of acute psychotic disorders. He is remembered as the inventor of the "padded room." A more sinister invention of Autenreith's was a metal mask that would fit over the faces of mental patients, preventing them from making too much noise by limiting the amount of movement of their jaws. He also devised bulblike gags to perform the same function.

See also MECHANICAL RESTRAINT.

autism Eugen BLEULER coined this term in 1910 as one of the "FOUR A's" (ASSOCIATION DISTURBANCES, AFFECTIVE DISTURBANCES, AMBIVALENCE, AUTISM) that Eugen Bleuler proposed as the FUNDAMENTAL SYMPTOMS that uniquely distinguish SCHIZOPHRENIA from other MENTAL DISORDERS. It refers to the unresponsiveness of many schizophrenics to their environment, thus seeming like they are in a "world of their own." In *Dementia Praecox, Or the Group of Schizophrenias* (1911), Bleuler makes the following observations on autism:

> The most severe schizophrenics, who have no more contact with the outside world, live in a world of their own. They have encased themselves with their desires and wishes (which they consider fulfilled) or occupy themselves with the trials and tribulations of their precursory ideas; they have cut themselves off as much as possible from any contact with the external world.

Bleuler then concludes, "This detachment from reality, together with the relative and absolute predominance of the inner life, we term autism." This symptom in children has led to the identification of infantile autism.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenias.* Translated by Joseph Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

autism, infantile A brain disease of infancy and childhood first described by psychiatrist Leo Kanner (1894–1981) in 1943. It was formerly called Kanner's syndrome but is now known as autistic disorder, the most severe and prototypical form of the general diagnostic category known as pervasive developmental disorders in *DSM-III-R*. Through the years, many other diagnostic terms have been used for this class of disorders, including atypical development, symbiotic psychosis, childhood psychosis, and childhood schizophrenia, but all these terms are now obsolete.

Autistic disorder is usually apparent in a child's behavior within the first two to three years of life. The child generally does not respond well to touching or other forms of social interaction, is slow to develop language, develops many unusual stereotyped and repetitive behaviors, and can become fascinated with certain inanimate objects (such as a spinning fan or faucets). Although some children can experience improvements in language, social, and other skills around the ages of five or six, this is not true in every case. Puberty can bring about marked changes either for the better or worse. The disease has a lifelong manifestation, although a small minority of these children go on to live relatively independent lives. The majority remain handicapped, with about 25 percent experiencing epileptic seizures before adulthood. About 50 percent remain within the mentally retarded range of intellectual functioning.

Studies in England and the United States have found that the prevalence of autistic disorder in the population is about four to five children out of every 10,000. Males are three to four times more likely to be afflicted with this disorder than females.

It is now known that autistic disorder is a brain disease that has nothing to do with child-rearing practices—especially the supposedly monstrous REFRIGERATOR MOTHER of autistic children, who Kanner believed was the cause of the disorder. Autistic disorder has been associated with maternal rubella, anoxia during birth, encephalitis, infantile spasms, tuberous sclerosis, untreated phenylketonuria, and the fragile X syndrome. A genetic basis is indicated by studies that show that autistic disorder is more common in siblings than in the general population. Candidate genes for autism have been found.

It was formerly thought that autism was a form of a childhood psychosis that would eventually develop into SCHIZOPHRENIA, but most recent research seems to indicate that they are two different disorders. Sancte de Santis described a childhood psychotic disorder in 1906, *dementia praecoxissima,* which he thought was related to DEMENTIA PRAECOX in adults. There was much confusion over whether infantile autism was a form of CHILDHOOD SCHIZOPHRENIA, until Kanner separated the two in 1943. Autism was officially removed from the diagnostic class of schizophrenic disorders in the 1970s, primarily as a result of the six published studies on the childhood psychoses published by Kolvin and his colleagues in 1971.

Autism, like schizophrenia, is viewed by many researchers as being a "spectrum disorder": that is, the disease manifests in several forms to a greater or lesser degree and may have underlying genetic relationships to other mental disorders. *DSM-IV-TR* (2000) includes Autistic Disorder in the category of Pervasive Developmental Disorders, many of which, in decades past, were diagnosed as infantile autism or childhood schizophrenia. These include Rett's Disorder, Childhood Disintegrative Disorder, and Asperger's Disorder. Autistic Disorder is characterized by a triad of impairments: qualitative impairment in social interaction (inability to look others in the eye, lack of curiosity in the world around them except for certain objects or movements of objects that fascinate them), qualitative impairments in communication (particularly delay in, or total lack of, development of spoken language), and restricted repetitive and stereotyped patterns of behavior, interest, and activities. Many children diagnosed with autism also have a secondary diagnosis of mental retardation due to an IQ below 70 and severe deficits in their ability to perform typical activities of daily living. In the first four years of life, autism is often easily distinguished from mental retardation as a primary diagnosis because mentally retarded children tend to seek out social interaction and are more interpersonally "present" than children who are developing autism. Asperger's disorder is a separate diagnosis in *DSM-IV-TR,* but many researchers and clinicians still argue that

it may be a form of "higher-functioning" autism. Although impairments in social interactions and repetitive and stereotyped patterns of behavior are part of the picture, unlike Autistic Disorder, there is no clinically significant general delay in language (for example, single words are used by age two, communicative phrases by age three). Also unlike Autistic Disorder, there is no clinically significant delay in cognitive development or in the development of age-appropriate self-help skills, adaptive behavior (other than social interaction), and curiosity about the world around them. In Asperger's disorder, IQ levels are generally higher and the possibility of holding jobs and engaging in other "normal" activities is greater as they become adults. The disorder is named after Viennese pediatrician Hans Asperger (1906–80), who published a paper in 1944 in the medical journal *Archiv fuer Psychiatrie und Nervenkrankheiten* on a condition he called "autistic psychopathy." This paper went largely unnoticed until 1981, when Lorna Gladys Wing, a child psychiatrist working at the Maudsley Hospital in London, published a paper in *Psychological Medicine* proposing that a new diagnostic term, Asperger's syndrome, be given to those autistic children who do not display developmental delays in language and communication. She distinguished Asperger's syndrome from the typical definition of autism of Leo Kanner. An earlier clinical description of a child with Asperger's syndrome actually appeared in an article by G. E. Ssucharewa in 1926 in the *Monatsschrift fuer Psychiatrie und Neurologie.*

DeMyer, M. K., J. N. Hingtgen, and R. K. Jackson. "Infantile Autism Reviewed: A Decade of Research," *Schizophrenia Bulletin* 7 (1981): 388–451.

Kolvin, J., et al. "Studies in the Childhood Psychoses. II. The Phenomenology of Childhood Psychosis," *British Journal of Psychiatry* 118 (1971): 385–395.

autistic savants Formerly called idiot savants, a term coined in 1887 by the pioneer in the study of mental retardation, J. Langdon Down, for "children who, while feebleminded, exhibit special faculties which are capable of being cultivated to a very great extent." Autistic savants, though often mentally retarded, almost invariably develop from an early history of autistic disorder. Psychiatrist Darold Treffert proposes that this phenomenon be renamed the "savant syndrome" in his book, *Extraordinary People: Understanding "Idiot Savants"* (1989). He identifies two subtypes: "talented savants" or "Savant I," who have "skills that are remarkable simply in contrast to the handicap"; and "prodigious savants" or "Savant II," which is a much rarer form of the condition in which "the ability or brilliance is not only spectacular in contrast to the handicap, but would be spectacular even if viewed in a normal person."

The savant syndrome is six times more likely to occur in males than females. Although the condition is rare, some estimates indicate that as many as 9.8 percent of those children diagnosed with autistic disorder may exhibit this syndrome. And even more rare are the cases of the "prodigious savants," or "Savant II," with less than 100 cases on record in the past 150 years.

The common talent of all children and adults with the savant syndrome is phenomenal memory ability. This enables the sometimes spectacular performance of skills in the following areas: calendar calculating, music (usually the piano), rapid numbers calculating and mathematics, art (painting, drawing, and sculpting), and sometimes mechanical ability. The memorization of enormous amounts of information has been documented in some prodigious savants.

Treffert has found that one of the more common patterns is a "triad" of blindness, mental retardation, and musical ability.

In 1988 a movie, *Rain Man,* won the Academy Award for best picture for its depiction of a prodigious savant, or "Savant II." The many remarkable feats of memory ability and calculating ability dramatized in the film were all based on actual anecdotes reported in the clinical literature and are generally accurate re-creations.

Treffert, D. "The Idiot Savant: A Review of the Syndrome," *American Journal of Psychiatry* 145 (1988): 563–572.

autoimmune hypothesis See IMMUNE SYSTEM ALTERATIONS IN SCHIZOPHRENIA.

autointoxication as the cause of dementia praecox (schizophrenia) There were two primary biological theories about the cause of DEMENTIA PRAECOX and SCHIZOPHRENIA from 1896 until the 1930s: heredity (genetics) and autointoxication. Whereas histories of biological psychiatry have focused almost exclusively on HEREDITY—since it has turned out that genetics does indeed play an influential role in the cause (ETIOLOGY) of the disease—they have tended to ignore the autointoxication or focal infection (focal sepsis) theories that were so promising a century ago. This is due to the fact that such theories of the cause of schizophrenia lost prominence by the 1930s. Breakthroughs in bacteriology and endocrinology had a profound influence on not only Emil KRAEPELIN (1856–1926) but many others as well, all of whom were convinced of the rationality of the notion that perhaps all diseases, both physical and mental, were caused by self-poisoning processes in the body. Kraepelin was not alone in the belief that dementia praecox was due to an endogenous process of autointoxication or focal infection which led to a poisoning of the brain and the production of the characteristic signs and symptoms of this chronic, devastating form of insanity. Then as now, the etiologic heterogeneity of dementia praecox and its successor, schizophrenia, cannot be explained by heredity or genetics alone. To understand fully Kraepelin's view of dementia praecox and its implications for subsequent research on the causes of schizophrenia, we must first understand the cognitive categories of the medical world in which he lived and worked, an era dominated by the new bacteriological and endocrinological paradigms emerging from the laboratory revolution in medicine that began in the late 1800s.

Autointoxication theory in medicine and psychiatry With the general acceptance of the germ theory of disease by 1880 due to the efforts of Louis Pasteur in France and Robert Koch in Germany, the new medical science of bacteriology offered a novel and potentially fruitful paradigm for comprehending illness. Following the replicable laboratory demonstration that bacteria or microbes were involved in processes such a putrefaction, fermentation, and infection, it was a natural cognitive leap to hypothesize that they were involved in the etiology and pathophysiology of many—if not most—diseases. Initially it was argued that diseases were not caused by the bacterial organisms acting directly but instead by the toxins they produced. Poisonous ptomaines (the products of proteins formed in putrefaction) or "toxalbumins" were formed that could be circulated through the body's bloodstream and produce a wide variety of diseases affecting almost every organ. In the original, classical form of autointoxication theory, the intestines were most often cited as the locus of this systemic self-poisoning process, with the kidneys and liver assuming lesser importance in theoretical speculation.

The disease theory of autointoxication first appears in the German medical literature. Hermann Senator (1834–1911), a clinical professor at Berlin University, had speculated as early as 1868 that "self-infection" arising in the intestines could be a source of disease elsewhere in the body. Later, in 1884, he argued that mental disturbances could be caused by this process, claiming that the acute delirium of diabetic coma may have its origin in *Selbstinfektion*.

However, it was the work of French physicians that fueled the rapid expansion of this theory to all categories of disease, including mental disorders. Autointoxication theory rose to international prominence in medicine after the 1887 publication of *Lecons sur les auto-intoxications dans les maladies* by Charles-Jacques Bouchard (1837–1915), an eminent professor of pathology at the University of Paris. For both Senator and Bouchard—the founders of autointoxication theory—the disease-causing poisons were the products of putrefactive processes in the intestines. Although a normal part of the digestive process, under certain conditions (such as fecal stasis) the overproduction of these toxins could not be filtered by the liver or kidneys and, as they entered other organs, disease would result. Bouchard's vision of the inner life of the human body is dramatic: "I have said that the organism, in its normal, as in its pathological state, is a receptacle and a laboratory of poisons. . . . Man is in this way constantly living under the chance of being poisoned; he is always working toward his own destruction; he makes continual attempts at suicide by intoxication."

It was not until 1893, however, that we find the first indications that autointoxication theory is being seriously discussed as a possible etiology for mental disorders. On August 1 of that year, at the Fourth Session of the French Congress of Psychological Medicine held in La Rochelle, "Rapporteurs" François-André Chevalier-Lavaure, a physician from Aix-en-Provence, and Emmanuel Regis, a physician from Bordeaux, drew attention to the value of autointoxication as a possible organic cause of madness by organizing and leading a panel on "Auto-intoxication in Mental Disease." This topic had been the subject of Chevalier-Lavaure's doctoral dissertation in 1890, the first substantive treatment of this issue in the history of psychiatry. In their presentation, they argued that it was difficult to distinguish between cases of autointoxication and those of infection from sources outside the body, but that a clear diagnostic distinction should be made between "infectious" insanity (mental disturbances following acute infectious diseases, such as meningio-encephalitis) and "visceral insanity," which is "associated with disease of the internal organs" and is "also very probably due to autointoxication." As Kraepelin would be three years later, in 1896, when he speculated that dementia praecox was caused by autointoxication, Regis and Chevalier-Lavaure were cautious about the extant scientific basis of their claims: "Indeed, we are inclined it [visceral insanity] as the most typical illustration of the influence of auto-intoxication on the mental faculties. There is not as yet sufficient experimental evidence, however, in favor of this assumption to enable us to assert that such is actually the case; for in respect especially of the mental disturbances that are dependent on digestive troubles we know next to nothing about the concomitant changes in the chemistry of the gastric digestion and toxicity of the intestinal contents."

Hermann Senator had already proposed in 1884 that such self-infection would have profound effects on the nervous system and the brain. When Bouchard's book first appeared in English in January 1894, Thomas Oliver noted in his translator's preface that, "The part played by auto-intoxication in mental diseases is attracting attention." In 1895 systematic extensions of autointoxication theory to psychiatry were offered in the German medical literature by D. E. Jacobson of Copenhagen and in the American medical literature by Albert E. Sterne of Indianapolis. Even Julius von Wagner-Jauregg (1857–1940), who would later win a Nobel Prize for his therapy for neurosyphilis, speculated that disturbed mental states may be caused by the influence of intestinal toxins on brain cells (Wagner-Jauregg 1896). According to Veronika Jahn in a 1975 monograph on this subject, the gastrointestinal tract continued to be the most often cited etiologic locus of "autointoxication psychoses" in psychiatric circles.

Although the rise of the bacteriological paradigm after 1880 initiated and fueled autointoxication theory, advances in the understanding of metabolic processes and the endocrine system between 1890 and 1905—the year Ernest Starling first proposed the modern concept of the "hormone"—added a new endogenous etiological hypothesis: metabolic or "interstitial autointoxication" due to the over- or underproduction of internal secretions in the glands with ducts (liver, pancreas, and kidney), those without ducts (thyroid, adrenals, pituitary), and especially the sex glands (gonads). The medical and psychiatric literatures on autointoxication prior to World War I reflect the confusion in the emerging discipline of endocrinology regarding the nature of hormones and their similarities to enzymes, general metabolites, drugs, toxins, antitoxins, and vitamins. The noted Russian psychiatric researcher Aleksandr Ivanovich Iushchenko (1869–1936) of St. Petersburg extensively reviewed this confusing literature in a series of lectures in 1911, which were later published and translated into German in 1914. He argued that dementia praecox was not due to an autointoxication arising in the intestines but rather was caused by glandular dysfunctions, especially disease processes in the parathyroid. Dementia praecox as a disease arising secondarily from metabolic disorders causing autointoxication would remain a central (if unsupported) etiologic hypothesis for its first 40 years, beginning with the speculative medical cognition of Emil Kraepelin himself.

Emil Kraepelin: Metabolic autointoxication as the cause of dementia praecox Impressed with recent advances in the understanding of metabolic

disorders (*Stoffwechselerkrankungen*) and with the plausibility of autointoxication theory, Kraepelin positioned his new diagnostic entity of dementia praecox squarely within the context of these new medical paradigms. In the general discussion of the causes of the insanities that opens the 1896 fifth edition of his *Psychiatrie,* Kraepelin notes that many of the characteristic signs of glandular or metabolic disorders appear during the development of mental deterioration, especially in dementia praecox (pages 36–37). Later in this book (p. 439), in his very first detailed description of dementia praecox in a chapter on *"Die Stoffwechselerkrankungen,"* Kraepelin states that he has "serious objections" to the point of view that dementia praecox is caused by "inadequate constitutional faculties" or "hereditary degeneration (*erblischen Entartung*)." Instead, he offers an alternate hypothesis: "I consider it more likely that what we have here is a tangible morbid process in the brain (*einen greifbaren Krankheitsvorgang im Gehirne*). Only in this way does the quick descent into severe dementia become at all comprehensible." He admits the failure of neuropathological studies to find any characteristic cellular pathology in dementia praecox but attributes this to an inadequate effort to search for such morbid changes. What then causes this "tangible morbid process in the brain" if it is not heredity? Kraepelin is clear on this point: "In light of our current experience, I would assume that we are dealing here with an autointoxication (*Selbstvergiftung*), whose immediate causes lie somewhere in the body."

Kraepelin, however, makes a major departure from classic autointoxication theory by rejecting the intestines as the source of toxins. Instead, Kraepelin posits the *locus morbi* in the gonads: "If we consider the tendency for the illness to strike at the age when sexual development is still taking place, then it is not out of the question for there to be a connection between the illness and some processes taking place in the sexual organs. These are, of course, only provisional and very indefinite hypotheses."

Kraepelin's metabolic autointoxication theory of dementia praecox was not uniformly welcomed by psychiatrists. Perhaps the most direct attack on this thesis came from Adolf MEYER (1866–1950), later to become one of the most prominent psychiatrists in the United States, in his review of the 1896 fifth edition of Kraepelin's textbook. "As long as chemistry can not furnish more accurate data and methods, the theory of intoxication and auto-intoxication so often resorted to by Kraepelin will be a *terminus technicus* for our ignorance." But such critics did not deter Kraepelin. In the 1899 sixth edition of his textbook, Kraepelin continues to make the argument that the sex glands are the source of the toxins that poison the brain and produce dementia praecox, but his claims are now more nuanced: "In view of the close connection for the disease with the developmental age, with menstrual disorders and reproduction, and in view of the absence of any recognizable external cause, the most obvious thing to think of is probably an *autointoxication* which could possibly be in some close or distant connection with processes in the genital organs." However, Kraepelin now tempers his earlier dismissal of the role of heredity in the cause of dementia praecox, adopting a view that presages modern vulnerability models of the etiology of schizophrenia: "The frequency of hereditary disposition to mental disturbances and their physical and mental symptoms would only signify a lowered resistance to the actual cause of the disease."

Although many followed Kraepelin and accepted autointoxication as the probable cause of the dementia praecox/schizophrenia, most diverged from Kraepelin by insisting that the intestines were the true locus of the "self-infection" and not the sex glands. Still, metabolic autointoxication as a possible cause of dementia praecox was an hypothesis that intrigued Kraepelin for at least two decades. In the third volume of the final, 1913 eighth edition of his *Psychiatrie,* Kraepelin (p. 931) cautiously asserts that it is still too early to make etiological conclusions about dementia praecox, but that it generally might be said that "a number of facts" (*eine Reihe von Tatsachen*) about dementia praecox suggest "an autointoxication as a result of a metabolic disturbance might be probable to some extent" (*einer Selbstvergiftung infolge einer Stoffwechselstorung bis zu einem gewissen Grade wahrscheinlich*).

Dementia praecox soon became an accepted diagnostic entity in Britain, and slightly later in America, where the first serious publications on

dementia praecox began to appear in 1900. In these first American notices, the importance of Kraepelin's new scientific nomenclature is uniformly lauded, with heredity mentioned as the most probable cause of the disorder. Autointoxication is not mentioned. Perhaps this is due to the fact that the autointoxication theory of the etiology of mental disorders did not meet with the immediate interest that it did in Britain, where the theory mutated into a new variant that originated in dentistry: focal infection theory.

Focal infection as the cause of dementia praecox In 1900 the British physician William Hunter suggested that "oral sepsis" was the root source of bacterial infections that would spread to other parts of the body such as the heart, lungs, stomach, intestines, and—a speculation conducive to the application of this theory to Kraepelin's autointoxication theory of dementia praecox—even the sex glands. Secondary localized diseases would then develop from the pathogenic effect of these bacteria, producing toxins as by-products that would cause further systemic sequalae. With autointoxication theory gaining wider acceptance in medicine after 1900, especially through its promotion by the British surgeon Sir William Arbuthnot Lane and John Harvey Kellog of Battle Creek, Michigan, focal infection theory in British dentistry seemed to be the next logical step in its evolution, although it, too, eventually proved to be an unfounded theory that had no scientific evidence to back it up. Focal infection as a cause of insanity was proposed by the British psychiatrist Lewis Bruce of Scotland in 1906 and neurologist Henry Upson of Cleveland, Ohio, in 1907. In outlining his theory that dementia praecox was caused by dental impaction, Upson claimed in 1909, "In several cases I have watched the development of an alveolar abcess and the simultaneous development of an acute psychosis, which was finally relieved by the extraction of the offending teeth." After the prominent Chicago physician Frank Billings, a former president of the American Medical Association, publicized his conversion to focal infection theory in 1916, physicians and psychiatrists concerned with finding the cause and cure of dementia praecox were emboldened to consider radical new theories of etiology and the rational treatments that would follow from them.

Rational therapeutics and surgical solutions The theories of autointoxication and focal infection were attractive to Kraepelin and others not only because of their central assumptions about the etiology of dementia praecox but also because they held out the very real promise of viable treatments or even a cure. As Kraepelin well knew, without knowledge of the cause of dementia praecox, there could be no effective rational therapy. Yet, despite his belief in autointoxication, Kraepelin did not direct his energies, or those of his talented research associates such as Franz Nissl and Alois ALZHEIMER, to finding internal sites of autointoxication or focal infection. Rather, he focused his research group on neuropathological studies, studies of hereditary patterns of transmission, and the development of psychopharmacological agents designed specifically for use in psychiatry.

Sources of autointoxication or infection in the body, if located properly, could be treated with Listerizing sprays or ointments, colonic irrigations, or, as Sir William Arbuthnot Lane demonstrated with his colectomies as a cure for chronic constipation, surgery. For the cure of mental illness, several physicians in America and Britain decided that surgery would be the most rational treatment. The first to do so was Newdigate M. Owensby (1882–1952), chief physician at the Bay View Asylum in Baltimore, Maryland. His experimental procedure was reported in *The New York Times* on December 20, 1907. Hypothesizing that the symptoms of dementia praecox were caused by an oversecretion of the thyroid gland (due to diseased blood vessels in the gland), which poisoned the brain, in July 1907 Owensby chose "the worst patient in the asylum" and cut away the diseased portion of the thyroid. In October 1907 the man was discharged, symptom-free. By December 1907 Owensby had operated on at least four other patients, reporting therapeutic success in all of them. The second to do so was Bayard Taylor HOLMES (1852–1924), a professor of medicine and a specialist in abdominal surgery in Chicago. Holmes was an avid proponent of biological psychiatry and founded and edited the journal *DEMENTIA PRAECOX STUDIES* between 1918 and 1922, a periodical devoted to disseminating scientific information about the possible organic causes of dementia praecox. It is believed to be the first med-

ical journal named after a mental disorder. After conducting less than a year of his own laboratory research, in 1915 Holmes hit upon a focal infection theory of the etiology of dementia praecox—an ergotism-like toxemia caused by fecal stasis in the cecum. The following year Holmes began performing cecostomies and appendicostomies, constructing a stoma in the side of his subjects to allow daily irrigations of the colon with water and magnesium sulfate to eliminate psychotic symptoms. Between 1916 and 1918, in private hospitals and in his short-lived (1917–18) Psychiatric Research Laboratory of the Psychopathic Hospital at Cook County Hospital in Chicago, Holmes and his associates performed major surgery on at least 22 persons suffering from dementia praecox. The first one was his own son, Ralph Loring Holmes, who had developed dementia praecox at age 17 while in his first year of medical school. Ralph never recovered from his May 1916 cecostomy and died four days after the experimental surgical procedure.

The third physician to advocate surgery as a treatment of dementia praecox was Henry A. COTTON (1876–1933), the superintendent of the New Jersey State Hospital at Trenton from 1907 to 1930 and an innovative psychiatrist who had studied with Kraepelin and Alzheimer in Munich for two years. Heavily influenced by Kraepelin's own belief in autointoxication as a cause of dementia praecox, and impressed by the dental theory of focal infection, starting in 1918 Cotton routinely had all the teeth removed from the psychiatric patients to stem the production of psychotic symptoms. By the following year he began even more radical procedures, removing part or all of the colon, cervix, ovaries, testes, or appendix of dementia praecox patients and claimed enormous success. More than 2,000 persons received experimental surgery as psychiatric treatment at the state hospital in Trenton and in Cotton's private clinic, although the pace of this endeavor slowed considerably after a political investigation into Cotton's excesses led to a public scandal and his own mental breakdown. Hundreds of his patients died following surgery. Historian Andrew Scull relates the details of this horrific gothic tale in his 2005 book, *Madhouse: A Tragic Tale of Megalomania and Modern Medicine.* The fourth physician to treat dementia praecox through dental and abdominal surgery was Thomas C. Graves, the medical superintendent of the Rubery Hill and Hollymoore Mental Hospital in Birmingham, England.

Autointoxication or focal infection as explanations for the cause of a wide variety of diseases, both acute and chronic, continued to be promoted as a general theory in medicine and biological psychiatry until the early 1930s. By that time, numerous clinical studies spurred by advances in medical technology had found little scientific evidence for endogenous autointoxication as the presumed cause of dozens of diseases, as the theory's proponents had claimed. The autointoxication and focal infection theories of dementia praecox likewise vanished from serious consideration, never to return in their original form, as "schizophrenia" supplanted the Kraepelin's old nosological category and etiological speculation. However, viral infections, endocrine disturbances, and even theories of too much of the neurotransmitter dopamine "poisoning" the brain and causing schizophrenia are all analogues to the autointoxication theory of the cause of dementia praecox/schizophrenia proposed by Kraepelin and other physicians more than a century ago.

See also DEMENTIA PRAECOX; ENDOCRINE DISORDER HYPOTHESIS; VIRAL THEORIES OF SCHIZOPHRENIA.

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Kraepelin, E. *Psychiatrie. Ein Lehrbuch für Studirende und Aerzte. Achte, vollstandig umgearbeitete Auflage.* 3 vols. Leipzig: Verlag von Johann Ambrosius Barth, 1908–1913.

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Meyer, A. "Book Review," *American Journal of Insanity* 53 (1896): 298–302.

Noll, R. "Historical Review: Autointoxication and Focal Infection Theories of Dementia Praecox," *World Journal of Biological Psychiatry* 5 (2004): 66–72.

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Scull, A. *Madhouse: A Tragic Tale of Megalomania and Modern Medicine.* New Haven, Conn.: Yale University Press, 2005.

Senator, H. "Ueber ein Fall von Hydrothionamie und uber Selbstinfektion durch abnorme Verdauungsvorgange," *Berliner klinische Wochenschrift* 5 (1868): 254.

———. "Ueber Selbstinfektion durch abnorme Zersetzungsvorgange und ein dadurch bedingtes (dyskrasisches) Coma (Kussmaulscher Symptomenkomplex des "diabetischen Coma)," *Zeitschrift für klinische Medizin* 7 (1884): 7–8.

avolition See ABOULIA.

Awl, William See "CURE-AWL, DR."

axonal pruning See CORTICAL PRUNING AS A CAUSE OF SCHIZOPHRENIA.

B

bad news technique Perhaps one of the earliest "cognitive" psychotherapeutic techniques on record is the practice of inventing false "bad news" to tell patients in order to quell their manic mood states. There is evidence that this rather sadistic "counter-cognitions" technique was used in the BETHLEM ROYAL HOSPITAL in England as early as the 1500s to change the behavior of unmanageable patients.

Baillarger, Jules-Gabriel-François (1809–1890) One of the most eminent of the French psychopathologists of the 19th century. Baillarger was a student of ESQUIROL and founded the famous *Annales Médico-Psychologiques* in 1843, the very first French professional publication devoted to the study of psychological medicine. His research contributions include one of the first descriptions (in 1854) of MANIC-DEPRESSIVE PSYCHOSIS, which he called *folie à double forme.* Baillarger's revolutionary connection between alternating melancholic and manic phases, which he hypothesized to be of a single disorder and independent of MENTAL DISORDERS characterized solely by DEPRESSION or solely by MANIA, is a concept later used by KRAEPELIN in his definition of manic-depressive psychosis and is still employed today in modern diagnostic systems. A mere two weeks after Baillarger presented his new diagnostic entity, another student of Esquirol's, Pierre FALRET, claimed instead that it was he who had first described such a condition in a paper published in 1851—but only in 1854 did he call it *la folie circulaire,* the term historically associated with Falret. Both Baillarger and Falret are thus given the distinction of being the first clinicians to describe manic-depressive psychosis or BIPOLAR DISORDER.

See also BIPOLAR DISORDER; CIRCULAR INSANITY; MANIC-DEPRESSIVE ILLNESS.

balderdash syndrome Another name for GANSER'S SYNDROME.

balmy Slang for "eccentric" or "mad." Some scholars have suggested that the term is derived from a 17th-century private madhouse in London known as Balmes House. It was later known as the Whitmore House or Warburton's madhouse.

Barison, Ferdinando An influential theorist—particularly in Italy—of schizophrenic thinking styles. Differing from those theorists who held that schizophrenics tended to be more concrete in their thinking than normals, Barison argued that schizophrenics become overly abstract in their ideas and speech. Barison thought that schizophrenics employed abstractions in order to cover up the gaps in their thought processes caused by the disease process, thus repairing the "dissociative" breaks in the organization of the typical schizophrenic mind. This viewpoint was largely adopted by psychiatrist Silvano ARIETI in his discussion of the "pseudoabstract form and content" of schizophrenic thought and language in his *Interpretation of Schizophrenia* (1974).

Barison, F. "L'Astrazione formale de pensiero quale sintomo di schizofrenia," *Schizophrenie* 3 (1934).

basket men The colloquial term used to refer to the male attendants of the BETHLEM ROYAL HOSPITAL in

London as late as the 17th century. It was a holdover from medieval times when the hospital was a monastery. "Basket men" was a term for the hospitallers (usually monks or nuns) who would go out into the community—baskets in hand—begging for alms and food, which would then be carried back to the hospital for the care of the hospitallers, their patients, and prisoners in the public jails. Such "alms-baskets" held a highly symbolic significance, for the phrase "to go to the basket" meant to go to prison—a common place to find the mentally ill prior to the reforms of the 19th century. Along with other unfortunate individuals, the mentally ill person might also be termed a "basket-scrambler," meaning one who scrambles for the dole from a basket (i.e., who lives on charity).

Bateson, Gregory (1904–1985) An anthropologist by training, Bateson (and his associates) in 1956 formulated the famous DOUBLE-BIND THEORY of communication patterns in the families of schizophrenics. Bateson was the son of the famous British biologist William Bateson, who coined the word *genetics;* his father named him after Gregor Mendel. After completing his M.A. in anthropology at Cambridge, Bateson conducted fieldwork in New Guinea. He met and married Margaret Mead, a pioneer in cultural anthropology, with whom he conducted important fieldwork in Bali. Their marriage lasted 14 years. Bateson is noted for his broad theoretical concerns in cybernetics, communications theory (which has influenced family-therapy theorists), the family dynamics of SCHIZOPHRENIA, and his work with John Lilly on man-dolphin communication at the Oceanographic Institute in Hawaii. Until his death in 1985, Bateson was a frequent lecturer and scholar-in-residence at the Esalen Institute in Big Sur, California.

Lipset, D. *Gregory Bateson: The Legacy of a Scientist.* Englewood Cliffs, N.J.: Prentice Hall, 1980.

bath of surprise A type of immersion therapy, used until the 19th century, in which the mentally ill person was plunged without warning into cold water. ESQUIROL, in his *Mental Maladies: A Treatise on Insanity* (first English translation, 1845), lists several forms of cold water treatment for patients, but the bath of surprise "consists of plunging the patient into water when he least expects it." Esquirol goes on to say that, "We administer it, by precipitating him into a reservoir, a river, or the sea. It is the fright which renders this means efficacious in overcoming sensibility. We can conceive the vivid impression that a patient experiences, who falls unexpectedly into the water, with the fear of being drowned." However, Esquirol admits that he has no data supporting the usefulness of this form of therapy and confesses, "I have never made use of it, but I am certain it has been fatal." Incredibly, instead of the bath of surprise, Esquirol recommends throwing the patient out of a third-story window in order to effect a cure: "When I hear of it (the bath of surprise) being prescribed, I should prefer rather, that they advised to precipitate the patient from the third story, because we have known some insane persons cured by falling upon the head."

Esquirol, J. E. D. *Mental Maladies: A Treatise on Insanity.* Translated by E. K. Hunt. 1838. Reprint, Philadelphia: Lea and Blanchard, 1845.

baths One of the most ancient forms of treatment for mental illness. It is included by Philippe PINEL as one of the three forms of the "usual treatment" ("bleeding, bathing, and pumping") for the mentally ill in asylums circa 1801. Various pseudoscientific theories were put forth at the time to account for the calming or shocking effect of baths that seemed temporarily to reduce active psychotic symptoms. In Daniel Hack Tuke's *A Dictionary of Psychological Medicine* of 1892, a full 10 pages is devoted to the variations on this basic form of treatment for the mentally ill. Indeed, 15 different categories of "bath" are listed in that reference work, as follows:

1. Prolonged warm or hot baths
2. Prolonged warm baths with the addition of cold to the head
3. Prolonged warm sitz baths
4. Prolonged warm baths medicated with mustard
5. Prolonged cold baths

6. Dip baths
7. Baths of surprise
8. Suffusion of tepid and cold water from pails
9. Douches
10. Showers
11. Packing in the wet sheets
12. Packing in the dry sheets
13. Packing in mustard and water sheets
14. Hot air (Turkish) baths
15. Vapour (Russian) baths

Many of these types of bath treatments survived until well into the 20th century.

See also HYDROTHERAPY.

Williams, D. "Baths." In *A Dictionary of Psychological Medicine,* Vol. 1, edited by D. H. Tuke. London: J. & A. Churchill, 1892.

Battie, William (1703–1776) An English physician and anatomist who was the first (and only) psychiatrist ever to be elected president of the Royal College of Physicians, a distinction he earned in 1764. Beginning in 1742 he served on the board of governors of the BETHLEM ROYAL HOSPITAL. However, due to the abusive conditions for patients at "Bedlam," in 1751 Battie founded Saint Luke's Hospital for Lunatics and later acquired two private madhouses. Battie instituted important reforms for the treatment of the mentally ill, many of which were outlined in his classic *Treatise on Madness* (1758), which is a milestone in the history of psychiatry. He advocated the training of the caretakers of the insane and called for research into the causes of insanity for the purposes of prevention. Battie is also remembered for his vicious battles fought with John Munro, who ran "Bedlam," over administrative and treatment philosophies for the care of the insane. The slang expression that a mentally ill person is "batty" or has "gone batty" may have originated in England with the expression that a person has "gone to Battie's," i.e., to Battie's private madhouse.

Beck, Samuel Jacob (1896–?) Romanian-born psychologist, later educated at Harvard and Columbia, who eventually headed the psychology laboratory at the Michael Reese Hospital in Chicago, Illinois. After psychologist David Levy imported the RORSCHACH TEST from Switzerland around 1925, Beck was the first American psychologist to publish research using the test; he also published the first Rorschach manual in English in 1937. Beck pioneered the use of the Rorschach as a diagnostic test for SCHIZOPHRENIA.

bedlam A well-known euphemism, even today, for pandemonium or chaos—like that found in "mad-houses." There was never a place officially named Bedlam. Instead, the word was a colloquial corruption of Bethlem, from the BETHLEM ROYAL HOSPITAL in London. An arresting portrayal of what the real "Bedlam" may have been like is to be found in certain scenes in the motion picture *Bedlam* (RKO, 1946), produced by Val Lewton, in which the chilling chiaroscuro suggests horrors of the asylum that the camera itself does not fully depict for the audience. However, the asylum images of life in "Bedlam" that are explicitly revealed bear a striking resemblance to those in the famous painting *Courtyard with Lunatics,* completed by Spanish artist Francisco Goya in 1793, which gives a graphic portrayal of asylum life in the 18th century. Since Lewton was known for the many literary and artistic allusions in his films (including many to Goya), he probably drew upon this painting (as well as Goya's etchings) for his motion picture conception of "Bedlam."

bed saddle A severe form of MECHANICAL RESTRAINT for patients that survived into the 20th century. For example, the bed saddle was reported in use at St. Elizabeth's Hospital in Washington, D.C., until removed from use by William Alanson White after he became superintendent of that institution in October 1903. In his memoirs, White describes the bed saddle:

> One day in my first month at the hospital. In going through the wards of the institution I found a colored patient strapped to the bed by means of what was known as a "bed saddle." This bed saddle was

made of thin strips of metal in the form of a cross strapped to the bed, and the patient was strapped to it with his arms extended in the position of crucifixion. I had never seen such an apparatus before and immediately issued an order discontinuing its use. I had been trained in the belief that physical restraint was unnecessary, yet in the very hospital where this was a fundamental principle a certain amount of physical restraint had actually been used. I had never seen such a cruel apparatus as this, so I felt justified in ordering its discontinuance.

A standing form of this device was known as the CRUCIFORM STANCE or harness.

White, W. A. *William Alanson White: An Autobiography of a Purpose.* Garden City, N.Y.: Doubleday, Doran, 1938.

Beers, Clifford W. (1876–1943) Beers, an American businessman, underwent a mental breakdown and attempted to commit suicide by jumping out of a window in June 1900, at the age of 24. PARANOIA, AUDITORY HALLUCINATIONS, and continual thoughts of suicide had plagued him for several years. After regaining his sanity and his eventual release, Beers wrote an autobiography, *A Mind That Found Itself* (1908), which detailed his treatment—and abuse—in mental institutions. The horrors of these institutions as depicted by Beers shocked the public of his day and helped to win him supporters for his National Committee for Mental Health (later called the National Association for Mental Health), the first major psychiatric patient-advocacy organization in the United States. Beers relates in his book how he would deliberately get himself transferred to the worst wards of the hospital—the "violent wards"—so that he could thoroughly investigate the institution for his later reform efforts. The sad fact is that the reader of Beers's book today who has worked any significant amount of time in psychiatric hospitals will find many of Beers's experiences familiar—suggesting that almost a century after the publication of this book many ugly conditions have still not changed in public institutions for the care of the mentally ill.

See also ABUSE OF PSYCHIATRIC PATIENTS.

Beers, C. *A Mind That Found Itself.* Garden City, N.Y.: Doubleday, 1908.

behavior therapy The behavioral model of MENTAL DISORDERS holds that SCHIZOPHRENIA should not be considered the expression of an underlying mental "disease" but instead reflects the learning of a repertoire of "maladaptive behaviors" that can be corrected through using the operant conditioning techniques of behavior therapy. However, behaviorists have never constructed a complete theory about the recalcitrant maladaptive behaviors of schizophrenics, and long-term success, with behavioral techniques, of patients with schizophrenia has not been demonstrated. Behavior therapists focus on changing selected target behaviors of a patient (e.g., bizarre dressing, excessive smoking or coffee drinking, AUDITORY HALLUCINATIONS) and try to eliminate them systematically through the manipulation of "reinforcement contingencies" based on the general principles of learning that have been found to be effective in changing the behavior of animals and "normals."

The studies of psychologist T. Ayllon and his colleagues in the 1960s were some of the first applying behavior therapy to institutionalized schizophrenics. A much-publicized behavioral technique that was designed to shape the behavior of entire wards of patients was the "token economy programs" that were popular in the late 1960s and early 1970s. Tokens were introduced on wards as a money substitute that could reward adaptive behaviors and help extinguish or reduce maladaptive ones. The problem with such programs was that they could only work in small environments where there was a highly motivated and highly trained staff on all three shifts of a 24-hour day—committed to following the rules of the behavioral program to the letter without "giving in" to the immediate maladaptive demands of the patients. Currently, social skills training programs based on learning theory and behavior therapy paradigms are gaining attention. Modeling, problem solving, and reinforcement techniques are used to improve the ability of schizophrenics to hold a conversation, be assertive, etc.

Whether any of the above forms of behavior therapy techniques for individuals or groups has long-

lasting effects is questionable. Schizophrenics who do well in such programs in the highly structured environment of an institution lose such skills as soon as they are back in the community and without constant support and reminders as environmental cues. The evidence suggests that the newly learned behaviors instituted by these programs are thus not generalizable. Furthermore, the disease process itself—as schizophrenia is more and more viewed as a brain disease of as yet unknown etiology—seems to sabotage the ability of the nervous system to allow psychosocially induced changes in thinking and behavior to remain permanently and lead to long-term improvements in the level of social and occupational functioning. Behavior therapy—and social skills training programs based on these principles—is thus of limited value in the treatment of schizophrenia.

Ayllon, T. "Some Behavioral Problems Associated with Eating in Chronic Schizophrenic Patients." In *Case Studies in Behavior Modification,* edited by L. Ullman and L. Krasner. New York: Holt, Rinehart & Winston, 1965.

Kazdin, A. E. "The Failure of Some Patients to Respond to Token Programs," *Journal of Behavior Therapy and Experimental Psychiatry* 4 (1973): 7–14.

Lieberman, R. P., W. D. Spaulding, and P. W. Corrigan. "Cognitive-Behavioural Therapies in Psychiatric Rehabilitation." In *Schizophrenia,* edited by S. R. Hirsch and D. R. Weinberger. London: Blackwell Science, 1995, pp. 605–625.

Penn, D. L., and K. T. Mueser. "Research Update on the Psychosocial Treatment of Schizophrenia," *American Journal of Psychiatry* 153 (1996): 607–617.

Belgian cage A wooden cage for the restraint of individuals with severe MENTAL DISORDERS. It stood on short posts. Such a cage was on display at a national exhibition in Brussels in 1880. Older names for such forms of MECHANICAL RESTRAINT, were the "idiot's cage" or "lunatic's cage."

Bellevue Hospital A hospital in New York City whose psychiatric ward achieved the notoriety in the United States that "Bedlam" had earned in England. Special wards reserved specifically for the mentally ill, called "insane pavilions," were first instituted at Bellevue Hospital in 1826. In 1839 a city "mad-house" was constructed and opened on Blackwell's Island (now Roosevelt Island) on the East River of New York City to handle the overwhelming population of the mentally ill that Bellevue was unable to confine. In the mid-20th century, saying that someone "belongs in Bellevue" was equivalent to saying that they were insane. By 2005 such references to Bellevue in popular culture and in everyday conversation had virtually disappeared on a national level, although it maintains a diminishing reputation as a "mad-house" to locals.

Bell's mania or disease A late-19th-century term for CATATONIC EXCITEMENT.

Benadryl The trade name for DIPHENHYDRAMINE, an antihistamine and anticholinergic drug that is used to treat the sometimes severe side effects that patients can experience after the initiation of antipsychotic drug therapy or after a significant increase in dosage. These side effects (stiffness; tremors; lockjaw; involuntary motions of the mouth, tongue, and hands; involuntary eye rolls), which usually occur within hours or days of administering ANTIPSYCHOTIC DRUGS, are acute dystonic reactions that can be reversed with antiparkinsonian agents such as Benadryl, Cogentin, or Akineton. These side effects are acute and are not to be confused with chronic reactions (to years of treatment with antipsychotic drugs) that are known as TARDIVE DYSKINESIA, which is treated with drugs other than Benadryl.

See also ANTIPARKINSONIAN DRUGS.

benign stupors Swiss psychiatrist August HOCH (1868–1919) proposed this term to refer to a certain "reactive type" of manic-depressive insanity that mimicked the symptoms of the catatonic type of DEMENTIA PRAECOX but which did not have the poor prognosis suggested by KRAEPELIN. Stanley McCormick (1874–1947), an insane heir to the

fortune of the famous McCormick family of Chicago, was treated by Hoch in the final years of his life and may have been the model for this proposed psychiatric disorder. Hoch's concept of benign stupors, influenced by the "reactive psychiatry" of Adolf MEYER, never became popular and is no longer in use.

Hoch, A. *Benign Stupors: A Study of a New Manic-Depressive Reaction Type*. New York: Macmillan, 1921.

Noll, R. "Styles of Psychiatric Practice, 1906–1925: Clinical Evaluations of the Same Patient by James Jackson Putnam, Adolf Meyer, August Hoch, Emil Kraepelin, and Smith Ely Jelliffe," *History of Psychiatry* 10 (1999): 145–189.

benztropine See ANTIPARKINSONIAN DRUGS.

Bethlem Royal Hospital ("Bedlam") The oldest mental hospital in England, which stood at the present site of the Liverpool Street Railway Station in London. Originally established as a priory in 1247, by 1329 records show that it was functioning as a hospital. The patients were serviced by a religious order of Hospitallers founded in the 13th century and called the "Bethlehemites." The insignia on their habits was a red star with a dark blue center. In 1346 the City of London took control of the priory and hospital from the bishop of Bethlehem, and by 1403 it is recorded that six mentally ill patients resided there.

The person who was brought to the Bethlem Hospital for incarceration when it was relocated in Moorfields entered gates that were topped, on either side, with sculptures of reclining but manacled male nudes, created by Caius Gabriel Cibber in 1677. Such a person may very well have felt that he or she were crossing through the gates of Hell and into the netherworld. These depicted "Raving Madness" (a heavily chained, taut-muscled and -fisted madman whose mouth is opened in an anguishing grimace) and "Melancholy Madness" (a more passive figure, lying on his stomach, a stuporous expression on his face). Noted English poet Alexander Pope referred to them as the "brazen brainless brothers" in his work *The Dunciad*.

Financial scandals and stories of abuse and torture in the public media marked the next several centuries of the institution's existence—until the 1870s, when official investigations finally reported nothing out of the ordinary at the hospital. Probably not without coincidence, this change followed a period of over a century (from 1728 to 1852) in which the Bethlem Royal Hospital was directed by physician members of the Monro family for four generations (James, John, Thomas, Edward Thomas). In an investigative report of the Committee on Madhouses presented to the House of Commons in 1815 it was noted that many patients were chained and manacled with heavy irons. An American Marine named James Norris had been chained continually for 12 years (since 1804), and a female patient was found to have been restrained in such a manner for eight years. Due to these abuses, particularly of Norris, superintendent Thomas Monro and apothecary John HASLAM were fired from the Bethlem Royal Hospital (Monro through forced retirement). Surgeon Bryan CROWTHER, who was responsible for routinely bleeding all the patients at Bethlem every spring regardless of the type or severity of illness, escaped a similar fate when he died shortly before the committee began its hearings. Monro's only defense against the charges of abusive treatment of patients made by the investigative commission was a weak one: "It was handed down to me by my father, and I do not know any better practice."

An autobiographical account of confinement in "Bedlam" was circulated in 1818 by a former patient, Urbane Metcalf. He describes the hospital as having four main "galleries" (more like cellblocks than wards), with the worst, the "basement gallery," described as follows:

> It is to be observed that the basement is appropriated for those patients who are not cleanly in their persons, and who, on that account have no beds, but lay on straw with blankets and a rug; but I am sorry to say, it is too often made a place of punishment, to gratify the unbounded cruelties of the keepers.

The hospital was first made into a royal institution in 1547, and the official name became the

Hospital of St. Mary of Bethlehem. Later this was shortened to Bethlehem Hospital and then to the Bethlem Royal Hospital. The institution moved several times over the years, with the final move occurring in 1920, to its present location in Monks Orchard, Eden Park, Beckenham, Kent. In 1948 it formed an association with Maudsley Hospital and now serves as a postgraduate teaching hospital for psychiatry.

Recent scholarship by the archivist at the Bethlehem Royal Hospital, Patricia Allderidge, questions the "house of horrors" image of "Bedlam" that has been perpetuated for the past 200 years. While noting in a paper published in 1985 that some patients were chained at the hospital, this was standard practice in asylums at the time (see BICÊTRE). After examining the original hospital records in the famous case of Norris (whose real first name is James and not William, as is often reported), she notes that he was quite possibly the most dangerous patient that the hospital staff had ever encountered. A large, strong seaman, Norris was continually making murderous assaults on staff until finally, in 1804, he was cuffed in an iron harness and chained to a post for good (as he is often pictured in drawings). The media attention to the Committee on Madhouses enquiry into this case truly helped to develop the stereotype of the hellish Bedlam, although Allderidge claims that the primary source materials (which have only been open since 1967) do not reveal much else that was extraordinary about the treatment at Bedlam vis-à-vis other asylums at that time.

See also BEDLAM.

Allderidge, P. "Bedlam: Fact or Fantasy?" In *The Anatomy of Madness: Essays in the History of Psychiatry,* Vol. 1, edited by W. Byrnum, R. Porter & M. Shephard. London: Tavistock, 1985.

———. *Cibber's Figures from the Gates of Bedlam.* London: Victoria and Albert Museum Masterpieces, No. 14, 1977.

Metcalf, U. *The Interior of Bethlehem Hospital.* London: 1818.

———. *Report of the Committee for Better Regulation of Madhouses.* London: Baldwin, Craddock, & Joy, 1815.

Tuke, D. H. *Chapters in the History of the Insane in the British Isles.* London: Kegan Paul, Trench, 1882.

bibliotherapy The reading of books as a therapeutic activity for the mentally ill. Such an activity can help focus the mind of some afflicted persons and give them a sense of structure and organization to help combat chaotic thought processes. For psychotic patients the value is extremely limited, but some patients—particularly those who have PARANOID SCHIZOPHRENIA or BIPOLAR DISORDER—seem to get satisfaction from the activity. Due to the religious preoccupations of many psychotic patients, the Bible remains one of the most common books read and reread by patients in today's psychiatric hospitals, as has been the case for almost two centuries.

In his *Medical Inquiries and Observations on the Diseases of the Mind* (1812), American psychiatrist Benjamin RUSH recommended that the person responsible for the care of the mentally ill should engage them in bibliotherapy: "His business should be, to divert them from conversing upon all the subjects upon which they had been deranged, to tell them pleasant stories, to read to them select passages from entertaining books, and to oblige them to read to him." A pioneer in the psychotherapy of schizophrenia, Swiss psychiatrist and psychoanalyst C. G. JUNG reports in his autobiography the case of a "schizophrenic old woman" whose auditory hallucinations of "voices" told her to let Jung test her knowledge of the Bible. As Jung (1961) tells it,

> She brought along an old, tattered, much-read Bible, and at each visit I had to assign her a chapter to read. The next time I had to test her on it. I did this for about seven years, once every two weeks. At first I felt very odd in this role, but after a while I realized what the lessons signified. In this way her attention was kept alert, so that she did not sink deeper into the disintegrating dream.

Jung reports a partial cure with this bibliotherapy method, admitting that "I would not have imagined that these memory exercises could have a therapeutic effect."

Jung, C. G. *Memories, Dreams, Reflections.* New York: Pantheon, 1961.

Rush, Benjamin. *Medical Inquiries and Observations Upon the Diseases of the Mind.* Philadelphia: Kimber & Richardson, 1812.

Bicêtre In 1793, following the French Revolution, Philippe PINEL was appointed as physician in charge of this mental institution in Paris, renowned as one of the worst in the world. The Bicêtre became a hospital in 1656 but was essentially a holding tank for all of the undesirables of society. By the time Pinel took charge of the institution, it contained only insane males, whereas the females were kept at the SALPÊTRIÈRE, also in Paris. Scores of patients, regardless of their illness, were heavily chained and often beaten by sadistic attendants. Records show that riots by the patients were not infrequent and led to the injuries and deaths of many of the attendants—often convicted criminals themselves. Pinel is frequently depicted as stunning the world by unchaining scores of these patients and by instituting policies for the minimum mechanical restraint necessary for maintaining order. Etchings and an 1876 painting by Tony Robert-Fleury depicting Pinel singlehandedly unchaining the mentally ill helped perpetuate this myth, although in the 1809 second edition of his famous textbook Pinel gives credit to the chief male nurse of the Bicêtre, Jean-Baptiste Pussin (1746–1809), for freeing the first 40 patients on May 23, 1789.

In his 1801 classic, *A Treatise on Insanity* (tr., 1806), Pinel argues that "coercion must always appear to be the result of necessity," and that with the changes he brought about at the Asylum de Bicêtre with his philosophy of "moral treatment:"

> I can assert, from accurate personal knowledge, that the maxims of enlightened humanity prevail throughout every department of its management; that the domestics and keepers are not allowed, on any pretext whatever, to strike a madman; and that straight waistcoats, superior force, and seclusion for a limited time, are the only punishments inflicted.

Pinel, P. *A Treatise on Insanity* (1801). Translated from the French by D. D. Davis and M. D. Sheffield. England: W. Todd, 1806.

biochemical theories of schizophrenia Biochemical theories of the causes of SCHIZOPHRENIA are among the oldest in history. Almost all the biochemical theories assume that schizophrenia is caused by abnormal metabolic or enzymatic processes in the chemistry of the brain. Thus, when present-day mental health professionals explain to the family member of a schizophrenic that the brain disease is caused by a "chemical imbalance," it is because of the suggestive evidence for certain aberrant "autointoxicating" chemical processes in the brain. However, there are many different theories involving many different chemicals and biochemical processes in the nervous system, and no one biochemical theory can as yet be targeted as the best explanation for the sole cause of schizophrenia (or of all its subtypes).

Autointoxication The idea that schizophrenia was perhaps caused by such an "autointoxicating" process in the brain was proposed from the very first by Emil KRAEPELIN in his initial description of dementia praecox in 1896. He wrote:

> For these reasons I consider it more likely that what we have here is a tangible morbid process occurring in the brain. Only in this way does the quick descent into severe dementia become at all comprehensible. It is true that morbid anatomy has so far been quite unable to help us here, but we should not forget that reliable methods have not yet been employed in a serious search for morbid changes. In the light of our current experience, I would assume that we are dealing with an autointoxication, whose immediate causes lie somewhere in the body.

Another early theorist to propose a metabolic disturbance as the cause of schizophrenia was the Swiss psychiatrist C. G. JUNG. In his 1907 classic, *The Psychology of Dementia Praecox,* Jung proposes that purely psychological causes (COMPLEXES) may be primary but are not enough to explain the devastating effects of schizophrenia. He proposed in addition the presence of a mysterious "hypothetical X, or metabolic toxin (?)" as perhaps the organic cause of this mental disorder. "Dementia praecox favors the appearance of anomalies in the metabolism—toxins, perhaps, which injure the brain in a more or less irreparable manner, so that the highest psychic functions become paralyzed,"

Jung wrote early in his monograph. Furthermore, he expressed the hope in 1907 that "a more perfect chemistry or anatomy of the future will perhaps demonstrate the objective metabolic anomalies or toxic effects associated (with dementia praecox)."

Endocrine theories By the mid-1930s most of the prominent proponents of AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX (SCHIZOPHRENIA) had vanished from the scenes. Sources of internal foci of infection were no longer thought to be the cause of poisons sent to the brain that caused psychotic symptoms. However, with the rise of endocrinology as a medical science, ENDOCRINE ALTERATIONS IN SCHIZOPHRENIA became a major focus of biochemical research in schizophrenia beginning in the 1920s. A significant proponent of such research was Nolan D. C. Lewis (1889–1979), a noted child psychiatrist who for a time served as the head of the New York State Psychiatric Institute. "Internal secretions" (hormones), enzymes, and a wide variety of other biochemical substances were examined in persons with schizophrenia. Then as now, findings were inconsistent and difficult to understand. The various CONVULSIVE THERAPIES that became popular in the 1930s (such as electroshock therapy or insulin coma therapy) were thought to work by producing biochemical changes in the brain, but there was never any conclusive evidence to support this.

Transmethylation hypotheses Based on studies of how hallucinogenic drugs, particularly LSD-25, worked on the brain to produce "psychotogenic" (psychosis-causing) effects, from at least 1957 to the mid-1970s the dominant theories of schizophrenia were based on various "inappropriate methylation" or TRANSMETHYLATION HYPOTHESES. The term *transmethylation* was coined by the organic chemist John Harley-Mason of Cambridge University in England. The first publication advocating this hypothesis was published in 1952 in the *Journal of Mental Science* and coauthored by Humphrey Osmond (1917–2004) and John Smythies. The assumption was that if the body of a person with schizophrenia was producing LSD-like or mescaline-like substances, then metabolites of these chemicals should be detectable in the blood or urine. For two decades schizophrenia researchers searched for enzymes that converted one biochemical molecule into another less-active substance or its detectable metabolite after breakdown. A prominent proponent of this line of research during this era was Seymour Kety (1915–2000), the head of the neuroscience laboratories at the NATIONAL INSTITUTE OF MENTAL HEALTH.

No endogenous psychotogen, no psychosis-causing metabolite, was ever found in persons with schizophrenia. However, the basic research conducted within the framework of the transmethylation hypotheses led to many useful discoveries, including the metabolites of DOPAMINE and serotonin, which had applications to other fields of research, such as psychopharmacology. By the late 1960s the focus of research had shifted from the search for toxic metabolites to instabilities of the methylation process itself. By the late 1970s the transmethylation hypothesis had been replaced by a new one: the DOPAMINE HYPOTHESIS. Research into the various transmethylation hypotheses slowed to a trickle and had virtually disappeared by the 21st century. The last such publication in this tradition appeared in 1999, reporting the "experimental psychosis" induced by the ingestion of Ayahoasca, a South American hallucinogenic beverage prepared by boiling two plants found in the Amazon region.

Neurotransmitters Following the discovery of receptors for acetylcholine, dopamine, serotonin, and other NEUROTRANSMITTERS starting in 1970, biochemical research in schizophrenia has been dominated by the study of neurotransmitter systems in the central nervous system. The hypothesis that an excessive production of dopamine flooded its receptor sites and caused the POSITIVE SYMPTOMS of schizophrenia led to a "single-system" theory of the cause of schizophrenia. With increased knowledge about the involvement of some of the other 100 or more neurotransmitter systems in schizophrenia (GABA, serotonin, glutamate, and so on), such single-system theories are no longer held to be valid. Changes in the biochemistry of specific parts of the brain, such as the hypothalamus and portions of the frontal lobe, have emerged from this research. A comprehensive review of research on the neurotransmitters implicated in the pathophysiology of schizophrenia can be found in the chapter on the neurochemistry of schizophrenia by Moghaddam and Krystal published in Steven Hirsch and Daniel Weinberger's 2003 volume, *Schizophrenia* (2nd ed).

By 2005 research on the biochemical/neurochemical theories of schizophrenia focused on three major areas of abnormal processes in the brain involving (1) monoamine mechanisms (dopamine, serotonin, and noradrenaline, and their common degraditive enzyme, MAO); (2) amino acid neurotransmitters (the inhibitory amino acid neurotransmitter pathways of gamma-aminobutryic acid [GABA] and glutamate, an excitatory neurotransmitter); and (3) neuropeptides (opioids and cholecystokinin [CCK]).

Given the fact that there are more than 100 neurotransmitters in the brain, and many of them interact with each other and with neuropeptides, researchers in this field are increasingly reluctant to believe in "single-system" theories of the neurochemistry of schizophrenia. Neurochemical studies are now regularly combined with postmortem work, functional brain imaging data, and other sources of information about what really happens in the brain of a person with schizophrenia. New theories of schizophrenia no longer propose simple "chemical imbalances" but instead are highly complex, interactive models that combine multiple neurotransmitter systems with neural circuitry. Most of these theories focus on pathways between the cortex and the subcortical regions of the limbic system of the brain. An entire issue of *Schizophrenia Bulletin* published in 1998 (vol. 24, no. 2) was devoted to these "New Models of the Pathophysiology of Schizophrenia."

With the promising findings in genetics regarding schizophrenia, biochemical theories have been linked to genetic theories of the causes of schizophrenia. The assumption is that a particular genetic abnormality predisposes an individual to developing a metabolic disorder in the brain. However, while this linkage is suggestive based on our knowledge of the genetic causes of other types of diseases, concrete evidence linking the two in the causes of schizophrenia is still lacking. Furthermore, it must be remembered that, other than through genetic causes, biochemical imbalances may derive from such things as environmental stress, infectious diseases, and trauma—all of which have historically been implicated in various theories of the cause of schizophrenia.

Jung, C. G. *The Psychology of Dementia Praecox,* in *The Collected Works of C. G. Jung.* Vol. 3. Princeton, N.J.: Princeton University Press, 1960; first published, 1907.

Kraepelin, E. "Dementia praecox," from *Psychiatrie.* In *The Clinical Roots of the Schizophrenia Concept: Translations of Seminal European Contributions on Schizophrenia,* edited by J. Cutting and M. Shepherd. 1896. Reprint, Cambridge: Cambridge University Press, 1987.

Moghaddam, B., and J. H. Krystal. "The Neurochemistry of Schizophrenia." In *Schizophrenia.* 2nd ed., edited by S. R. Hirsch and D. Weinberger. Cambridge: Blackwell, 2003.

Osmond, H., and J. R. Smythies. "Schizophrenia: A New Approach," *Journal of Mental Science* 98 (1952): 309–315.

Pomilio, A. B., et al. "Ayahoasca: An Experimental Psychosis that Mirrors the Transmethylation Hypothesis of Schizophrenia," *Journal of Ethnopharmacology* 65 (April 1999): 29–51.

biogenic amine hypothesis The hypothesis that abnormalities in the structure, production, and transmission of the biogenic amines are the cause of many mental disorders, especially psychotic disorders. The three primary groups of biogenic amines that are suspected to play this role are the CATECHOLAMINES (such as the NEUROTRANSMITTER DOPAMINE), the INDOLAMINES (such as the neurotransmitter serotonin), and the HISTAMINES.

biological markers of schizophrenia The search for certain biological "signs" or "markers" in the biochemistry and neurophysiology of SCHIZOPHRENIA is one of the most important searches presently underway in schizophrenia research laboratories. If it can be shown that certain biochemical or neurophysiological processes are different in schizophrenics than in normals, then further tests can be devised to determine why this is so, perhaps giving scientific clues to the causes of schizophrenia. Furthermore, certain measurable differences found in schizophrenics may then be developed into a useful physiological method for making the diagnosis of schizophrenia (much as we now have tests for many other physical diseases). Ideally, such tests could then be used in GENETIC COUNSEL-

ING (if genetics tests are developed) or in prenatal screening by determining the liability to schizophrenia. At present, although it is almost certain that schizophrenia is a brain disease with a physiological cause, there are no certain biological markers that can be looked for through medical tests in the same way that, for example, diabetes can be diagnosed.

Biological markers for schizophrenia are sought in research on the following areas: neuroanatomy, both gross and histologic (neuropathology, computed tomography, magnetic resonance imaging); dynamic brain functioning (positron emission tomography, mapping of the brain's electrical activity); neuroendocrine measures; neurophysiological measures (tracking of eye movements, electroencephalogram); molecular genetics; biochemical measures; and the biochemical response to the administration of various psychoactive drugs.

See also BRAIN ABNORMALITIES IN SCHIZOPHRENIA; BRAIN IMAGING TECHNIQUES; BIOCHEMICAL THEORIES OF SCHIZOPHRENIA; CARDIOVASCULAR HYPOPLASIA; ENDOCRINE DISORDER HYPOTHESIS; EYE-MOVEMENT ABNORMALITIES IN SCHIZOPRENIA; PLATELET MONOAMINE OXIDASE ACTIVITY HYPOTHESIS.

biperiden See ANTIPARKINSONIAN DRUGS.

bipolar disorder Until the publication of *DSM-III* in 1980 and *ICD-10* in 1992, a person suffering from a major depressive episode was diagnosed with MANIC-DEPRESSIVE ILLNESS even though they may have never experienced a manic episode. This was due to the conceptualization of manic-depression proposed by Emil KRAEPELIN in 1899 as a single disease resulting in the manifestation of almost all the known severe and/or chronic AFFECTIVE DISORDERS (now termed "mood disorders"). Evidence that there may actually be "monopolar" syndromes of DEPRESSION and MANIA in addition to the "bipolar" manic-depressive illness was first presented in 1957 in a book by a German psychiatrist, Karl Leonhard (1904–88), *Die Aufteilung der endogenen Psychosen* (The Classification of Endogenous Psychoses). Leonard borrowed the term *bipolar* to refer to manic-depressive illness from another German psychiatrist, Karl Kleist (1879–1960), who first used the term (and *unipolar* as well) in 1953. His conclusions were based on years of longitudinal research on the course and outcome of manic-depressive disorder. Leonhard's work inspired numerous studies of this issue by other researchers throughout the 1960s, and by the 1970s it was believed that unipolar depression and bipolar manic-depression were in fact separate syndromes.

In 1980 *DSM-III* introduced the new terms *major depression* and *bipolar disorder* to replace manic-depression as it had been defined since 1899. As forms of Affective Disorders (a new umbrella category), the diagnosis of a manic episode was now the key to receiving a bipolar diagnosis. This still implied that persons who are "bipolar" would one day experience at least one bout of major depression, but we now know that this is not the case. In *DSM-IV* (2000), the category of Mood Disorders includes separate categories for (plural) Depressive Disorders and Bipolar Disorders. Bipolar Disorders are divided into Bipolar I Disorder (where a full manic episode has been diagnosed) and Bipolar II disorder (where hypomanic episodes are present with recurrent episodes of major depression). Each of the forms of Bipolar I disorder is defined according to whether the most recent episode was major depression, mania, or a mixed episode. Specifiers for each of the bipolar disorders are added if psychotic features present, if there is a seasonal pattern, if there is or is not interepisode recovery, if there are catatonic features, if the onset was postpartum, and if the course of a person's illness indicated rapid cycling (four or more manic, major depressive, or mixed episodes in a 12-month period).

Most of the research conducted since the adoption of the RESEARCH DIAGNOSTIC CRITERIA (1978) and *DSM-III* (1980) supports the notion that unipolar depression and bipolar disorder are in fact two separate syndromes. However, the focus has primarily been on major depression, which has a lifetime risk of approximately 5 percent in the United States, and not on bipolar disorder, which has a risk of approximately 1 percent (almost identical to schizophrenia). Studies conducted in Europe indicate the

prevalence rate for bipolar disorder may be as high as 5 percent. Prior to 1980, manic-depressive illness also tended to be neglected by researchers, with most of the attention going to dementia praecox and schizophrenia.

Symptoms and Diagnostic Path

Despite the prominence of this disorder in psychiatry since 1899, very little is still known about the various courses of bipolar disorder, its various outcomes, its ETIOLOGY (causes), and its pathophysiology (underlying biological abnormalities associated with the disease process that causes it). What is known can be summarized below:

Age of onset The rule of thumb since Kraepelin was that most persons with manic-depression or bipolar disorder experienced their first manic episode prior to age 25. This assumption has been disputed in a major study conducted by the Institute of Psychiatry in London by Noel Kennedy and colleagues that was published in the *American Journal of Psychiatry* in 2005. In this study, all cases of first-episode PSYCHOSIS, mania, or hypomania in adults treated at a psychiatric facility in London between 1965 and 1999 were analyzed. They found that the average age of onset of a manic episode was 32.9 years. A major gender difference was found, with an average age of onset for men at 30 years and one for women at 35 years. Half of all the men experienced a manic episode before age 25, and by age 35 almost 80 percent of men had done so. In women, only one-third had experienced mania before the age of 25, and just 64 percent by the age of 35.

A family history of affective disorders is associated with an earlier age of onset. Onset before the age of 17 is associated with a more severe course of the illness.

Comorbidity Persons with bipolar disorder are extremely likely to develop another mental disorder at some point in their lives. The two most common comorbid conditions are anxiety disorders (primarily panic disorder and social phobia) and substance abuse (primarily alcohol and marijuana).

Season of birth effect As with schizophrenia, studies have found season of birth effects for bipolar disorder and unipolar depression. Persons with bipolar disorder are more likely than the general population to be born in December through March. Persons with unipolar depression are more likely to be born in the period from March through May.

Frequency of episodes Studies have indicated that, for most persons with bipolar disorder, the disease starts slowly and picks up severity over the years. The durations between the first, second, and third episodes are much longer than the time between bouts of mania, depression, or mixed states as the years go by. Earlier age of onset is associated with an increased frequency of episodes and a continuity of symptoms between full episodes. Later episodes are less likely to include euphoric mania and more likely to become increasingly dysphoric and/or psychotic.

Cycle patterns The classic CIRCULAR INSANITY pattern identified by Falret in 1854 of mania alternating with depression is actually quite rare. Most persons with bipolar disorder have a variety of alterations (mania-mania-mania-depression-mania, for just one example). Untreated, depressive episodes last longer than manic episodes. Seasonal patterns have been noted, with depression more likely in the winter and mania or hypomania more likely in the spring and summer. Anniversary reactions to past traumatic events seem to trigger annual manic or depressive episodes in some persons.

Rapid cycling Rapid cycling is defined in *DSM-IV-TR* as four distinct episodes in a calendar year, each separated by two months of normal functioning or by a switch in polarity (mania to depression, or vice versa). One consistent finding is that rapid cycling is far more common in women than in men. Continuous or ultradian (ultrafast) cycling is associated with a severe course of the illness.

Mixed episodes Since the early 1990s, a great deal of research has been devoted to those episodes that seem to be a mixture of mania and depression. Such MIXED STATES are now generally termed *dysphoric mania.* They are associated with later stages of the illness, with more suicidal thoughts and suicide attempts, and with poorer outcomes than patients who experience pure or euphoric mania. Mixed states occur in about 40 percent of persons with bipolar disorder during the course of a lifetime.

Psychotic features Pronounced and persistent delusions or hallucinations are a bad prognostic

sign in bipolar disorder. Psychotic features are associated with greater disability and a more severe and chronic course of the illness.

Sleep For a person with bipolar disorder, the duration and quality of sleep is the key to preventing relapse. Lack of sleep has been known to ignite a manic episode.

Treatment Options and Outlook

LITHIUM has been the standard treatment for manic episodes since the 1950s. However, it was only approved for use in the United States in 1970. Lithium also works to alleviate the depressive episodes in bipolar disorder. However, lithium does not work for everyone. Recent recommended treatment algorithms (decision trees) for psychiatrists to follow suggest that the type of manic episode is the most important determinant of what medication to use. For euphoric mania (the classic type), lithium is the first choice. Lithium works less well for dysphoric mania and psychotic mania. Antipsychotic drugs such as olanzapine (Zyprexa) or mood-stabilizers such as divalproex sodium or valproate (Depakote or Depakene), carbamazepine (Tegretol), lamotrigine (Lamictal), topiramate (Topamax), or gabapentin (Neurontin) are found to work better for these two types of mania. Some antidepressant drugs (such as some of the SSRIs) have actually been known to ignite a manic episode and therefore are not usually prescribed.

Genetics Like schizophrenia, bipolar disorder runs in families. Twins studies and adoption studies have indicated patterns that support the suspicion that genetics plays a role in family transmission. Although far fewer studies of bipolar disorder have been conducted than those on schizophrenia, concordance rates for identical twins have averaged around 44 percent. No strong candidate genes for bipolar disorder have been identified.

Bipolar disorder and schizophrenia Near the end of his career, Emil Kraepelin admitted that, in practice, it was sometimes quite difficult to diagnose cases differentially of manic-depression from cases of schizophrenia. When pronounced psychotic features are present in a mood disorder, especially during a manic episode, this is indeed the case. In reviewing the evidence for a connection between manic-depression and bipolar disorder in their excellent book *Surviving Manic-Depression* (2002), E. Fuller Torrey and Michael Knable of the Stanley Research Foundation of Bethesda, Maryland, concluded, "In fact, the findings for manic-depressive illness more closely approximate those for schizophrenia than for unipolar depression."

The issue of whether schizophrenia and bipolar disorder were one disease or two separate diseases was the subject of a one-day symposium on April 17, 1999, associated with the International Congress on Schizophrenia Research. The results of this symposium were published in a special issue of *Schizophrenia Research* in 1999. The basic conclusion that many of the RISK FACTORS for the two disorders were similar (family history, roughly the same season of birth effect, similar 1 percent lifetime risk for the disorder in the general population), but that the clinical pictures of the two disorders were quite different (course and outcome, neuropsychological findings, neuroimaging findings, gender differences). Whether schizophrenia and manic-depression are two separate disorders or different expression of an underlying "unitary psychosis" is still an open question.

Akiskal, H. S., et al. "Re-evaluating the Prevalence of and Diagnostic Composition within the Broad Clinical Spectrum of Bipolar Disorders," *Journal of Affective Disorders* 59 (2000): S5–S30.

Kennedy, N. et al. "Gender Difficiences in Incidence and Age at Onset of Mania and Bipolar Disorder over a 35-year Period in Cambridge, England." *American Journal of Psychiatry* 162 (2005) 257–262.

Goldberg, J. F., and M. Harrow, eds. *Bipolar Disorders: Clinical Course and Outcomes.* Washington, D.C., and London: American Psychiatric Press, 1999.

Sato, T., et al. "The Boundary between Mixed and Manic Episodes in the *ICD-10* Classification," *Acta Psychiactrica Scandinavica* 106 (2002): 109–116.

Suppes, T., E. B. Dennehy, and E. Wells Gibbons. "The Longitudinal Course of Bipolar Disorder," *Journal of Clinical Psychiatry* 61 (2000): 23–30 (supplement 9).

Suppes, T., et al. "Report of the Texas Consensus Conference Panel on Medication Treatment of Bipolar Disorder 2000," *Journal of Clinical Psychiatry* 63 (April 2002): 288–299.

Torrey, E. F., and M. B. Knable. *Surviving Manic Depression: A Manual on Bipolar Disorder for Patients, Families and Providers.* New York: Basic Books, 2002.

Birch, John (1745–1815) Birch was a British surgeon and is perhaps the first to use ELECTROSHOCK THERAPY for mental illness. In the late 1700s Birch founded an "electric department" at London's St. Thomas Hospital and used electricity to treat his patients stricken with MELANCHOLIA and other assumed MENTAL DISORDERS. He "passed shocks through the brain," as is reported in a book by George Adams (the man who made Birch's special electrical instrument), *An Essay on Electricity, Explaining the Principles of That Useful Science, and Describing the Instruments* (London, 1799).

birth order and schizophrenia In the late 1950s and early 1960s many studies were conducted to determine whether a person's rank in birth order among his or her siblings was correlated to the later development of SCHIZOPHRENIA. This research was partially conducted to test hypotheses generated by psychoanalytic theory, which predicted that the extraordinary oedipal demands made upon the first-born male child might (in combination with a "SCHIZOPHRENOGENIC MOTHER") produce adult schizophrenia. The make-up or "constellation" of schizophrenic families, determined by such things as the sex and birth order rank of children, was also of interest to "family systems" theorists who practice family therapy. However, major reviews of these studies have almost uniformly concluded that there is no association between birth order and the development of schizophrenia.

Erlenmeyer-Kimling, L., E. Van Den Bosch, and B. Denham. "The Problem of Birth Order and Schizophrenia: A Negative Conclusion," *British Journal of Psychiatry* 115 (1969): 659–678.

bizarre ideation A common descriptive term found in the diagnostic assessments of clinicians examining psychotic patients. It refers to the grossly aberrant expressed thoughts of someone with a psychotic mental disorder. It is often used as a more colorful euphemism for the more clinical term DELUSION.

blacks, incidence of schizophrenia in In the United States, blacks are given the diagnosis of SCHIZOPHRENIA at a greater rate than whites. The most conservative studies indicate that the rate for blacks is at least one and a half times that for whites. There are several reasons suggested for this discrepancy. One is that most clinicians in the United States are white, and that the labeling of blacks with such a serious diagnosis is an expression, consciously or unconsciously, of racism. Others have suggested reasons based on epidemiological grounds, namely that there is a strong association between schizophrenia and lower socioeconomic status—regardless of race—in large cities. This association does not seem to be as strong for smaller cities or rural areas. Demographic studies show that blacks tend to be clustered in major metropolitan areas and less so in smaller cities or rural areas. Studies of schizophrenia rates in rural American areas show no difference between whites and blacks. Thus, those who cite such epidemiological data suggest that the higher schizophrenia rates among black Americans are due to environmental factors—the harsh life of poverty in large urban areas—rather than racial factors.

Kramer, M. "Population Changes and Schizophrenia, 1970–1985." In *The Nature of Schizophrenia,* edited by L. Wynne et al. New York: Wiley, 1978.

bleeding The deliberate opening of a blood vessel (venesection) or the more localized use of cupping glasses and leeches to draw blood was one of the most common forms of medical treatment for both physical and MENTAL DISORDERS for thousands of years. It gained in popularity as a psychiatric treatment after William Harvey's discovery of the circulation of blood in 1628 and was extensively employed for many physical and mental diseases until the 19th century. Galen, in the second century A.D., recommends it as a treatment for fevers. Due to the HUMORAL THEORY OF MENTAL ILLNESS of Hippocrates (fifth century B.C.) it was thought that insanity was caused by an excess of "hot blood"

or of particular humors, which thus needed to be drawn off from the body. The word for this condition of excess—the Greek *plethora*—is still used today, although not in its original, humoral sense.

Bloodletting was a common medical practice for centuries, although in the 12th century priests and monks (who were long involved in the medical treatment of the sick and poor) were forbidden to use it or other physical treatments by Pope Innocent II and instead were ordered to concentrate on religious matters of the soul. To compensate for this loss of medical specialists, a group of lay specialists known as barbers or barber-surgeons arose to meet the demand for bloodletting services. In England, a subspecialty group known as Lay-Barbers or Surgeons of the Short Robe was one of the groups represented in the Guild of the Barber-Surgeons, which was formed in 1210. Later legislation restricted the Lay-Barbers to bloodletting, wound surgery, cupping, leeching, the extraction of teeth, the giving of enemas, and—the only service that the barbers of today still perform—shaving. To distinguish themselves from the Surgeons of the Long Robe, who performed amputations and other services that the surgeons of today still provide, the Lay-Barbers placed a striped pole or sign outside their doors, under which was attached a "bleeding bowl" to advertise the nature of their services. The barber-pole represented the stick held and squeezed in the patient's hand to help increase the flow of blood from a wound produced on a vein in the arm (the same place where blood is most commonly drawn today), with the white stripe on the pole symbolizing the tourniquet tied around the arm above the opened vein and the red stripe, of course, symbolizing the blood. This is the way barber poles still appear today. Sometimes on the older poles a blue line might appear, which symbolized the appearance of the veins in the body.

There were three main bloodletting techniques. In venesection, sometimes called "breathing a vein," a vein (usually on the arm or foot) was opened with a sharp-pointed, double-edged, and straight-bladed cutting instrument known in ancient Greece and Rome as a phlebotome (from the Greek words for "a vein" and "to cut") or later as a lancet. The noted British medical journal *The Lancet* is named after this bloodletting instrument. A practitioner would be advised to carry a variety of lancets of various sizes for different-size veins. They could be either the manually applied type or, later, a "spring-lancet," in which a spring-propelled device could be released to mechanically push into and puncture a vein. Special "bleeding bowls" with internal gradations marked to measure the amount of blood collected were used, with some of the finer ones made of pewter. It was considered an art not to spill a drop of blood anywhere but in these bowls.

A second method, "wet cupping," involved the application to the surface of the skin of a glass (usually) cup that had first been exhausted of air inside (usually through holding it over a flame until the flame expired), causing the skin to puff up (tumefy). After the skin responded in this manner, the cup was lifted and several incisions were made (sometimes with special devices, with multiple, razor-sharp blades, known as "scarificators"), and the cup reapplied to collect the blood.

The third method, "leeching," involved applying the freshwater parasitic invertebrate still known as *Hirudo medicinalis* to various parts of the body. The animal would then attach itself to the skin through its three-pronged bite and would engorge itself until full (in the largest leeches, about an ounce of blood). Cupping the wound after the leech was removed would then obtain much more blood, since leeches inject an anticoagulant substance into the blood and such wounds would not readily clot or heal. The word *leech* is actually an old Anglo-Saxon word for a "healer" or "to heal," and for many centuries the animal was more commonly known by its ancient Latin name, *hirudo.* With the popularity of the medical practice of bloodletting, the word *leech* only later began to refer to the animal itself.

That the anemia caused by an excessive loss of blood could weaken anyone—and thus diminish their symptoms of mental illness—is no surprise. Many individuals lost their lives through this misguided form of treatment based on an incorrect theory. The history of psychiatry seems to be particularly prone to such tragic treatments, usually based upon some new scientific discovery (as the treatment of bleeding followed the discovery of the circulation of the blood), particularly since there are also modern examples of dangerous treatments based on little or no scientific theory—20th-century

equivalents of "bleeding," such as PSYCHOSURGERY, the COMA THERAPIES, and the CONVULSIVE THERAPIES for schizophrenics.

Up until the 19th century, all the patients in the BETHLEM ROYAL HOSPITAL in London were bled several times every summer, regardless of the severity or type of disorder, and as a commonly reported form of punishment. In 18th-century France, prior to their transfer to the care of Philippe PINEL at the BICÊTRE Asylum in the 1790s, the mentally ill patients of Paris's oldest hospital were bled so often that the general public referred to bleeding as the *"traitement de l'Hôtel-Dieu."* French mental patients were usually bled once or twice in the spring and autumn and then bathed (or simply cast) into cold water. Pinel did not advocate bleeding, nor did J. E. D. ESQUIROL, who bluntly stated in his 1838 psychiatric manual that "I do not believe it necessary to prescribe bloodletting in the treatment of insanity."

Perhaps the greatest advocate of bleeding among the fathers of modern psychiatry was the American Benjamin RUSH of Philadelphia. In his 1812 textbook, *Medical Inquiries and Observations on the Diseases of the Mind,* he gives modern readers a glimpse into this long-rejected practice as a treatment for "mania":

> Blood-letting is indicated by the extraordinary success which has attended its artificial use in the United States, and particularly in the Pennsylvania Hospital. In the use of bleeding in this state of madness, the following rules should be observed:
>
> It should be copious on the first attack of the disease. From 20 to 30 ounces of blood may be taken at once, unless fainting be induced before that quantity be drawn. It will do most service if the patient be bled in a standing posture. The effects of this early and copious bleeding are wonderful in calming mad people. It often prevents the necessity of using any other remedy, and sometimes it cures in a few hours.

Rush's treatment of choice (which he picked up during his training in Edinburgh and London, where he witnessed the regime at Bedlam and St. Luke's) did not meet with widespread approval in the United States, and by 1832 was no longer in use in American asylums. By the mid-1800s, the use of bleeding as a treatment for mental illness had almost entirely disappeared in Europe as well, leading the noted German psychiatrist Wilhelm GRIESINGER to write in 1845 that, "The use of bleeding . . . has in recent times been considerably restricted, and all are agreed that the necessity for venesection is not to be inferred from delirium, or any of its forms, even the most active, excited, and furious."

The best source of information on the medical practice of bleeding for modern readers is the essay and illustrations in a catalog of "bloodletting instruments" in the collection of the Smithsonian Institution in Washington, D.C., published in 1979 by Audrey Davis and Toby Appel.

Brain, P. *Galen on Bloodletting: A Study of the Origins, Development and Validity of His Opinions, with a Translation of the Three Works.* Cambridge: Cambridge University Press, 1986.

Davis, A., and T. Appel. *Bloodletting Instruments in the National Museum of History and Technology,* Smithsonian Studies in History and Technology, Number 41. Washington, D.C.: Smithsonian Institution Press, 1979.

Earle, P. "Bloodletting in Mental Disorder," *American Journal of Insanity* 10 (1854): 387–405.

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity,* trans. E. K. Hunt. Philadelphia: Lea & Blanchard, 1845; first published, 1838.

Griesinger, W. *Mental Pathology and Therapeutics.* 2nd ed., trans. C. L. Robertson. 1845. Reprint, New York: William Wood & Co., 1882.

Rush, B. *Medical Inquiries and Observations Upon the Diseases of the Mind.* Philadelphia: Kimber & Richardson, 1812.

Bleuler, Eugen (1857–1939) An empathetic healer and prominent Swiss psychiatrist who coined the term *SCHIZOPHRENIA* in a 1908 paper and who gave its clearest and unsurpassed description in his classic book, *Dementia Praecox, Or the Group of Schizophrenias,* in 1911. Bleuler was born in Zollikon, near Zurich, where his ancestors were largely farmers. After earning his diploma, he served his medical residency at the Waldau mental hospital near Bern. He then left to study in Paris with such noted French psychiatrists as Jean Martin Charcot

and Victor Magnon. In 1885 he returned to Zurich to serve as assistant to August Forel, the chief of the BURGHÖLZI HOSPITAL. The following year, Bleuler at the age of 29 became the director of a mental hospital, the Reinau, located in a former monastery on an island in the Rhine River.

Bleuler's next 12 years were spent at Reinau and provided him the intimate experience of the everyday life of schizophrenics that he based his later theoretical work on. Bleuler lived in the same building with 800-plus patients (considered some of the worst and most chronic in this "backwater" institution) and devoted himself selflessly to every aspect of their care. Still a bachelor, Bleuler spent almost all his waking hours with his patients and succeeded in his goal of attaining a close emotional rapport (*affektiver Rapport*) with each of them. Despite his relative youthfulness, the patients and the attendants addressed him as "Father" out of reverence.

This devotion to understanding the inner world of the schizophrenic patient he carried with him to the Burghölzi mental hospital when he succeeded his mentor Forel as the director in 1896. His lectures to his new staff, based on his observations made during his 12 years at Reinau, were the basis of his later book on schizophrenia. He organized work therapy programs (*Arbeitstherapie*) for the patients and would visit the wards several times at any hour during the day. He was also insistent that his staff demonstrate the same devotion as Bleuler himself to understanding the patients—a revolutionary approach in the days when physicians were rarely seen by the patients at all, let alone involved in discussions with them. Over the years, his staff contained individuals who would later become famous for their own contributions to psychiatry and psychoanalysis: C. G. JUNG, Karl Abraham, A. A. Brill, Ernest Jones, and Ludwig Binswanger. Alphonse Maeder (cited in Ellenberger's book, *The Discovery of the Unconscious*), who also became well known, described what life was like with Eugen Bleuler in those legendary days at the Burghölzi:

> The patient was the focus of interest. The student learned how to talk with him. Burghölzi was in that time a kind of factory where you worked very much and were poorly paid. Everyone from the professor to the young resident was totally absorbed by his work. Abstinence from alcoholic drinks was imposed on everyone. Bleuler was kind to all and never played the role of the chief.

Bleuler was briefly associated with Sigmund FREUD's psychoanalytic movement but broke with Freud in 1910. He is credited with coining the word *depth psychology*, which refers to the psychology of the unconscious mind made famous by Freud and Jung.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenias.* Translated by Joseph Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

Ellenberger, H. *The Discovery of the Unconscious.* New York: Basic Books, 1970.

Bleuler, Manfred (1903–1990) Son of Eugen BLEULER and a major contributor to the study of schizophrenia in his own right. Manfred assumed his father's former position as the director of the Zürich Psychiatric University Clinic at the Burghölzi in 1942. He remained in this position for 27 years and was known for his long-term studies of schizophrenic patients and their families. Like his father, Manfred also placed a great importance on understanding the inner world of those afflicted with schizophrenia. In 1979 he wrote:

> A healthy life exists buried beneath this confusion. Somewhere deep within himself the schizophrenic is in touch with reality despite his hallucinations. He has common sense in spite of his delusions and confused thinking. He hides a warm and human heart behind his sometimes shocking affective behavior. We must know how to approach the schizophrenic. We must enter and feel with him his vision of reality. We must never relinquish this endeavor.

Bleuler, M. "My Sixty Years with Schizophrenics." In *Disorders of the Schizophrenic Syndrome,* edited by L. Bellak. New York: Basic Books, 1979.

———. *The Schizophrenic Disorders: Long-Term Patient and Family Studies,* trans. S. M. Clemens. 1972. Reprint, New Haven, Conn.: Yale University Press, 1978.

Bleuler's syndrome The eponymous label given by British psychiatric researcher T. J. Crow to his proposed "Type I" SCHIZOPHRENIA, which is the variety characterized by positive symptoms, good response to psychotropic medication, and a relative lack of intellectual impairment. This last characteristic is why Crow named Type I schizophrenia after Eugen BLEULER, whose contribution to the study of schizophrenia was his recognition that there were forms of schizophrenia that did not necessarily follow the strict degenerative course that Emil KRAEPELIN thought characterized all dementia praecox. Kraepelin's concept of dementia praecox more closely fits Crow's Type II schizophrenia, which he named the PINEL-HASLAM SYNDROME after the two famous alienists who each, apparently, provided the first clinical descriptions of this disorder in books that they published in 1809.

See also CROW'S HYPOTHESIS.

Crow, T. J. "The Two-syndrome Concept: Origins and Current Status," *Schizophrenia Bulletin* 11 (1985): 471–485.

blocking A very common symptom of SCHIZOPHRENIA wherein a person has an abrupt loss of their train of thought, feeling as though he or she is suddenly "blanking out" in mid-sentence. Many schizophrenics describe this experience as a sudden loss of all thoughts and feelings, leaving awareness "empty" or filled with "nothingness." Often they cannot remember what they were previously saying or thinking when asked after such an experience. One paranoid schizophrenic patient that the author knew would scream out, "They just killed me right now!" to describe his anxiety over the frequent, sudden loss of his inner world. The term was used by Eugen BLEULER as early as 1911.

bloodletting See BLEEDING.

blood of the insane, studies of Blood has always been regarded as a carrier of information about the essence—physical, mental, spiritual—of the individual person. Humoral medicine, of course, posited blood as one of the primary causative factors in disease and offered rational treatments—such as BLEEDING—for the cure of physical and mental maladies. For asylum physicians and researchers intrigued by the stories that blood may reveal, there were at least four questions that needed to be addressed:

(1) Is the blood of diseased persons different from the blood of healthy ones?
(2) Can specific diseases be diagnosed by specific changes in the blood?
(3) Is the cause of madness in the blood itself? In other words, is "mad" blood "bad" blood? (the question of etiology)
(4) Are differences in the blood of the insane merely clues to the hidden causes of madness that are to be found elsewhere in the body? (the question of pathophysiology)

Unclear about the exact parameters of the clinical syndromes confronting asylum physicians, and not knowing how to define operationally mental illnesses such as DEMENTIA PRAECOX or manic-depressive insanity except as vaguely "organic" or "biological," most laboratory researchers simply applied methods inspired by the latest conceptual or technological innovations in the various medical sciences and hoped there would be a serendipitous payoff in the search for the ETIOLOGY, pathophysiology, and treatment of psychiatric disorders.

In the past 150 years, four general approaches to the examination of the blood of the insane have framed experimental research:

(1) the corpuscular richness paradigm (1854)
(2) the metabolic paradigm (circa 1895)
(3) the immunoserodiagnostic paradigm (1906)
(4) the medical genomics paradigm (2005)

The corpuscular richness paradigm The first quantitative laboratory investigation of the blood of asylum patients was conducted in 1854 by W. Lauder Lindsay, then an assistant physician at the Crichton Royal Institution at Dumfries, and published in January 1855 just as he assumed a new position as superintendent and chief medical officer of James Murray's Royal Asylum for Lunatics in Perthshire, Scotland. Lauder Lindsay created the

initial paradigm for this type of laboratory research in PSYCHIATRY by focusing on the relative numbers or proportions of the structural elements of blood as counted through microscopic observation. In doing so, Lauder Lindsay was applying laboratory logic—but not the time-consuming procedures—inspired by Karl Vierordt's pioneering 1852 publication in which the first blood cell counts were reported. The studies of Vierordt and Lauder Lindsay were conducted within the context of the first phase in the history of modern hematology in which the focus was on the quantification of various cell types within the blood. Staining techniques that could more accurately reveal the structural characteristics of the blood only came into general use after 1877, when Paul Ehrlich (1854–1915), while still a medical student, developed a triacid stain that enabled the clear microscopic definition of the nucleus, cytoplasm, and other details of cells in thin films of dried blood on glass slides.

In his unprecedented experiment, Lauder Lindsay used a needle to prick the fingers of 236 insane patients and 36 officers and attendants of the Crichton Royal Institution and Southern Counties Asylum at Dumfries. A simple blood smear on glass slides was examined using a microscope from Nachet in Paris, with a magnifying power of "180 to 380 diameters." His procedural remarks are colorful:

> As a general rule, the insane are extremely bad subjects for such experiments. . . . They are extremely sensitive, restless and suspicious of operative interference, even of a slight nature. Many obstinately refused to allow their fingers to be pricked. Some did so from a firm conviction that a deep-laid conspiracy against their lives or welfare lurked under the cloak of apparently simple experiment; others simply objected to become tools of experiment or amusement; some declined on the plea that in their greatly debilitated condition they could ill afford to spare even a single drop of blood; others lacked courage to submit to the operation; some demanded full explanations of the motives which led to my making the singular request of allowing their finger to be pricked by a needle; in others this formed the keynote of their delusions, delirium or vituperation, for days or weeks after the experiment was attempted in them. On the other hand, many, who could not appreciate the objects of experiment, submitted cheerfully . . . some presented their fingers under the impression that, from the single drop of blood, the state of their constitution, the chances of cure, and the period of their removal, could infallibly be predicted; others from curiosity to see the appearance from which their own blood, or that of their companions, presented under a microscope . . . some carried this laudable curiosity to a great extent, begging most earnestly not only to see their own blood at different periods of the day, but that of fellow-patients and attendants, evidently strongly impressed with the belief that between their own blood and that of companions who exhibited most different traits of character or conduct, or between that of insane patients and sane attendants, there should exist a perceptible difference. On various occasions, I was obliged to demonstrate the condition of my own blood under the microscope, to satisfy the curiosity thus awakened (1855: 82).

Documenting the relative proportion of serum, fibrin, and globules in the blood of the insane and noninsane, as well as a comparison of the form and structures of the red and white corpuscles, he attributed differences in the blood of the insane to the presence of other physical diseases that were equally present in noninsane persons. Diagnostic differences among the insane did not yield corresponding differences in the blood. His negative findings are summarized more succinctly in his later June 1857 annual report as superintendent and chief medical officer of Murray's Royal Asylum for Lunatics: "insanity and the different types and phases thereof are not characterized by a particular morbid state of the blood, and tend to show that insanity must be placed in the category of ordinary physical diseases" (1857: 15).

Lauder Lindsay was a Scottish precursor to what historian Edward Shorter referred to as "the first biological psychiatry" launched in the 1860s by Germans such as Wilhelm GRIESINGER (1817–68). Additionally, Lauder Lindsay expressed his faith in laboratory medicine as a means not only to discover the causes of mental disorders but also as a medium for dispelling discrimination against the mentally ill:

> Researches of this nature will tend greatly to break down the unfounded prejudices still existing in the public mind regarding the special nature of insanity, and to propagate, among the profession as well as the public, more correct opinions of the mutual relations of the healthy and morbid states of mind and body, and more particularly the reaction of physical disease on mental phenomena. It will hereby be found that insanity is much more a corporeal disease than is at present believed, or, at least, is more intimately connected with, or inseparable from, various of the ordinary physical diseases to which human flesh is heir (1855: 78).

Reflecting the assumptions and practices of the "morphologic era" in the early history of hematology, subsequent innovators in biological psychiatry also focused on the "corpuscular richness" of the blood. Blood was taken from insane persons, diluted, and then the corpuscles in a certain volume of that dilution were counted using such instruments as Gower's Haemacytometer. The relative proportion of red and white blood cells (blood dyskrasias) was of particular interest, as was the amount of hemoglobin, and many who followed this research paradigm claimed these amounts differed before, during, and after an individual's bout with madness. By 1892 S. Rutherford Macphail could review the extant literature up to that time and conclude that there was an overall "deficiency of the corpuscular richness of the blood met with in the first stages of insanity," and that a "close connection" exists "between improvement in the quality of the blood, and mental recovery, the converse which exists in cases of persistent and incurable dementia." The corpuscular richness paradigm continued to be followed not only by American and British researchers but also by those in Germany and France.

Following the division of dementia praecox from manic-depressive insanity by Emil KRAEPELIN in the 6th edition of his *Psychiatrie* (1899), serological studies focused on distinguishing these two diseases from each other and from persons without MENTAL DISORDERS. Experiments designed to test the corpuscular richness hypothesis were, not surprisingly, often contradictory. This was especially true with regard to MANIC-DEPRESSIVE ILLNESS. However, a 1920 review by Bayard Taylor HOLMES (1852–1924)—an ardent American proponent of biological psychiatry and the founder (in 1918) of *DEMENTIA PRAECOX STUDIES,* the first medical journal named after a mental disorder—concluded that the blood in dementia praecox "is at times highly concentrated, exhibiting polycythemia [an excess of red blood cells] with leucopenia [a decrease in white blood cells]," and that "the morphological changes in the blood are excessively rapid, almost instantaneous, and when the ratio of corpuscles approaches the normal, there is often a betterment in the mental condition of the patient." This latter statement by Holmes referred to a phenomenon known as the "blood crisis," in which the exacerbation of psychotic symptoms was correlated with a rapid diminishing of white blood cells and an overproduction of red blood cells, the reversal of which accompanied a return to relative normalcy. A rational treatment for dementia praecox derived from this experimental observation involved the injection of patients with sodium nucleate (salts of yeast acids used in the treatments of anemia, rheumatism, and gout) to increase the white blood cell count.

By the 1920s serological studies in psychiatry were no longer conducted within the corporeal richness paradigm. Two more promising serological paradigms—the metabolic paradigm and the immunoserodiagnostic paradigm—captured the imagination of researchers after 1900 following advances in endocrinology and immunology.

The metabolic paradigm Throughout the latter half of the 19th century, physiologists sought to understand the mechanisms of metabolism. For most of that time, physiological changes in the body were explained by theories of nervous regulation. Between 1890 and 1905—the year Ernest Starling first proposed the modern concept of "hormone"—metabolism was increasingly explained by theories of chemical regulation through secreting organs such as glands. Endocrinology emerged from physiology in a recognizable form in the years following British physiologist Edward Schaefer's address "On Internal Secretions" to the British Medical Association in Physiology in London on August 2, 1895. *Internal secretions* was a term introduced by physiologist Claude Bernard in 1855, but reframed by

Schaefer in terms of clinical medicine. Metabolic diseases as a separate category of illness were caused by the overproduction or underproduction of internal secretions in the glands with ducts (liver, pancreas, and kidneys), those without ducts (thyroid, adrenals, pituitary), and the sex glands (gonads). As Schaefer proposed in his famous lecture, secreting organs, both with and without ducts, return secreted materials to the blood. The ductless glands, however, produce only internal secretions. Blood thus became the medium through which to detect and measure internal secretions, or, later in the 20th century, hormones and NEUROTRANSMITTERS.

This emerging new endocrinological paradigm was immediately seized upon by the first biological psychiatrists. If an overproduction or underproduction of internal secretions could produce physical diseases such as diabetes, why not also insanity? Since it was clear that the brain was the organ underlying mental diseases, perhaps the true etiology of the insanities originated elsewhere in the body, places where substances toxic to the brain (internal secretions, ptomaines, bacteria, and so on) were produced and then transmitted to the central nervous system via the blood. This autointoxication theory of mental disorders first became prominent in France in 1893 and influenced a generation of ALIENISTS, neurologists, and psychiatric researchers. And indeed the most prominent among them was Emil Kraepelin. From the fifth edition of *Psychiatrie* in 1896 until the eighth edition in 1913, autointoxication (*Selbstvergiftung*) arising from a metabolic disturbance, probably in the sex glands—and not heredity—was Kraepelin's prime candidate for the cause of dementia praecox.

The early experimental literature on the search for traces of internal secretions in the blood of the insane reflects the confusion in the emerging field of endocrinology regarding the nature of hormones and their similarities to enzymes, general metabolites, drugs, toxins, antitoxins, and vitamins. These studies are too numerous, perplexing, and contradictory to summarize here. Perhaps the most extensive early review of this literature was conducted by the Russian psychiatric researcher Aleksandr Ivanovich Iushchenko (1869–1936) in a series of lectures delivered in 1911 and then translated into German and published in 1914. He hypothesized that dementia praecox was caused by glandular dysfunctions, especially disease processes in the parathyroid. Modern endocrinological research into the biological substrates of dementia praecox/SCHIZOPHRENIA began in the 1920s, increased in number from the late 1950s to the 1980s due to researchers looking for metabolites as part of the TRANSMETHYLATION HYPOTHESIS and has declined somewhat in the past 20 years. The early literature was reviewed in the work of one of its major proponents, Nolan D. C. Lewis (1889–1959), who believed the thyroid, adrenal, and gonads were implicated in dementia praecox.

Most of the research into the metabolic disorder hypothesis of schizophrenia has yielded little of value. The past half-century of research is confounded by the fact that endocrine abnormalities in schizophrenia may be due to stress caused by the illness itself or the effects of antipsychotic medications. The best evidence for an endocrine link to schizophrenia involves the anterior pituitary gland. The anterior pituitary contains gland cells that respond to releasing or inhibiting factors from the hypothalamus, which eventually may be found to be the source of the myriad confusing findings of endocrine dysfunction in schizophrenia.

Endocrinological research provided a direct and important analogical bridge that led to the discovery of neurotransmitters in the brain. Following the 1921 discovery by Otto Loewi (1873–1961) of a substance in the brain later identified as acetylcholine, neurotransmitters were referred to as neurohormones or neurohumors. Indeed, the term *neurotransmitter* did not come into use until the 1960s. Neurotransmitter theories of the pathophysiology of schizophrenia (not the etiology—an important distinction to remember) involving the measurement of serotonin (1954), DOPAMINE (1966), glutamate (1980), and so on, in the blood or cerebral spinal fluid (CSF), evolved directly from the metabolic paradigm in studies of the blood of the insane.

The immunoserodiagnostic paradigm By 1890 the discovery of "reactions" in the blood to foreign organisms or substances, as evidenced by the production of detectable "antitoxins," "antigens," "defensive ferments," or "antibodies," led to the

rise of immunology in medicine. Following the general acceptance of the germ theory of disease by 1880 and advances in bacteriology that demonstrated microorganisms could directly or indirectly cause diseases, between 1890 and 1910 the development of serologic tests such as agglutination, the precipitin reaction, and complement fixation revolutionized the diagnosis of infectious diseases. The development of the Wasserman reaction test for neurosyphilis in 1906 was a turning point for biological psychiatry. It had long been suspected that the many asylum patients with GENERAL PARALYSIS OF THE INSANE were suffering from the long-term effects of the syphilis bacterium in their nervous systems. For the first time, there was a blood test for madness—at least for one variety of madness, anyway. Could such immunoserodiagnostic tests for the other insanities be developed? Could one serologic test be developed that could differentially diagnose the major forms of insanity, dementia praecox, and manic-depressive illness?

In 1909 two German researchers from Eppendorf created a minor sensation when they injected patients with cobra venom and found that all the dementia praecox patients, and a portion of the manic-depressive subjects, invariably reacted to the toxin, while other psychiatric patients and normals did not. The excitement over the "Much-Holzmann psycho-reaction" was over within two years. Although the "Much-Holzmann psycho-reaction" was quickly discredited by other researchers, it was the first promising differential diagnostic immunoserologic finding for dementia praecox and manic-depressive insanity. Another more promising BLOOD TEST FOR SCHIZOPHRENIA, the Abderhalden defensive ferments reaction test, would cause an international sensation in 1913.

In an era in which autointoxication theory influenced medical and psychiatric cognition, researchers posited that bacteria in the intestines spread throughout the body and caused damage to internal organs. These damaged organs would release debris such as "toxic albumins" into the bloodstream, which would then be carried to the brain and cause the symptoms of insanity. Such theories were many and varied, as were the hypothetical substances that could be detected in the blood of the insane. In only one example, Bayard Taylor Holmes of Chicago believed he had produced experimental support for the theory that fecal stasis in the cecum led to the bacterial production of the same toxic amines that were implicated in ergotism, resulting in the poisoning of the brain and eventual psychosis. An excess of histamine in the blood was claimed as evidence for this mechanism.

The immunoserodiagnostic paradigm continues to this day in schizophrenia research, with not only the blood but also the cerebral spinal fluid examined for antibodies to possible pathogens. Evidence for allergic reactions to foods, viruses transmitted from cats to humans, and a lengthy list of other possible pathogens is weak. Viruses in particular are suspected to be involved in the etiology of some forms of schizophrenia and bipolar disorder, although no confirmatory antibodies have yet been detected.

In the late 1990s there was renewed interest in searching for IMMUNE SYSTEM ALTERATIONS IN SCHIZOPHRENIA and other mental disorders. A 2004 review of this literature by researchers from the Netherlands led to the hypothesis that lymphocytes—which make up about 20 percent of all white blood cells—might carry information that reflects the metabolism of brain cells and might be utilized as an indirect probe of a limited number of cellular functions, including gene expression. They proposed focusing on the T (thymus-derived) cell, B (bone-marrow-derived) cell, and NK cell subpopulations of lymphocytes. Other increases or decreases in specific lymphocytes have been found in schizophrenia. The return of interest to numerical or morphological changes in the white blood cells harkens back to the early 20th century research by Lundvall, Holmes, and others intrigued by correlating changes in the blood with changes in symptoms in dementia praecox.

Medical genomics In January 2005 an international team of researchers reported the results of a pilot study in which they claimed to have developed a blood test that could differentially diagnose schizophrenia from bipolar disorder and from normal controls. Collecting RNA from blood samples, the researchers found that schizophrenia and BIPOLAR DISORDER exhibited unique expressed genome signatures. If the follow-up studies confirm the

preliminary report published in the *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics* by Ming T. Tsuang, C. C. Liew, and colleagues, this development signals not only a new paradigm in serological studies of mental disorders—that of medical genomics—but also promises the attainment of the holy grail of biological psychiatry: a blood test for madness.

Is this the dawning of a "third biological psychiatry"? The trajectory of history from a solitary Scottish asylum physician counting the blood cells of his lunatic patients under a weak microscope in 1854 to this recent report by a team of geneticists in three different countries is nothing less than breathtaking.

See also ENDOCRINE ALTERATIONS IN SCHIZOPHRENIA; GENETICS STUDIES.

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blood test for schizophrenia There is no diagnostic blood test for schizophrenia or any other MENTAL DISORDER. The cause of SCHIZOPHRENIA is unknown, the nature of the biological disease process is unclear, and even today it is not known if it is one disease with many forms or many diseases with similar symptoms, courses, and outcomes. Given this situation, it is next to impossible to develop a blood test that could differentially diagnose schizophrenia from other mental disorders and from persons with no mental disorders. However, twice in history—once in 1913 and again in January 2005—the world's attention was caught by the announcement of the development of just such a blood test for schizophrenia.

The story of the first blood test for dementia praecox (1912) In May 1913 at the annual meeting of the German Psychiatrists Association in Breslau, a presentation of experimental research findings by August Fauser (1856–1938), a psychiatrist from Stuttgart, created an international sensation that would capture the imagination of medical researchers for the next several years. At that conference, Fauser reported that he had used a recently invented immunodiagnostic test in an examination of the blood of 250 psychiatric patients and found it could differentially diagnose DEMENTIA PRAECOX from other psychiatric disorders. Furthermore, Fauser claimed that this blood test could also differentiate normal controls from persons suffering from severe mental disorders. Fauser's stunning announcement of the discovery of a blood test for madness held out the promise that PSYCHIATRY would now share in the success of other medical sciences that had been revolutionized by laboratory studies in bacteriology, endocrinology, and serology. This remarkable new immunoserodiagnostic tool was known as the Abderhalden defensive ferments reaction test, originally developed in 1909 by the Swiss biochemist Emil Abderhalden (1877–1950) as a purported method of diagnosing pregnancy. Abderhalden continually refined his procedure and central concept—that of the "defensive ferments," the *Schutzfermente* or *Abwehrfermente*—and a 1912 book on his discovery went through two more editions by 1914. The third edition of 1913 included a bibliography of more than 400 published studies using his serodiagnostic technique.

In a lecture on October 27, 1912, in Halle at a congress of German Psychiatrists and Neurologists,

Abderhalden himself had suggested that his new blood test might be applied to the study of nervous and mental disorders. Fauser, under the direct guidance of Abderhalden, carried out this research plan and published a short research report on his findings on December 26, 1912. But it was Fauser's presentation at the May 1913 meeting of the German Psychiatrists Association that caught the world's attention. For a very brief—but exciting—period in the history of psychiatry, many researchers in Europe and North America believed that psychiatry now had the equivalent of the Wasserman reaction test for dementia praecox.

Fauser's claim to have found a blood test that could differentially diagnose dementia praecox from other psychiatric illness and from healthy persons was, for a time, internationally accepted as valid because of the congruence of his specific findings with the etiological speculations of Emil Kraepelin. Kraepelin believed the disease was caused by "a tangible morbid process in the brain (*einen greifbaren Krankheitsvorgang im Gehirn*)." Furthermore, Kraepelin speculated that the brain is affected by "an autointoxication (*Selbstvergiftung*)" that originated elsewhere in the body. Rejecting notions prevalent in medicine at the time that bodily autointoxications primarily arose from the intestines, KRAEPELIN held to the notion that dementia praecox was caused by a metabolic disturbance originating in the sex glands.

One of the major claims of Abderhalden's defensive ferments reaction test was that it could identify diseased internal organs in the body through a reaction of hypothesized "defensive ferments (*die Abwehrfermente*)" in the blood of a patient when it came into contact with tissue from corresponding human organs taken from a cadaver. The assumption by Abderhalden was that debris from a diseased organ, toxalbumins, would end up in the bloodstream. Since such material was poisonous to the blood and not excreted through the kidneys, the blood produced "defensive ferments" or enzymes which dissolved this debris, catabolizing it and making it into a peptone and amino acid. Specific defensive ferments would be produced in the blood only when coming into contact with tissue from specific organs, and this process could be experimentally replicated in a test tube outside of a living body. An experimental reaction indicating the creation of defensive ferments in the blood in response to contact with corresponding tissue would result in a bright violet color. Such a color would confirm which organ in a patient's body was diseased.

Thus, Fauser found that defensive ferments in the blood of all persons with severe mental disorders caused a reaction against tissue from the cerebral cortex, thereby supporting Kraepelin's contention that dementia praecox is caused by a tangible morbid process in the brain. Fauser further corroborated Kraepelin when he reported that he found defensive ferments reacted against sex gland tissue only in the blood of persons with dementia praecox and not in those diagnosed as manic-depressive, hysteric, or with purely degenerative insanity. The serum of male patients reacted only with testicular tissue, and the serum of female patients only with ovarian tissue.

Fauser's report, and subsequent research publications from his clinic, immediately inspired replication efforts around the world. The most notable of these was a study conducted with the blood of 106 psychiatric patients at the Sheppard and Enoch Pratt Hospital in Baltimore by the noted virologist Charles E. Simon. In an article published in the May 30, 1914, issue of *The Journal of the American Medical Association,* Simon provided a critical review of the work of Fauser and subsequent researchers who did not confirm Fauser's findings, pointing out possible flaws in their use of Abderhalden's complex methodology as a reason for conflicting results. In Simon's own study, the sex-gland reaction was found in nearly all dementia praecox patients, but he directly rejects Fauser's claim that such a reaction is exclusive to dementia praecox. Simon also directly accused Fauser of manipulating his data to achieve the expected outcome. According to Simon,

> In surveying the literature just outlined, one cannot help being impressed . . . by the wonderful apparent uniformity of the results reported by Fauser, and on the other by the total lack of uniformity of those obtained by others. . . . The thought naturally suggests itself that two factors may have been operative to this end, namely that

> Fauser was carried away by his enthusiasm and allowed himself to be influenced unduly in the direction of his own wishes, and that [others] lacked complete control of the technic. As a matter of fact, there is good ground for the belief that both factors were operative (p. 1,703).

Despite an acute awareness of the chaos in the medical literature on what Simon renamed the "Abderhalden-Fauser Reaction," he insisted on the reality of Abderhalden's proposed "defensive ferments" and on the method for detecting them: "It is my firm conviction that . . . Abderhalden's basic work in this field should be viewed as one of the most important contributions to modern experimental science" (Simon, 1914: 1702).

Charles E. Simon never again mentioned the "Abderhalden-Fauser Reaction" in any subsequent publications—and for a very good reason. In the four months before Simon's paper appeared in print, a series of devastating critiques of Abderhalden's defensive ferments reaction test began to appear in German medical journals. Serious criticisms of Abderhalden's methods and even the veracity of the defensive ferments continued in English language journals.

With the wisdom of hindsight, it is known why the Abderhalden defensive ferments reaction test did not revolutionize biological psychiatry: Abderhalden's defensive ferments simply do not exist. They never did. All the reports of positive results with the Abderhalden reaction test were based on error—if not worse. Indeed, in an article published in the May 14, 1998, issue of *Nature,* two German scholars accuse Emil Abderhalden of outright fraud rather than incompetence. The issue of error versus fraud was explored in depth in a 2000 article by Kaasch.

But surely the hundreds of published experimental reports of positive findings using Abderhalden's test were not fraudulent? There is, of course, another explanation: human fallibility. Since the reaction depended on the ability to perceive a particular color, the method was not quantitative. Instead, it was highly subjective. Some researchers saw the color all the time, some saw the color some of the time, and some never saw it no matter how carefully they followed Abderhalden's procedures. The story of the rise and fall of Abderhalden's blood test is more akin to a social psychology experiment on perceptual bias and the consensual nature of reality rather than fraud perpetuated on a massive international scale. August Fauser and his colleagues in Stuttgart clearly saw the color every time it fit their preconceptions about the locus of the diseased organs in dementia praecox. Because of this highly subjective element, the hundreds of experimental reports often wildly conflicted in their results. Charles Simon was therefore correct in his suspicion of experimental bias on the part of Fauser but failed to discern the essential weakness in Abderhalden's method. By 1917 it was clear to most of the world that Abderhalden's defensive ferments did not exist and that the method purported to detect them was flawed. In 1920 Jacques Loeb could write to a biochemist colleague, "Nobody speaks of the Abderhalden reaction any more in the United States and I am very much surprised to see that in his journal Abderhalden still continues that myth." However, scientific articles reporting the use of Abderhalden's test continued to appear in German publications for several more decades.

Despite the general rejection of Abderhalden's defensive ferments and the test purporting to detect them, a minority of physicians in the United States continued to believe in them and in their promise to revolutionize biological psychiatry. These physicians were Albert Sterne of Indianapolis, Bayard Taylor HOLMES of Chicago, and Henry A. COTTON of Trenton. What united these men in their continued belief in Abderhalden and his test was their strong belief in autointoxication and focal infection theories of the cause of dementia praecox and other mental disorders.

The second blood test for schizophrenia (2005) It has been known for some time that both schizophrenia and MANIC-DEPRESSIVE ILLNESS (BIPOLAR DISORDER) have a significant genetic component. Blood relations of persons with schizophrenia or bipolar disorder are more likely also to have the same disorder than persons with whom there is no genetic relatedness. Although the specific genes underlying these disorders are still largely unknown, some candidate genes have been tentatively identified on chromosomes that are implicated in both disorders (specifically, chromosomes 10, 13, 18, and

22). The promise of medical genomics for finding the causes and potential treatments for schizophrenia and bipolar disorder has long been promoted by pharmaceutical and genomics companies. But the genetic heterogeneity of both disorders, and the complex environmental factors that surely must also be involved in the ETIOLOGY of these disorders, has seemed to push the pay-off of basic genetics research further and further into the future. This is why the January 2005 report of a pilot study of a gene-based diagnostic blood test for schizophrenia and bipolar disorder is so stunning.

Ming T. Tsuang, director of the Institute of Behavioral Genomics at the University of California, San Diego, and his international team of colleagues from the United States, Canada, and Taiwan employed a procedure for using RNA derived from white blood cells. This procedure—known as "the Sentinel Principle"—was invented and patented by C. C. Liew, chief scientist of ChondroGene, a private genomics firm in Toronto, Canada. They took blood from 30 subjects with schizophrenia, 16 with bipolar disorder, and 28 normal controls. Using a microarray analysis, they found that each disease state exhibited a unique expressed genome signature, allowing for the objective biological differential diagnosis of mental disorders for perhaps the first time in history. They examined eight candidate biomarker genes and with 95 to 97 percent accuracy were able to use them as blood biomarkers to discriminate between schizophrenia, bipolar disorder, and normal controls. As they conclude in their abstract: "We therefore propose that blood cell–derived RNA may have significant value for performing diagnostic functions and identifying disease biomarkers in schizophrenia and BPD."

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Tsuang, M. T., N. Nossova, T. Yager, et al. "Assessing the Validity of Blood-based Gene Expression Profiles for the Classification of Schizophrenia and Bipolar Disorder: A Preliminary Report," *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics* 133B (January 2005): 1–5.

blood transfusion Down through the centuries the idea has persisted that mental illness might be caused by abnormalities in the blood. The practice of BLEEDING attempted to cure the mentally ill by drawing significant quantities of blood from the afflicted until a change in symptoms could be noted. Similarly, the idea of blood transfusions as a possible treatment of mental illness developed in Europe in the late 1550s. A French physician, Jean-Baptiste Denis, performed the first recorded transfusion of blood from dog to dog. At a meeting of the Royal Society on November 23, 1667, Richard Lower demonstrated the transfusion of sheep's blood into a divinity student, Arthur Coga. This event was recorded by Samuel Pepys in his famous diary. Besides France and England, these transfu-

sion treatments were recommended in Germany by physicians Klein and Ettmüller, the latter of which suggested this form of treatment in his 1682 *Chirurgia Transfusoria*.

A 20th-century resurrection of this "bad blood" theory of the cause of mental illness was made in 1977 by psychiatrists J. Wagemaker and R. Cade, who noticed a significant improvement in a paranoid schizophrenic patient following hemodialysis for kidney disease. They hypothesized that an unknown "toxin," which caused schizophrenic symptoms, may have been removed through hemodialysis. Although a further study using hemodialysis on schizophrenics with no kidney disease proved promising and attracted media attention, replications of this study by others have not found the same results.

See also HEMODIALYSIS TREATMENT OF SCHIZOPHRENIA.

blood vessel alterations in schizophrenia Beginning with the ancient Greek and Roman humoral theory of medicine, blood has been associated in various ways with the cause of insanity. By the 19th century, the focus shifted to the vessels that transported blood throughout the body. The possibility that psychotic disorders might be caused by pathological changes in the circulatory system was proposed by the great neuroanatomist Theodor Meynert (1833–92). In 1884 Meynert proposed that the insanities were caused by pathological changes in the circulatory system. Since the brain was fed oxygen and nutrients through the blood-brain barrier (as we now call it), any damage to the blood vessels feeding the brain would cause neuropathology. Meynert, who is best remembered for his contributions to our understanding of the structure and functioning of the central nervous system (as well as for being Sigmund FREUD's professor in Vienna), was a major influence on the first biological psychiatrists of the late 19th century by convincing them that the foundation of mental illnesses illness could be found in studies of neuroanatomy and neuropathology.

After the introduction of DEMENTIA PRAECOX (1893) and SCHIZOPHRENIA (1908) as identifiable psychotic syndromes, attention again turned to the structure and function of the blood vessels in persons with this disease. In his classic 1911 volume *Dementia Praecox, or the Group of Schizophrenias,* Eugen BLEULER discusses abnormalities of the "vasomotor system" in schizophrenia, stating, "We do not yet know anything fundamental about the tensions within the vascular system in psychoses (p. 166)." A page later he then adds the observation, "The fragility of the blood vessels which appears in many schizophrenics, both acute and chronic, seems to indicate a real vascular pathology."

Between 1923 and 1925, while working as a staff psychiatrist under superintendent William Alanson White (1870–1937) of St. Elizabeth's Hospital in Washington, D.C., Noland D. C. Lewis (1889–1979) and his colleagues performed or reviewed the records of autopsies on 4,800 mental patients, of which 601 were diagnosed with dementia praecox (schizophrenia). Lewis concluded that a biological marker of schizophrenia was a primary hypoplasia (underdevelopment or atrophy of tissue or an organ) of the cardiovascular system. Dementia praecox patients, it was found, were characterized by small hearts and a hypoplasia through the vascular system. This, it was hypothesized, led to a general reduction of oxygen to the brain (cerebral hypoxemia), thereby contributing to the development of dementia praecox. According to Lewis, another contributing factor to the development of dementia praecox was the dysfunction of the thyroid and adrenal glands and the gonads. Several confirmatory replications of Lewis's study were performed by others and reported until about 1940. After that time, there was little interest in the role of the vascular system in the etiology or pathophysiology of schizophrenia until 2005.

The inflammatory-vascular theory of schizophrenia (2005) In 2005 D. R. Hanson and Irving L. Gottesman, two prominent researchers in the genetics of schizophrenia, proposed a "genetic-vascular-inflammatory" theory of schizophrenia in the online electronic journal *BMC Medical Genetics*. The theory proposes that the physiological abnormalities leading to illness involve the disruption of the "exquisitely precise regulation of the delivery

of energy and oxygen required for normal brain function." They propose that abnormalities in the metabolism of the central nervous system (as evidenced by abnormal cerebral regional blood flow) arise because genetically modulated inflammatory reactions damage the microvascular system of the brain in reaction to environmental agents. These would include infections, hypoxia, and physical trauma. Damage would accumulate with repeated exposure to triggering agents resulting in exacerbation and deterioration, or healing with their removal. Hansen and Gottesman are proposing "a chronic, smoldering, inflammation of the blood vessels alone" as the source of the many BRAIN ABNORMALITIES IN SCHIZOPHRENIA. And since blood must feed the cells in all areas of the brain, it is no surprise that a century of brain studies in schizophrenia have implicated almost every area of the brain to the disease at one time or another. This theory also brings IMMUNE SYSTEM ABNORMALITIES back into consideration with the hypothesis of the inflammation of the blood vessels leading directly to damage of the blood-brain barrier.

Hansen, D. R., and L. L. Gottesman. "Schizophrenia: A Genetic-Inflammatory-Vascular Synthesis," *BMC Medical Genetics* 6 (2005): 1,471–1,492.

Lewis, N. D. C. "Pathology of Dementia Praecox," *Journal of Nervous and Mental Disease* 62 (1925): 25–260.

Meynert, T. *Klinische Vorlesungen uber Psychiatrie.* Vienna: Braumuller, 1890.

blunted affect A commonly used descriptive term for a significant reduction in the (normal) intensity of the expressed emotions of a person. This is one of the major symptomatic expressions of SCHIZOPHRENIA but can also be witnessed in those persons who are depressed. A related term, FLAT AFFECT, refers to the nearly complete absence of any emotions whatsoever, with the voice sounding monotonous and the face rigid.

Bly, Nellie (1867–1922) The pseudonym of an American journalist for the *New York World,* Elizabeth Seaman (née Cochrane), who faked insanity and gained admittance to the New York City Lunatic Asylum (formerly "mad-house") on Blackwell's Island (now Roosevelt Island). Her serialized exposé was entitled "Ten Days in a Mad House," with the engaging subtitle "Feigning insanity in order to reveal asylum horrors. The trying ordeal of the *New York World*'s girl correspondent." Her articles were published in book form the following year.

Bly detailed abuses involving the unnecessary use of restraints, cruelty to patients by attendants, and unsanitary conditions. These were the same kinds of maltreatment documented by Charles Dickens when he went to the asylum on Blackwell's Island during his trip to America in 1842.

Bly, N. *Ten Days in a Mad House.* New York: 1888.

boarding homes The mentally ill have long resided in boarding homes in the United States, but this type of residence has proliferated since the DEINSTITUTIONALIZATION of psychiatric patients from state hospitals, which began in the 1950s. The idea was that it would be more "normal" for patients to live in the community in such homes. However, in the United States such homes are often found to be undersupervised, with their high turnover rates not infringing upon their profitability to the private owners, who generally have no professional training for supervising such patients. Many psychiatric patients actually prefer the relatively close supervision of the psychiatric hospital, where there are always other people around in case of danger. A cogent critique of the problem of the "homeless mentally ill" in the 1980s is provided in a book by psychiatrist E. Fuller Torrey.

Torrey, E. F. *Nowhere to Go: The Tragic Odyssey of the Homeless Mentally Ill.* New York: HarperPerennial, 1988.

body image in schizophrenia A commonly reported phenomenon in SCHIZOPHRENIA is the experience of distortions in body image. The afflicted person feels, fears, or believes that the physical body itself is changing and will look different to others. Such body distortions can take bizarre

forms in people with schizophrenia and are fully experienced as "real" by them. A former patient of the author's was fully experiencing the feeling that his face had turned into that of a dog's, and that this was how people were actually perceiving him. Others may believe that they have huge, gaping holes in the middle of their torsos through which they experience the wind passing, or feel much thinner or fatter than they really are. The issue of a person's body image has been much discussed in recent years, with the phenomenon of females with anorexia nervosa having the delusional belief that they are being perceived as fat when, in fact, they are emaciated.

Boerhaave, Hermann (1668–1738) A Dutch physician, known for his psychiatric interests. He is acknowledged as the inventor of the "spinning chair," a device of mechanical restraint that was designed to render patients unconscious.

See also CIRCULATING SWING.

borderline cases No diagnostic system is perfect, especially when it comes to identifying mental disorders, and so over the years they must constantly be revised. New categories must be added and others discarded. In the 20th century, the concept that there could be cases that fall between "NEUROSIS" and "PSYCHOSIS" because they have the features of each began to take hold when it was discovered that more and more patients could not be evenly classified by this simple dichotomy. These have been called "borderline cases." However, following the dichotomy of psychotic disorders identified by KRAEPELIN in 1899s, it has generally been found that these so-called borderline cases seemed to be related either to SCHIZOPHRENIA (DEMENTIA PRAECOX) or to BIPOLAR DISORDER (manic-depressive psychosis). Those borderline cases that seemed more closely to resemble schizophrenia are now labeled SCHIZOTYPAL PERSONALITY DISORDER (see BORDERLINE SCHIZOPHRENIA), and those that are allied with manic-depressive psychosis are now called BORDERLINE PERSONALITY DISORDER. However, this distinction was also reflected in the clustering of other types of similar personality disorders in the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised* (1987), with "Cluster A" consisting of schizotypal, paranoid, and schizoid personality disorders. These people are said to appear "odd or eccentric." "Cluster B" is grouped into borderline, antisocial, histrionic, and narcissistic personality disorders, in all of which an individual's behavior appears "dramatic, emotional or erratic."

Spitzer, R. L., J. Endicott, and M. Gibbon. "Crossing the Border into Borderline Personality and Borderline Schizophrenia," *Archives of General Psychiatry* 36 (1979): 17–24.

borderline neuroses See BORDERLINE SCHIZOPHRENIA.

borderline personality disorder Although the descriptions of this disorder differ, the most widely accepted diagnostic description is an erratic pattern of interpersonal relationships characterized by extremes of overidealization and devaluation, problems with self-identity, emotional instability (usually depicted as vaccillating between intense feelings and displays of anger and an "emptiness" depression), and, in the most severe forms of the disorder, self-mutilation and suicide threats and attempts. During stressful periods, psychotic symptoms (such as BIZARRE DELUSIONS or HALLUCINATIONS) can appear. For example, a woman whose daily occupation requires a significant amount of reasoning ability and responsibility (e.g., as a social worker) may nonetheless suddenly be afraid to open the door of her apartment to pay for the pizza she ordered over the telephone, for fear that the delivery boy had poisoned it.

Borderline personality disorder is apparently becoming more common than in the past and is generally diagnosed more in females than in males. Males with similar symptoms tend to be involved in antisocial activities (e.g., stealing, violence, substance abuse) acted-out against others and thus are usually given the diagnosis of antisocial personality disorder. Since this disorder is often difficult for most people to identify, fictional examples from motion

pictures or television are sometimes referred to in the training of mental health professionals. Some fictionalized examples of extreme forms of the disorder are the roles of actresses Glenn Close in the movie *Fatal Attraction* (1987) and Meryl Streep in the movie *Plenty* (1985).

Borderline personality disorder is the best example of the types of BORDERLINE CASES that resemble affective disorders, such as BIPOLAR DISORDER, rather than those that resemble schizophrenia.

See also ANTISOCIAL BEHAVIOR.

borderline schizophrenia A term that became popular in the 1920s but is no longer in use for the type of disorder in which a person has what resembles SCHIZOPHRENIA across many traits but is not fully psychotic and does not have all the symptoms of schizophrenia. Such individuals might now be commonly diagnosed as having a SCHIZOTYPAL PERSONALITY DISORDER. The concept that some patients fall between "NEUROSIS" and "psychosis" with their mental illness is expressed in the use of the word *borderline.* In psychoanalytic publications, this concept formerly meant patients who were intermediate between the groups that were clearly "analyzable" (such as those with neurotic disorders) and "nonanalyzable" (those who are psychotic).

Other clinical terms used over the years that overlap with borderline schizophrenia (with the person who coined them and in what year) are as follows: borderline neurosis (L. P. Clark, 1919); impulsive character (W. Reich, 1925); INCIPIENT SCHIZOPHRENIA (Glover, 1932); SCHIZOAFFECTIVE DISORDER (Kasanin, 1933); AMBULATORY SCHIZOPHRENIA (Zilboorg, 1941); "as-if" personality (H. Deutsch, 1942); LATENT PSYCHOSIS (Federn, 1947); pseudoneurotic schizophrenia (Hoch & Polatin, 1949); and LATENT SCHIZOPHRENIA (Bychowski, 1953). It is also thought that Eugen BLEULER attempted to identify this type of "borderline" person with the term *compensated schizophrenic* in 1911.

Stone, M. H. "The Borderline Syndrome: Evolution of the Term, Genetic Aspects, and Prognosis." In *Essential Papers on Borderline Disorders: One Hundred Years at the Border,* edited by M. H. Stone. New York: New York University Press, 1986.

bouffée délirante Throughout the history of PSYCHIATRY, there has been a distinction been psychotic disorders that are chronic (such as SCHIZOPHRENIA) and those that have a sudden onset, a brief duration, and then just as suddenly disappear. *Bouffée délirante* is a brief psychotic disorder characterized by a sudden onset ("like a bolt from the blue") of DELUSIONS and HALLUCINATIONS of any kind (auditory, visual, tactile, olfactory, gustatory) with a rapid acceleration of often changing delusional features (for example, persecution, megalomania, or hypochondriasis). The disorder disappears completely after a period of weeks or months. Persons who suffer such disorders return to their previous level of functioning and usually remain in full remission. In French psychiatry, the brief or acute psychotic disorder known as the *bouffée délirante* has been an important diagnostic category for more than a century. In the past, this diagnosis was three times more likely to be used by French psychiatrists than that of ACUTE SCHIZOPHRENIA. As recently as 1999, it was reported that the diagnosis of *bouffée délirante polymorphe* was given to as many as one-third of persons admitted with acute psychotic symptoms.

Bouffée délirante was first described in separate books published in 1886 by Honore Saury (1854–?) and Paul-Maurice Legrain (1860–1939), students of the French *alieniste* Valentin Magnan (1835–1916) of the Ste.-Anne Mental Hospital in Paris. In 1893 Magnan proposed this diagnostic category in the context of DEGENERATION THEORY, of which he was a major proponent. The connection of this disorder with degeneration began to disappear in French psychiatry around 1910. The prominent French psychiatrist Henry Ey (1900–77) emphasized the distinction in course and prognosis between *bouffée délirante* and schizophrenia rather than the symptoms, a characteristic feature of French psychiatry as a whole.

See also ACUTE AND TRANSIENT PSYCHOTIC DISORDERS; BRIEF PSYCHOTIC DISORDER; POLYMORPHIC PSYCHOTIC SYMPTOMS.

Ferrey, G. "Evolution et prognostic des troubles psychotiques aigus (bouffée délirante polymorphe)," *Encéphale* 25 (1999): 26–32.

Legrain, P.-M. *Du Délire Chez Dégénérés.* Paris: Deshaye et Lecrosoier, 1886.

Magnan, V. *Lecons cliniques sur les maladies mentales.* 2nd ed. Paris: Battaille, 1893.

Pichot, P. "The Concept of 'Bouffée Délirante' with Special Reference to the Scandinavian Concept of Reactive Psychosis," *Psychopathology* 19 (1986): 35–43.

boundary disturbances in schizophrenia This is a type of perceptual distortion that many schizophrenics report in which they feel they are merging or blending into or are part of another person. Such persons may describe the anxiety felt when in the presence of others as being due to the frightening feeling that they are "sliding into" another person and thus losing the sense of individual identity. Such experiences—although terrifying for most psychotics—have been reported by "normals" who have ingested certain hallucinogens, thus giving rise to the research in the experiential similarities between SCHIZOPHRENIA and hallucinogenic states.

bradykinesia One of the triad of signs of PARKINSONISM that is an adverse effect of the administration of ANTIPSYCHOTIC DRUGS. Along with tremor and rigidity, bradykinesia (or AKINESIA) can occur in patients within weeks to months after the beginning of antipsychotic drug therapy. Bradykinesia is a slowness of motion, whereas akinesia (less common and more severe) is an absence of motion that is not caused by a general paralysis. The person with bradykinesia will frequently seem to have a masklike face, with little expressiveness and infrequent and slow eye blinking. The motions of such a patient can seem "zombielike." The bradykinetic patient is said to turn his or her body "en bloc," as if rigidly frozen into a body without joints. Drooling is a common associated phenomenon with the triad of Parkinsonian symptoms.

Brady- is a prefix that means "slow" and is used in many other clinical behavioral terms.

See also ANTIPARKINSONIAN DRUGS.

brain abnormalities in schizophrenia The search for abnormal structures in the brains of schizophrenics has a long history, beginning with the 19th-century ABLATION STUDIES and continuing with the sophisticated technology of BRAIN IMAGING TECHNIQUES today. It is known that autopsies were performed on the deceased patients at the BETHLEM ROYAL HOSPITAL in London, England, in the early 1800s, as well as in Paris, France, by PINEL and ESQUIROL at about the same time. Between 1802 and 1804, Pinel conducted more than 250 autopsies or "openings" (*ouvertures*) of corpses of deceased mental patients. Only about one-fourth of these patients showed cerebral lesions, thus confirming the belief of Pinel and his student Esquirol after their *recherches cadavériques* that insanity was more likely to be caused by visceral lesions than by brain abnormalities.

The brains of persons with SCHIZOPHRENIA have been studied using two basic approaches, one for dead brains and one for living brains.

The first—and oldest—of these is called *neuropathology.* Neuropathology is the science that correlates autopsy findings in dead brains with the symptoms and behaviors of the person with schizophrenia when they were alive. There are two general types of evidence in neuropathology: macroscopic findings, which involve the observation and measurement of larger structures in the brain (such as the early ablation studies that found lesions with the naked eye); and histological findings, which involve the microscopic examination of the structure and neurochemistry of the various types of cells in the brain (neurons, glial cells). The earliest neuropathological study of the brains of persons with DEMENTIA PRAECOX (schizophrenia) and other psychotic disorders was conducted in Germany by Alois ALZHEIMER (1864–1915) and published in 1897. Alzheimer and Franz Nissl (inventor of a famous staining technique that allows for the study of nerve cells) continued their neuropathological investigation of dementia praecox under Emil KRAEPELIN (1856–1926) in Germany in the very first multidisciplinary research program devoted to discovering the biological causes of MENTAL DISORDERS. The findings of this remarkable research group were summarized in the thick third volume (1913) of four in the eighth edition of Kraepelin's textbook *Psychiatrie.* In the United States, this neuropathological approach was continued in a 1915 study of the brains of

persons with dementia praecox by the prominent Harvard Medical School neuropathologist E. E. Southard (1876–1920). Southard counted himself with Kraepelin and Alzheimer as one of the "brain spot men" in psychiatry who believed schizophrenia was a brain disease. He and the other Kraepelinians were opposed to "mind twist men" such as Adolf MEYER (1866–1950) and Sigmund FREUD, who denied the importance of heredity and brain disease and instead claimed that mental disorders were caused by reactions to environmental stresses (Meyer) or early childhood experiences (Freud).

Due to the lack of technological breakthroughs in the methods of neuropathological research, and the rise of the influence of Freud and psychoanalysis in psychiatry in the United States and Great Britain after the First World War, virtually no neuropathological studies of schizophrenia were conducted from the mid-1920s to the early 1950s. During that time, there were no neuropathological investigations of AFFECTIVE DISORDERS such as manic-depressive illness, a state of affairs that persisted into the late 1990s, when the Stanley Foundation of Bethesda, Maryland, began collecting and comparing the brains of persons with schizophrenia, BIPOLAR DISORDER, and major DEPRESSION. At the 1st International Congress of Neuropathology, which was held in Rome, Italy, in 1953, the general consensus among the world's leading experts was that there were no pathological changes in the nervous system of schizophrenics—a conclusion that greatly strengthened the prominence of theories like Freudian psychoanalysis, which denied the role of biological disease processes in favor of the "schizophrenogenic mother" and other experiential/environmental causes of mental disorders. It would not be until 33 years later, at the 4th World Congress of Biological Psychiatry held in Philadelphia in 1985, that a symposium specifically on the "Neuropathology of Schizophrenia"—the first in history—would be held. By 1990 professional neuropathologists could no longer ignore the growing evidence of brain abnormalities in schizophrenia, and a workshop on "The Neuropathology of Schizophrenia" was held at the XIth International Congress of Neuropathology in Kyoto, Japan. The renewal of interest in the neuropathology of schizophrenia sprang almost directly from the innovative research of German neuropathologist Bernhard Bogerts. Bogerts and his research group published their first of many postmortem studies of schizophrenia in 1983.

The second major approach in neuropathology is the use of BRAIN IMAGING TECHNIQUES (or "neuroimaging" as it is now commonly called) to study the brains of living persons. Neuroimaging studies have examined both the structure and the functioning of living brains of persons with schizophrenia. The very first neuroimaging study of structural abnormalities in schizophrenia was conducted by E. D. Johnstone and colleagues using a CT SCAN. It was published in 1976. Since then, many other studies of structure have used not only CT but also MRI to measure size and volume of certain brain structures. Many other studies have used techniques that look at the functioning of living brains, such as positron emission tomography (PET) and single photo emission computed tomography (SPECT) and functional magnetic resonance imaging (fMRI), which combines both structure and function in its computer generated images.

The scientific literature on the neuropathology of schizophrenia is gigantic and growing weekly. Prominent experts in the field of schizophrenia disagree about the interpretation of almost every neuropathological finding. Neuropathological theories of schizophrenia come and go on a regular basis, with few of them ever completely ruled out. It is distressing to realize how little we know about the brains of persons with schizophrenia. However, a major critical review of the literature on the neuropathology of schizophrenia by Paul J. Harrison was published in the scientific journal *Brain* in 1999. Harrison weighed the strength of the evidence for various claims, and the strongest findings are as follows:

Macroscopic findings (in descending order of certainty):

1. Enlarged lateral and third ventricles of the brain. *Background:* Ventricles are the "spaces" between the lobes of the brain through which the cerebrospinal fluid passes. The first researcher to describe enlarged cerebral ventricles in the postmortem examination of brains from deceased psychotic patients was Ewald Hecker (1843–1909) in 1871.

Hecker described the psychotic disorder HEBEPHRENIA, which Kraepelin later incorporated as one of the three subtypes of dementia praecox. Enlarged ventricles were also described in Johnstone's 1976 CT study and have been described many times since, thus justifying Harrison's certainty about the strength of this finding.

2. Decreased cortical volume. *Background:* There have been many descriptions of the smaller, lighter brains of persons with schizophrenia.

3. Enlarged ventricles and decreased cortical volume are found in persons who have just suffered through their first experience of schizophrenia. *Background:* This strong finding means that brain abnormalities are not due to the progression of the disease, nor are they due to the effects of antipsychotic medications on the brain. The brains of persons who develop schizophrenia are structurally abnormal before they get ill for the very first time.

4. The temporal lobe (including the hippocampus) loses disproportionately more volume than the other areas of the brain.

5. Decreased thalamic volume. *Background:* The thalamus, a major relay center for circuits that send messages traveling throughout the brain, is smaller and lighter than normal in persons with schizophrenia.

6. Cortical volume loss affects gray matter rather than white matter. *Background:* The two large hemispheres of the cortex are made up of different types of cells. The shrinkage of the brains of people with schizophrenia seems to occur in the gray matter, largely made of neurons, rather than the white matter, largely made of glial cells.

7. Enlarged basal ganglia is secondary to antipsychotic medication. *Background:* The basal ganglia, an important structure in the extrapyramidal motor system of the brain, is rich in the NEUROTRANSMITTER DOPAMINE. Because so many antipsychotic drugs work by affecting dopamine pathways in the brain, long-term use of such drugs seems to affect the structure of the brain in areas such as the basal ganglia that are part of the dopamine system.

Histological findings (in decreasing order of certainty):

1. Absence of gliosis as an intrinsic feature
2. Smaller cortical and hippocampal neurons
3. Fewer neurons in dorsal thalamus
4. Reduced synaptic and dendritic markers in hippocampus
5. Maldistribution of white matter neurons
6. Entorhirnal cortex dysplasia
7. Cortical or hippocampal neuron loss
8. Disarray of hippocampal neurons

Harrison also added two additional neuropathological findings: (1) Contrary to speculation since the 1930s, evidence of Alzheimer's disease is not more common in the brains of persons with schizophrenia than in the general population and (2) pathology (brain abnormality) is connected to asymmetries in the cerebral hemispheres in the brain.

As so many others have concluded since Southard did in 1915, Harrison also suggests that the brain abnormalities in schizophrenia most likely originate in the developing embryo and fetus and continue on through childhood and adolescence, culminating in the first episode of schizophrenia in young adulthood in most cases. Such theories of FETAL NEURAL DEVELOPMENT AND SCHIZOPHRENIA, or "neurodevelopmental schizophrenia," as it is sometimes called, have dominated the field since 1986. Michael Knable and Daniel Weinberger of the NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH) argue that "schizophrenia is a developmental abnormality affecting the connectivity of the prefrontal and medial temporal cortices." This so-called disconnection hypothesis of schizophrenia has been defined in many different ways with reference to many different brain regions and neural pathways. Neuropathological studies of the brains of human fetuses at high-risk for developing schizophrenia later in life are lacking, which make it difficult to test hypotheses about the neurodevelopmental causes of schizophrenia.

Two of the major reviewers of the evidence for brain abnormalities in schizophrenia—P. J. Harrison of Oxford University in England and Bernhard Bogerts of the University of Magdeburg, Germany, agree that the best interpretation of all these findings is that much of the evidence clearly points away from the notion that schizophrenia is a progressively neurodegenerative disease, like Alzheimer's disease, and therefore, by default, the findings generally fit the NEURODEVELOPMENTAL

MODEL OF SCHIZOPHRENIA but do not prove it. They agree on consistent evidence for:

(1) cellular changes in the hippocampal formation, a finding first reported in 1984
(2) cellular changes in the dorsal prefrontal cortex (DPFC), first noticed in postmortem studies in the 1990s
(3) decreased volume in the mediodorsal thalamic nucleus

A problem with most neuropathological studies of schizophrenia until the year 2000 was that most changes in the brains of schizophrenics were compared to normal controls and not to the brains of persons who had suffered from other psychiatric disorders (such as bipolar disorder). It is not known if brain abnormalities are similar or distinctively different from persons suffering other psychotic disorders, affective disorders, or personality disorders (for which there are no postmortem brain studies).

Abnormalities in other areas of the brains of persons with schizophrenia have been proposed. Schizophrenia researcher Nancy Andreasen (1938–) of the University of Iowa, noted for leading the research group that published the first MRI study of schizophrenia in 1986, has proposed that abnormalities in the cerebellum, particularly shrinkage in size over time, is correlated with the persistence of negative symptoms, psychosis, and psychosocial impairment. These assumptions form the basis of her COGNITIVE DYSMETRIA theory.

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Knable, M. B., and D. R. Weinberger. "Are Mental Diseases Brain Diseases? The Contributions of Neuropathology to Understanding of Schizophrenic Psychoses," *European Archives of Psychiatry and Clinical Neuroscience* 245 (1995): 224–230.

Southard, E. E. "The Mind Twist and the Brain Spot Hypotheses in Psychopathology and Neuropathology," *Psychological Bulletin* 11 (1914): 117–130.

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Wassink, T. H., N. C. Andreasen, P. Nopoulos, and M. Flaum. "Cerebellar Morphology as a Predictor of Symptom and Psychosocial Outcome in Schizophrenia," *Biological Psychiatry* 45 (1999): 41–48.

brain imaging studies of schizophrenia Also called neuroimaging techniques, these are technologically sophisticated methods for studying the structure and functioning of the brains of living human beings by generating "pictures" or "images" that can then be studied and compared with images from the brains of others. These techniques have revolutionized the neurosciences.

Techniques for "seeing" into a living body and examining its internal structure has a long history in medicine. After the invention of the X-ray technique in 1895 by the German physicist W. C. Roentgen (1845–1923), it was applied the following year by Harvey Cushing (1896–1939) of Johns Hopkins University in Baltimore to a patient who had suffered spinal cord damage due to a bullet injury to the neck. The extensive diagnostic use of X-rays to investigate the living brain and nervous system was pioneered by Arthur Schuller (1874–1957) of Vienna, who published a book on this application in 1918. Beginning in 1918 another technique with a long history in 20th century medicine, the air encephalography, ventriculography, or pneumoencephalography, was introduced at Johns Hopkins. This technique involved injecting air into the space around the spinal cord, which allowed for a clearer contrast image in X-ray studies. The first application of pneumoencephalography to the study of SCHIZOPHRENIA in 1927 found an anomaly that has been a consistent finding in some (but not most) persons with schizophrenia: enlarged cerebral ventricles. This first study was conducted in a mental hospital near Jena, Germany, by Walter Jacobi and H. Winkler under the supervision

of Hans Berger (1873–1941), who had invented the EEG and was experimenting with it at this time. Other techniques that were introduced to image the living brain were carotid arteriography (1947), radionucleotide brain scanning (1948), and the measurement of cerebral blood flow (1948). The measurement of regional cerebral blood flow, or rCBF, played an important role in understanding schizophrenia in the years prior to the introduction of modern neuroimaging technologies. The first modern technique was the CT SCAN, pioneered for use by G. N. Hounsfield in 1973. The first report of the use of brain imaging techniques to study schizophrenic brains was the classic report by E. D. Johnstone and his colleagues published in the British medical journal *Lancet* in 1976. Many other types of brain imaging techniques have been developed and used in schizophrenia research since then.

CT (computerized tomography) scans and nuclear magnetic resonance (NMR), also called MAGNETIC RESONANCE IMAGING (MRI), generate images of the structure of the brain. MRI images are considered to be clearer and of more value. The dynamics of brain functioning, however, are studied with brain imaging techniques such as brain electrical activity mapping (BEAM), cerebral blood flow imaging (also known as regional cerebral blood flow, or rCBF), positron emission tomography (PET SCANS), single photon emission computed tomography (SPECT), and magnetoencephalography (MEG).

Brain imaging studies of schizophrenia have become an important area of research. The neuroimaging studies of the 1970s and 1980s focused on brain structure in schizophrenia, with the first CT study appearing in 1976 and the first MRI study appearing in 1984. However, since the first PET study of schizophrenia appeared in 1980, the vast majority of studies since then has examined the functioning brains of persons with schizophrenia, usually as they performed certain psychological tasks (memory tasks and so on). Most of these recent studies have used (1) a variety of different types of PET techniques using different radioactive materials to trace the many different ways in which brain metabolism works, (2) functional magnetic resonance imaging (fMRI), which came into use in the mid-1990s, and (3) three-dimensional magnetic resonance imaging (3D MRI), first used in schizophrenia research by DeQuardo in 1996.

After 24 years of the widespread use of neuroimaging techniques in schizophrenia research, one fact clearly stands out: almost every region of the brain has been implicated in schizophrenia by at least one or more of these hundreds of studies.

Since these technologies are new, and innovations seem to appear at a rapid rate, it is difficult to arrive at conclusions about schizophrenia with absolute certainty. It is hard to generalize findings from one study to another. Technologies differ; different regions of the brain are examined from one study to another, the tasks they are asked to perform while being scanned differ, and there are serious statistical issues regarding the ways in which this computerized technology measures the brain and then constructs a computer generated image from many thousands of tiny "approximate" measurements. Because these technologies are so new and relatively rare (because they are so expensive to obtain and maintain), researchers know that just about any brain imaging study of schizophrenia is a novel contribution to the field. Some, unfortunately, are not careful about the logic of their experimental design. Many principal investigators who manage neuroimaging research teams are medically trained psychiatrists with little or no background in experimental psychology, a problem that may lead to design flaws and to the wrong interpretation of neuroimaging results. A common bit of gossip among researchers in this field concerns some researchers with deep pockets whose goal is simply to produce impressive color photos of a schizophrenia brain "lighting up" when performing just about any task. Such images can be impressive to administrators with little expertise in neuroimaging when requesting grants or increases in funding. Fortunately, these researchers are in the minority. It is therefore not surprising to find that so many brain imaging studies seem to contradict one another, as has been the case with the issue of HYPOFRONTALITY as a "finding" about the brains of schizophrenics.

University of Pennsylvania schizophrenia researchers Ruben Gur and Raquel Gur remind researchers to keep four basic principles in mind before making claims of new scientific findings

about schizophrenia based on brain imaging studies:

1. First, carry out extensive studies on healthy subjects before leaping to patient studies.
2. Remember to incorporate standard resting measures of brain activity as well as activation measures (as when the subject is asked to perform a psychological task, such as a memory or spatial problem).
3. Suspend judgment until data are available on large, well-characterized, samples of persons with schizophrenia.
4. Integrate functional neuroimaging data with clinical variables and other measures of brain structure and function.

What have brain imaging studies of schizophrenia taught us about the disease? In general, there are two categories of findings which result from the brain imaging techniques used:

(1) Structural imaging studies (CT, MRI) have consistently provided support for evidence first noticed in autopsies that the brains of some schizophrenics have less tissue and less volume than normal brains. The problem seems to be worse for the tissue of the temporal lobes of the brain, particularly the left, and is also true for regions of the frontal lobe and other areas (the hippocampus, the cerebellum, and so on). The reduction in the volume of brain tissue results in the enlargement of the "spaces" or ventricles between the various lobes of the brain, a fact that has also been repeatedly confirmed in these imaging studies. Furthermore, brain imaging studies have confirmed that these structural abnormalities are present even in the earliest phases of the illness and therefore were most likely in existence before the first psychotic symptoms appeared.

(2) Functional imaging studies (PET, SPECT, fMRI) of schizophrenia have documented a widespread disturbance of brain functioning. This seems to be especially true for the connections between two areas: the frontal and temporal lobes. However, many other areas of the brain seem to function abnormally in schizophrenia as well when compared to the functioning of normal brains.

These functional imaging studies are the primary basis of the so-called DISCONNECTION THEORIES OF SCHIZOPHRENIA. These theories claim that there is a dynamic imbalance between different regions of the brain, and as such they do not cooperate with one another in a normal fashion. Various versions of this disconnection theory have been proposed that implicate different regions of the brain. The most prominent disconnection theory involves the "fronto-temporal network." As one of the most prominent researchers in functional imaging studies of schizophrenia, Peter F. Liddle, describes the general "disconnection" hypothesis, "the essential functional abnormality in schizophrenia is a disturbance of functional connectivity in the neural networks serving the supervisory mental functions responsible for the initiation, selection and monitoring of self-generated mental activity."

Some support for neurodevelopmental and disconnection theories of schizophrenia have come from MAGNETIC RESONANCE SPECTROSCOPY IMAGING (MRSI) studies of both adults and children with schizophrenia and their biological relatives. These studies show that people with schizophrenia, both children and adults, and their biological relatives have a smaller than normal regional NAA (N-acetylaspartate) chemical signal, indicating neuron damage or abnormalities in functioning of certain neural circuits or pathways.

The results of neuroimaging studies of schizophrenia have been combined with postmortem studies of BRAIN ABNORMALITIES IN SCHIZOPHRENIA and with studies of cognitive functioning (memory, spatial ability, and so on) to give us a fuller picture of what is happening inside the brain of a person with schizophrenia.

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Liddle, P. F. "Brain Imaging." In *Schizophrenia,* edited by Hirsch, S. R., and D. R. Weinberger. London: Blackwell Science, 1995, pp. 425–439.

McCarley, R. W., et al. "Neuroimaging and the Cognitive Neuroscience of Schizophrenia," *Schizophrenia Bulletin* 22 (1996): 703–725.

brain injury and psychosis See MEDICAL DISORDERS THAT MIMIC PSYCHOTIC DISORDERS.

brain tumors and psychosis See MEDICAL DISORDERS THAT MIMIC PSYCHIATRIC DISORDERS.

brief psychotic disorder In *DSM-IV-TR* (2000), a psychotic disorder lasting at least one day but less than one month that results in a full return to premorbid levels of functioning. The presence of one or more of the following symptoms must be in evidence: DELUSIONS, HALLUCINATIONS, disorganized speech, or grossly disorganized or catatonic behavior. There are three types:

(1) with a marked stressor preceding the onset of symptoms (*brief reactive psychosis*)
(2) without a marked stressor, indicating the psychosis is not a reaction to stress or trauma
(3) with postpartum onset (onset within four weeks of giving birth (postpartum psychosis) In *ICD-10* (1992) these are known as ACUTE AND TRANSIENT PSYCHOTIC DISORDERS. After one month, if the symptoms persist, in *DSM-IV-TR* the diagnosis is changed to SCHIZOPHRENIFORM DISORDER. If symptoms of schizophreniform disorder persist more than six months, the diagnosis may then be changed to schizophrenia, schizoaffective disorder, an atypical affective disorder, or a psychotic disorder not otherwise specified.

See also ATYPICAL PSYCHOTIC DISORDERS.

Brierre de Boismont, Alexandre (1798–1881) A noted French *aliéniste* who is most remembered for his comprehensive study of HALLUCINATIONS published in 1853. This study examined the phenomenon of hallucinations not only in the mentally ill, but also in hypnosis ("magnetic visions"), religious experience, and in other ALTERED STATES OF CONSCIOUSNESS. Brierre de Boismont was a disciple of ESQUIROL and was a member of the famous "Esquirol Circle."

Brierre de Boismont, A. *Hallucinations: Or, the Rational History of Apparitions, Visions, Dreams, Ecstasy, Magnetism and Somnambulism.* Philadelphia: Lindsay & Blakiston, 1853.

Brigham, Amariah (1798–1848) One of the original 13 founders of the American Psychiatric Association in 1844 (then called the Association of Medical Superintendents of American Institutions for the Insane). In 1843 he became the superintendent of the newly opened Utica State Hospital in New York. The following year, in 1844, he started the *American Journal of Insanity,* which later became the *American Journal of Psychiatry,* as it is known today. He printed it in the hospital with the assistance of patients in work programs.

Broadmoor Hospital Broadmoor has achieved notoriety in the British Isles as the place where the most homicidal of "homicidal maniacs" are kept. Since it opened its doors in 1863, Broadmoor has been where the most dangerous or violent mentally ill criminals have been placed. Prior to its construction in Crowthorne, Berkshire, such dangerous patients were kept in a special "gallery" at the BETHLEM ROYAL HOSPITAL in London.

Brosius, C. M. (1825–1910) A German psychiatrist who, along with Wilhelm GRIESINGER, is noted for quickly and successfully instituting policies of nonrestraint for the patients in German asylums and hospitals in the mid-1800s. German institutions took the lead in this more humane treatment of the mentally ill, whereas hospitals in the rest of Europe, notably England and France, only significantly improved near the end of the 1800s.

Broussais, Francois Joseph Victor (1772–1838) A French physician, army surgeon, and professor of general pathology of the University of Paris who was a bitter enemy of Philippe PINEL. Broussais entertained the theory that mental illness was caused by gastrointestinal "irritation." BLEEDING, PURGING, and diets were suggested as treatments for this irritation.

Broussais, F. J. V. *De l'irritation et de la folie.* Paris: 1828.

Bucknill, Sir John Charles (1817–1897) A major figure in 19th-century British PSYCHIATRY, Bucknill was an important advocate of nonrestraint policies and the boarding-out of mental patients from the hospitals to community placements. Superintendent of the Devon Asylum from 1844 to 1862, he also became the first president of the Association of Medical Officers of Asylums and Hospitals for the Insane (now the Royal College of Psychiatrists), and in 1862 he rose to the prominent position of Lord Chancellor's Visitor in Lunacy. Bucknill was also the first honorary member of the American Psychiatric Association; together with D. H. Tuke he wrote a standard textbook, *A Manual of Psychological Medicine,* in 1858 (2nd ed., 1882) that was widely used for many years.

Burghölzi Hospital The famous psychiatric hospital and clinic that is associated with the University of Zürich in Switzerland. After accepting a position as professor of medicine at the University in 1860, Wilhelm GRIESINGER assisted in planning and overseeing the construction of the new hospital. Griesinger also became its first director upon opening. Other famous directors of the Burghölzi over the years have been August Forel, Eugen BLEULER, and Manfred BLEULER. Burghölzi holds a special significance for the history of the scientific study of SCHIZOPHRENIA and the psychotic disorders because it was while they worked together there that Eugen Bleuler and C. G. JUNG wrote their famous monographs on "DEMENTIA PRAECOX," and it is the place where the term *schizophrenia* was first coined and used. Jung also carried out his famous diagnostic "word-association" experiments at Burghölzi in the early 20th century. The Burghölzi was the site of a noted longitudinal study of schizophrenia, carried out by Manfred Bleuler.

See also COURSE OF SCHIZOPHRENIA.

butyrophenones See ANTIPSYCHOTIC DRUGS.

C

cacodemonomania This is one of the two types of DEMONOMANIA identified by ESQUIROL in his chapter on the topic in his 1838 textbook, *Des Maladies mentales.* The word is used to refer to those mentally ill persons who believe they are possessed by, or in contact with, evil spirits or Satan himself. It is derived from two Greek words, *kakos* and *daimon,* for "bad" and "demon." The word *daimon* in the classical world did not have a bad connotation, as Esquirol notes, but had more of the meaning of a "guardian spirit" or "spiritual guide," which a person could consult. Esquirol asserts the diagnosis of cacodemonomania should be applied to "all those unfortunate beings who fancied that they were possessed by the devil, and in his power; who were convinced that they have been present at the imaginary assemblies of evil spirits, or who feared damnation, and the misery of eternal fire."

Possession by "evil spirits" has been attributed as a cause of mental illness for thousands of years. Cacodemonomania can still be witnessed from time to time in certain individuals even today, and a modern case of this disorder, reported in the psychiatric literature as recently as 1987, can be found reprinted in the volume by Richard Noll listed below.

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity,* trans. E. K. Hunt. 1838. Reprint, Philadelphia: Lea & Blanchard, 1845.

Kemp, S., and K. Williams. "Demonic Possession and Mental Disorder in Medieval and Early Modern Europe," *Psychological Medicine* 17 (1987): 21–29.

Noll, R. *Vampires, Werewolves and Demons: Twentieth Century Reports in the Psychiatric Literature.* New York: Brunner/Mazel, 1991.

Salmons, P. H., and D. J. Clarke. "Cacodemonomania," *Psychiatry* 50 (1987): 50–54.

Cameron, Donald (1901–1967) A British psychiatrist who became the first president of the World Psychiatric Association. While a professor of psychiatry at McGill University in Montreal, Canada, in the 1940s, Cameron helped popularize the form of treatment of SCHIZOPHRENIA known as INSULIN COMA THERAPY in North America.

camisole A heavy-canvas coat, reaching from neck to waist, with long, closed sleeves that are designed to wrap the wearer's arms across the chest and are tied with cords behind the wearer's back. Apparently, the 19th-century term *camisole* was merely a euphemism for a type of STRAITJACKET, a term that had taken on a negative connotation by the end of the 1800s. In *A Mind That Found Itself,* Clifford BEERS graphically describes his torturous experience of being placed in a camisole in 1902, and describes this type of mechanical restraint as follows: "A camisole is a type of straight-jacket; and a very convenient type it is for those who resort to such methods of restraint, for it enables them to deny the use of a straight-jacket all. A straight-jacket, indeed, is not a camisole, just as electrocution is not hanging."

Beers, C. *A Mind That Found Itself.* New York: Doubleday, 1908.

Canada The only major study of prevalence rates for SCHIZOPHRENIA in Canada was carried out by research psychiatrist H. M. B. Murphy and his colleagues in the 1960s. In a survey of 14 Canadian villages with different ethnic compositions, he found an overall age-corrected prevalence rate of 4.6 per 1,000 in Canada. However, considering that he used a much narrower (at the time)

definition of schizophrenia than was accepted in the United States, the Canadian rate would have been much higher if the broader, American criteria had been used. Murphy found that traditional, "Old French" villages had a much higher rate of schizophrenia than other types, measuring twice as high as Anglo-Protestant villages. Furthermore, Canadian Catholics as a whole had a much higher rate of schizophrenia than Canadian Protestants.

Many studies have also been conducted in Canada on the native Canadian Inuit populations. Hudson Bay Inuit groups were found to have higher prevalence rates for schizophrenia, with studies ranging from 12.7 to 30.4 per 1,000.

Schizophrenia may also be especially prevalent among Canadian Indians, particularly the Cree and Salteaux Indians of northern Saskatchewan, where the age-corrected prevalence rate was 11.0 in one study. The same study looked at the non-Indian population in the area and found that the age-corrected prevalence rate for schizophrenia was only 2.4 per 1,000.

Murphy, H. B. M., and M. Lemieux. "The Problem of High Schizophrenic Prevalence in One Type of French-Canadian Rural Community," *Canadian Psychiatric Association Journal* 12 (1967): 72–81.

Sampath, H. "Prevalence of Psychiatric Disorders in a Southern Baffin Island Eskimo Settlement," *Canadian Psychiatric Association Journal* 19 (1974): 363–367.

Roy, C., et al. "The Prevalence of Mental Disorders among Saskatchewan Indians," *Journal of Cross-Cultural Psychiatry* 1 (1970): 383–392.

candidate genes Genes that are believed to be implicated in the cause of a particular disease (pathogenesis).

See also BIOLOGICAL MARKERS OF SCHIZOPHRENIA; GENETICS STUDIES; GENOME.

Capgras syndrome A delusional condition that some psychotic individuals develop in which they believe that a person, usually closely related in some way, has been replaced by an impostor or a "double." The DELUSION is often quite fixed and can be very distressing for the concerned family member, friend, or caretaker whose identity is constantly denied even when confronted with the absurdity of the notion. Usually the person accused of being an "impostor" or a "replacement" is also thought to bear bad intentions toward the delusional person.

The very first case was described by Jean Marie Capgras (1873–1950) and J. Reboul-Lachaux in 1923: a woman with a chronic paranoid psychosis who insisted that various individuals involved in her life had been replaced by "doubles." Their name for the condition was *l'illusion des sosies*, or "the illusion of doubles," but it is now almost universally known as the Capgras syndrome.

Capgras syndrome is one of the MISIDENTIFICATION SYNDROMES that are sometimes witnessed in psychotic individuals. As is the case with many fictional works of horror or science fiction that exploit common human fears, the 1956 motion picture *Invasion of the Body Snatchers* is based on a premise very similar to the fearful experience of persons suffering from Capgras syndrome.

Recent neuroimaging and neuropsychological studies of Capgras syndrome suggest that this delusional disorder is associated with right hemisphere abnormalities in the brain.

Capgras, J. M., and J. Reboul-Lachaux. "L'illusion des 'soises' dans um delire systematize chronique," *Annales Medico-Psychologiques* 81 (1923): 186–193.

Edelstyn, N. M., and F. Oyebode. "A Review of the Phenomenology and the Cognitive Neuropsychological Origins of the Capgras Syndrome," *International Journal of Geriatric Psychiatry* 14 (1999): 48–59.

carbamazepine A drug generally known by its trade name, Tegretol, used to treat seizure disorders. However, it has come into use in psychiatric centers as a treatment for certain psychotic patients who tend toward violence. It is structurally related to the heterocyclic antidepressants (such as imipramine and others) and to another anticonvulsant, phenytoin (trade name, Dilantin). It is also used in the treatment of some forms of BIPOLAR DISORDER.

carbon dioxide therapy One of the somatic or physical therapies for SCHIZOPHRENIA that was used

by American psychiatrists from 1929 until the late 1940s. In 1929 Arthur Solomon Loevenhart of the University of Wisconsin published a report that indicated that the inhalation of carbon dioxide produced a "cerebral stimulation" that alleviated catatonic symptoms in schizophrenia, MANIC-DEPRESSIVE ILLNESS, and involutional MELANCHOLIA (DEPRESSION in late life). Patients breathed in a gas mixture of 30 percent carbon dioxide, far greater than the average atmospheric amount of .03 percent. Patients were given as many as 150 inhalation sessions. This form of therapy has not been used since the 1940s.

Loevenhart, A. S., W. F. Lorenz, and R. M. Waters. "Cerebral Stimulation," *Journal of the American Medical Association* 92 (1929): 880–883.

cardiazol therapy See METRAZOL SHOCK THERAPY.

cardiovascular hypoplasia See BLOOD VESSEL ALTERATIONS IN SCHIZOPHRENIA.

catalepsy Another name for CATATONIC WAXY FLEXIBILITY, or *flexibilitas cera*.

catathymic crisis The crisis state induced in a person who is aware that he or she is developing a psychosis, or for whom an existing psychotic state is worsening. The terrible fear and anxiety caused by this awareness of a loss of control and a degeneration into mental chaos somehow leads the person to commit a violent or other antisocial act. As first described by Wertham in 1937, the crisis-provoked act is intended as a cry for help by the afflicted person. Wertham writes: "One gains the impression that the violent act in these cases prevents the developments that would be far more serious for the patient's health. The overt act seems to be a rallying point for the constructive forces of the personality."

Wertham, F. "The Catathymic Crisis," *Archives of Neurology and Psychiatry* 37 (1937): 974.

catatonia, or catatonic type Catatonia is a syndrome of abnormal movement. It can be associated with mood disorders (such as major DEPRESSION) or with disorders of cognitive deterioration or deficit (SCHIZOPHRENIA). Catatonic behavior can take many forms (see the entries below), from stupor (the classic picture of catatonia that we all have), to excitement, catalepsy (catatonic waxy flexibility), negativism, mutism, apparently voluntary assumption of inappropriate or bizarre posturing, stereotyped movements, off mannerisms, prominent grimacing, echolalia, or echopraxia. All these characteristics are part of the clinical picture of the "catatonic type" of schizophrenia in *DSM-IV-TR* (2000), any two of which are necessary for a diagnosis of this type.

Catatonia was considered an independent psychotic disorder in its own right until 1899. In that year Emil KRAEPELIN reframed catatonia as a "form" of DEMENTIA PRAECOX along with hebephrenic and paranoid forms. In 1911 Eugen BLEULER likewise considered catatonia as a subtype of schizophrenia and not as an independent disorder.

Catatonia (*Katatonia*) was a term coined by Karl Ludwig KAHLBAUM as early as 1868, but he first used it in print in his 1874 monograph, *Die Katatonie, oder das Spannungsirresein*. In Kahlbaum's view, catatonia was essentially a motility psychosis, a disorder of movement, which manifested in overactive and underactive forms. In the decades after 1899, as first Kraepelin's dementia praecox, then Bleuler's schizophrenia, were accepted by psychiatrists in primarily German and English-speaking countries (but not so in France or French-speaking countries until, arguably, sometime after *DSM-III* appeared in 1980), catatonia lost its independence. After the introduction of CHLORPROMAZINE and the PHENOTHIAZINES in MENTAL HOSPITALS after 1954, it was claimed that catatonia had virtually disappeared because of the effects of ANTIPSYCHOTIC DRUGS. However, such symptoms do indeed still appear in patients treated with these drugs but are now often interpreted as aspects of their side effects, particularly a form known as the NEUROLEPTIC MALIGNANT SYNDROME (or NMS), which can be lethal. Indeed, "lethal catatonia" had long been described in the old psychiatric literature and the symptoms and lethal course are similar to that of

NMS. Catatonia has long been known to respond to treatment with barbiturates, benzodiazepines, and electroconvulsive therapy. There is no firm scientific evidence from biological, genetic, or longitudinal studies of schizophrenia that catatonia is a distinct subtype of schizophrenia, but for historical and clinical reasons it is kept within schizophrenia as a variant of this disorder.

Kahlbaum, K. *Die Katatonie, oder das Spannungsirresein.* Berlin: Hirschwald, 1874.

catatonic excitement A behavior that occurs intermittently in catatonic persons in which they move about in a very active fashion without any apparent purpose and seemingly unguided by environmental cues. This excited motor behavior can occur between periods of other types of less mobile catatonic behavior. In the late 19th century, catatonic excitement was sometimes thought to result in death from exhaustion, and other names for it included "acute delirium mania," "BELL'S MANIA," and "BELL'S DISEASE."

See also AKATHISIA; NEUROLEPTIC MALIGNANT SYNDROME.

catatonic negativism A seemingly purposeless resistance to all attempts, whether physical or verbal, to being moved. If the person is passive, he or she may simply be unresponsive. When in a more active state, the person may be oppositional and do the opposite of what is asked.

catatonic posturing The bizarre or unusual postures that catatonic persons can maintain for a long period of time.

catatonic rigidity The maintenance of a muscularly tense, rigid position by a catatonic person, despite the forceful efforts of others to move him or her.

catatonic stupor The common image of a catatonic person's behavior. The person behaves as if in a stupor, hardly moving and relatively unresponsive to his or her environment.

catatonic waxy flexibility This is a behavior found in persons with the rare catatonic subtype of SCHIZOPHRENIA in which a person's body or limbs can be molded into a particular position and will remain passively in place, as if the person were a doll or made of wax. An older medical term for waxy flexibility is *cera flexibilitas.*

catecholamines A class of biogenic amines that includes the NEUROTRANSMITTERS dopamine, epinephrine, and norepinephrine.

See also BIOGENIC AMINE HYPOTHESIS; DOPAMINE HYPOTHESIS; INDOLAMINES; HISTAMINES.

cats and schizophrenia The current widespread practice of humans keeping cats as house pets did not begin until the middle of the 1700s and became very popular by the end of the 1800s. The rise in rates of insanity from 1750 until the present parallels this phenomenon. The question is: Do cats cause insanity? At least two controlled studies have found that persons with SCHIZOPHRENIA and BIPOLAR DISORDER have had a greater exposure to cats in childhood compared with persons who do not have those MENTAL DISORDERS. This issue has been explored in the context of VIRAL THEORIES by E. Fuller Torrey of the Stanley Research Foundation in Bethesda, Maryland. In the past decade several studies have found evidence that *Toxoplasmosis,* an infectious disease caused by a virus in cat feces or in undercooked meat, may be implicated in schizophrenia. Several studies have found antibodies to this virus in persons with schizophrenia as well as in the mothers of persons with schizophrenia.

CAT scan See CT SCAN.

causality, teleologic An aspect of the thinking of schizophrenics, as identified by Silvano ARIETI, in

which events in the world are interpreted as purposeful and due to somebody's will. Arieti compares this aspect of schizophrenic cognition to the thought patterns of children and people in primitive societies. Teleologic causality is contrasted with "deterministic causality," the more rational and scientific way in which most "civilized" normal adults attribute causes to events they experience.

cautery treatment A rather primitive form of "shock treatment" used on the mentally ill in the 18th and early 19th centuries in which they would be touched on the head or neck with a hot iron poker. Alternatively, the ancient technique of igniting moxa (small combustible cones from a plant that was introduced into Europe from Asia) on the skin to cauterize it. A treatment manual advocating the use of this method was written by French psychiatrist L. Valentin and published in 1815. ESQUIROL was greatly influenced by this book and successfully applied the treatment himself. This is how he described its use:

> I cannot omit making some remarks respecting the use of fire and moxa, applied to the top of the head, and over the occiput or neck in mania. Doctor L. Valentin has published some valuable observations concerning the cure of mania by the application of fire. I have many times applied the iron at a red heat to the neck, in mania complicated with fury, and sometimes with success.

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity* (1838), trans. E. K. Hunt. Philadelphia: Lea & Blanchard, 1845; first published, 1838.

Valentin, L. *An Essay and Observations Concerning the Good Effects of the Actual Cautery, Applied to the Head in Various Disorders.* 8 vols. Nancy: 1815.

cera flexibilitas See CATATONIC WAVY FLEXIBILITY.

Cerletti, Ugo (1877–1963) Italian psychiatrist and inventor of ELECTROSHOCK (or "electroconvulsive") THERAPY. Cerletti was inspired to invent this treatment in a rather macabre way—by observing the reactions of pigs who were given electrical shocks just before slaughter. Together with his colleague, Lucio Bini, Cerletti perfected his new treatment, and the very first schizophrenic to receive this treatment did so on April 15, 1938. Electroconvulsive therapy, or ECT as it is commonly referred to, was considered a safer and more humane type of CONVULSIVE THERAPY than the one invented by Hungarian psychiatrist VON MEDUNA, in which convulsions were induced by pharmacological means.

Cerletti had a varied medical career, undergoing training in Turin, Rome, Paris, and Heidelberg, where he was exposed to Emil KRAEPELIN and his associates. Cerletti seems to have always been attracted to unconventional ideas about medical treatments for MENTAL DISORDERS. Near the end of his life, he attempted to find a chemical alternative to his own electroshock therapy, which would have none of the harsh side effects of the convulsive therapies. He concocted a serum, from the brains of animals that had been subjected to repeated electroshock sessions, that he thought would have the same therapeutic effect as electroshock therapy. This serum was alleged to contain a special chemical created in these animal brains from the treatments—vitalizing substances that Cerletti called *aeroagomines*—which he believed he could inject into schizophrenics and obtain similar results. However, Cerletti's work in this area has been discounted.

Cerletti, U. "Old and New Information about Electroshock," *American Journal of Psychiatry* 107 (1950): 87–94.

Cerletti, U., and L. Bini. "L'Electroshock," *Arch. Gen. Neurol. Psichiatr. Psicoanal.* 19 (1938): 266.

ceruloplasmin hypothesis In 1957 Swiss biochemist S. Akerfeldt announced research findings that suggested that an increased level of the copper-containing substance ceruloplasmin might be related to the development of SCHIZOPHRENIA. He developed a relatively simple test, which he thought could discriminate between the BIOLOGICAL MARKERS OF SCHIZOPHRENIA and other mental diseases.

Despite media attention, his theory was soon disproved when it was found that the level of ceruloplasmin depended on the amount of ascorbic acid (vitamin C) in the blood, and institutionalized psychiatric patients have been known to have low serum ascorbic acid levels.

See also TRANSMETHYLATION HYPOTHESIS OF SCHIZOPHRENIA.

Akerfeldt, S. "Oxidation of N_1N-Dimenthyl-p-phenylenediamine by Serum from Patients with Mental Disease," *Science* 125 (1957): 117–123.

Ceylon (Sri Lanka) A 1974 study of the prevalence rate for SCHIZOPHRENIA in Ceylon (now Sri Lanka) found a rate of 3.7 per 1,000.

Wijesinghe, C. P., et al. "Survey of Psychiatric Morbidity in a Semi-urban Population in Sri Lanka," *Acta Psychiatrica Scandinavica* 58 (1978): 413–441.

chemical restraint The use of drugs, as opposed to MECHANICAL RESTRAINTS (such as straps, STRAITJACKETS, MUFFS) to subdue psychiatric patients. Although ANTIPSYCHOTIC DRUGS were only brought into use in 1952 to treat psychotic disorders by reducing their symptoms, many different types of drugs have been used for centuries to restrain patients engaged in undesirable behaviors. Often such pharmacological agents were used as punishment. In the 18th and 19th centuries, such drugs may have been administered as a daily "physic" said to improve the health of a patient. Camphor and opiates in particular are mentioned in these early accounts. By the end of the 19th century many sedatives had been created that were then widely used (often to the point of excess) in mental hospitals. In his autobiography of his life as a mental patient, Clifford BEERS makes the following remarks about chemical restraint:

> Chemical restraint (sometimes called medical restraint) consists in the use of temporarily paralyzing drugs—hyoscine being the popular "dose." By the use of such drugs a troublesome patient may be rendered unconscious and kept so for hours at a time. Indeed, very troublesome patients (especially when attendants are scarce) are not infrequently kept in a stupefied condition for days, or even for weeks—but only in institutions where the welfare of the patients is lightly regarded.

Chemical restraint is one of the main instruments of psychiatric abuse in many countries.

See also ABUSE OF PSYCHIATRIC PATIENTS.

Beers, C. *A Mind That Found Itself*. New York: Doubleday, 1908.

chemistry of the brain See BIOCHEMICAL THEORIES OF SCHIZOPHRENIA.

cheromania A term used in the Middle Ages to describe the unnatural euphoric reaction to epidemics (such as the plague) and other disasters. It is equivalent to the elation reported in "maniacs" in archaic psychiatric textbooks and to the same behavior in persons undergoing a "manic episode" in today's nomenclature.

Chiarugi, Vincenzo (1759–1820) Sometimes referred to as the "Pinel of Italy." Chiarugi was an Italian physician appointed in 1789 by the Grand Duke Pietro Leopoldo of Tuscany to head the Hospital of Bonifacio in Florence. His work with the mentally ill at that hospital led to his publishing several works regarding mental illness, including a volume of 100 observations on mental illness. He believed that psychoses were the result of a deterioration of the brain, thus linking him with modern theories of the organic etiology of mental illness. He was also an early reformer and an opponent of cruel or unnecessary forms of restraint, and he shares an historic distinction as one of the earliest proponents of nonrestraint policies, with PINEL in France and William Tuke of the YORK RETREAT in England. A translation of an indicative passage from one of Chiarugi's works is provided by historian of psychiatry George Mora:

> It is a supreme moral duty and medical obligation to respect the insane individual as a person. It is especially necessary for the person who treats the mental patient to gain his confidence and trust. It is best, therefore, to be tactful and understanding and try to lead the patient to the truth and to instill reason in him little by little in a kind way. . . . The attitude of doctors and nurses must be authoritative and impressive, but at the same time pleasant and adapted to the impaired mind of the patient. . . . Generally it is better to follow the patient's inclinations and give him as many comforts as is advisable from a medical and practical standpoint.

Chiarugi, V. *Della pazzia in genere e in specie trattato medico analitico con una centuria di observazioni.* Florence: 1973–1974.

———. *On Insanity and Its Classification,* ed. and trans. G. Mora. Canton, Mass.: Science History Publications, 1987.

Mora, G. Vincenzo. "Chiarugi (1759–1820) and His Psychiatric Reform in Florence in the Late 18th Century," *Journal of the History of Medicine* 14 (1959): 431.

childhood-onset schizophrenia Childhood-onset schizophrenia is a very rare form of SCHIZOPHRENIA. It is defined by the onset of the typical psychotic symptoms of schizophrenia before the 18th birthday. This disorder is now sometimes called "neurodevelopmental schizophrenia." Although it had practically disappeared from the scientific literature, in 1994 several studies were published that resurrected interest in this disorder. Since then, there has been an explosion of research on the very small population of children who could be located that have childhood-onset schizophrenia. Although childhood-onset schizophrenia is rare, it resembles the "adolescent-onset" and "adult-onset" versions of schizophrenia. There are similarities between childhood, adolescent, and adult-onset schizophrenias in terms of their poor premorbid histories, their performance on psychological tests, and certain neuroanatomical and neuroimaging findings. Thus, it is thought that childhood-onset schizophrenia is continuous with at least some of the later-onset versions of schizophrenia and not a separate disease process. For example, abnormalities in the cerebral ventricles of children with schizophrenia tend to worsen in adolescence. Also, in MAGNETIC RESONANCE SPECTROSCOPY IMAGING studies, smaller than normal regional chemical signals for N-acetylaspartate (NAA) are found in childhood-onset schizophrenics, adult-onset schizophrenics, and biological relatives of schizophrenics. In general, the course of childhood-onset schizophrenia is more severe than the later-onset varieties of this disease.

No one knows why there is an earlier age of onset in this disorder. Several possible factors behind early onset are: (1) increased genetic load, especially if both parents are schizophrenic or have a high-risk for schizophrenia themselves, (2) increased exposure to harmful environmental forces, either during fetal development, infancy, or early childhood, that affect the brain and nervous system, (3) precocious brain maturation (the brain develops abnormally fast in some respects and not in others, causing a disconnection between different areas of brain functioning), and (4) perhaps a premature exposure of the nervous system to hormones that are only usually released during puberty.

Other names for this disorder that can still be found in the literature are childhood schizophrenia, developmental psychosis, childhood psychosis, symbiotic psychosis, and atypical development. *DSM-IV* (1994) allows the diagnosis of schizophrenia in children only if prominent DELUSIONS and HALLUCINATIONS are present for at least a month in a child who has already been known to have a history of autistic disorder or a pervasive developmental disorder.

Since the neurodevelopmental model of schizophrenia has emerged as a dominant scientific paradigm, the study of childhood-onset schizophrenia is combined with the data from studies of FETAL NEURAL DEVELOPMENT, adolescent-onset, adult-onset, and LATE-ONSET schizophrenia to construct a picture of the natural course of this terrible disease over the human life span.

Alaghband-Rad, J., S. D. Hamburger, J. N. Giedd, J. A. Frazier, and J. L. Rapoport. "Childhood-onset Schizophrenia:

Biological Markers in Relation to Clinical Characteristics," *American Journal of Psychiatry* 154 (1997): 64–68.
Howells, J. G., and W. R. Guirguis. "Childhood Schizophrenia 20 Years Later," *American Journal of Psychiatry* 41 (1984): 123–128.
McKenna, K., C. T. Gordon, and J. L. Rapoport. "Childhood Onset Schizophrenia: Timely Neurobiological Research," *Journal of the American Academy of Child and Adolescent Psychiatry* 33 (1994): 771–781.
Murray, R. M. "Toward an Aetiological Classification of Schizophrenia," *Lancet* 1 (1985): 1,023–1,026.
Rapoport, J. L., J. Giedd, S. Kumra, et al. "Childhood-onset Schizophrenia: Progressive Ventricular Change during Adolescence," *Archives of General Psychiatry* 54 (1997): 897–903.

childhood psychosis See CHILDHOOD SCHIZOPHRENIA.

children at risk for schizophrenia See HIGH-RISK STUDIES.

chiromania An archaic term for madness caused by MASTURBATION, a common belief of psychiatrists throughout the 19th century and earlier. It is derived from the Greek words for "hand" and "insanity."

chlorpromazine The first true ANTIPSYCHOTIC DRUG, approved for use in the United States in March 1954. The drug is a PHENOTHIAZINE and is more commonly known by its trade name, THORAZINE; it was named by the manufacturer, Smith, Kline, and French, after the Norse god of thunder, Thor.

choromania An archaic term for the uncontrollable impulse to dance or sway. The famous "dancing manias" that were epidemic in the Middle Ages are another example of this. Perhaps the classic reference to "dancing manias" or "frenzies" is the work of the 19th-century German scholar J. F. C. Hecker, and translations of representative excerpts of his writings can be found in the appendix to a book by psychiatrist Harold Mersky of the London Psychiatric Hospital, London, Ontario, Canada.

Hecker, J. F. C. *Die grossen Volkskrankheiten des Mittelalters, Historisch-pathologische Untersuchungen . . . ,* ed. August Hirsch. Berlin: Th.Chr.Fr.Enslin, 1865.
Mersky, H. *The Analysis of Hysteria.* London: Baillière Tindall, 1979.

chromosome Within the nucleus of each cell in the human body there are rodlike organic bodies (normally 46 in humans) called chromosomes, which are the bearers of GENES. Each chromosome is made up of an extended double helix of DNA and associated proteins. Chromosomes are arranged in 23 different pairs. One pair, made up of the X and Y chromosomes, is called the sex chromosomes and is responsible for the transmission of genetic information regarding sex differentiation. The other 22 pairs (numbered from 1 to 22) are called autosomes. The 46 chromosomes in humans were first observed directly by scientists when new techniques were developed by Tijo and Levan in 1956. Since that time, a series of studies have been conducted on large samples of psychiatric patients of varying diagnoses—especially schizophrenics—with little success in detecting specific abnormalities. This has changed with the development of clearer research diagnostic criteria for schizophrenia and the more advanced research technologies of molecular genetics.

A series of techniques known as chromosome mapping attempt to determine the position of specific genes on specific chromosomes and then construct a diagram of each chromosome showing the relative position of genes. There are estimated to be between 25,000 to 30,000 human genes, most of which are yet to be identified.

See also GENETICS STUDIES.

Tijo, H., and A. Levan. "The Chromosome Number of Man," *Hereditas* 42 (1956): 1–6.

chronic delusional states in French psychiatry National differences have always played a role in the history of science and medicine. In PSYCHIATRY, where most MENTAL DISORDERS are syndromes (clusters of symptoms) that do not meet the criteria for disease in the sense of having an identifiable

underlying cellular pathology, national traditions and culture-specific folklore shape (socially construct) clusters of symptoms into diagnostic syndromes that may differ from standard classification of mental disorders that are found in *ICD-10* and *DSM-IV-TR*. Historically, this has been especially true in France, where diagnostic systems arising in Germany (such as that of Emil KRAEPELIN) and "Anglo-Saxon" countries such as England and the United States have met with resistance. The French antipathy toward German psychiatric classification began in the early 1900s as a reflection of the political and cultural nationalism that played a role in bringing about the First World War (1914–18). Even today, definitions of what constitutes SCHIZOPHRENIA, the delusional disorders, and the brief psychotic disorders are viewed differently in French psychiatry.

Since approximately 1909, French psychiatry has placed delusions at the center of its definition of psychotic disorders. This trend began with the work of Valentin Magnan (1835–1916) and his colleagues in the 1880s on "chronic delusional insanity." However, although Magnan linked his "systematic delusions" to processes of DEGENERATION or nondegeneration, by the First World War, degeneration theory began to decline in importance in French psychiatry. Again, anti-German sentiment may have played a role, because German psychiatry emphasized hereditary causes and disorders with chronic, progressively deteriorating course like DEMENTIA PRAECOX. Since then, French psychiatry has adopted an elaborate classification system for chronic delusional states that, under current diagnostic systems, might be regarded as forms of PARANOID SCHIZOPHRENIA, PERSISTENT DELUSIONAL DISORDERS, DELUSIONAL DISORDER, and PARANOID PERSONALITY DISORDER. To this day French psychiatrists are more likely to emphasize nonschizophrenia delusional syndromes and more narrowly diagnose schizophrenia in everyday practice.

Currently, chronic delusional states are divided into three main categories:

(1) chronic interpretative psychosis (also known as systematized or paranoic psychoses)
(2) chronic hallucinatory psychosis
(3) chronic imaginative (or paraphrenic or fantastic) psychosis

Chronic interpretive psychosis There are two types of chronic interpretive psychosis, intellectual delusional states and emotional delusional states. Both were described in 1909 by Paul Serieux (1864–1947) and J. M. Capgras in their seminal book, *Les Folies Raisonnantes: le Delire d'Interpretation (Intelligent Insanity: Delusional Interpretation)*. In intellectual delusional states, facts that were perceived correctly at first are misinterpreted due to false reasoning. Eventually the delusions arising from this misinterpretation progressively conquer all other aspects of mental activity. The delusions are systematized and complex, there are no prominent hallucinations, intellectual functioning is unimpaired, and the course is chronic. In emotional delusional states, the delusional premise does not spread beyond the theme of the delusion and the persons or persons involved in the delusion. The two most common variants of emotional delusional states are (a) vindictive delusional states (e.g., the "litigious paranoia" of persons who are constantly involved in legal suits against others whom they perceive as having "wronged" them) and (b) sentimental delusional states (delusional jealousy and erotomania).

Chronic hallucinatory psychosis This disorder was first described in 1911 by Gilbert-Louis-Simeon Ballet (1853–1916), a Parisian psychiatrist working at the famous mental hospital the Hotel-Dieu. The symptoms of this disorder, which Ballet believed was rooted in HEREDITY, were:

(a) persistent hallucinatory activity
(b) delusions, most frequently of persecution
(c) clear sensorium, unimpaired speech, relatively normal behavior, and unimpaired intellectual functioning.

In more recent French psychiatric descriptions of this disorder, additional features are:

(a) onset in middle or late adult life
(b) absence of schizophrenic thought disorder
(c) relatively good functioning prior to the onset of the disorder

Chronic imaginative psychosis This delusional disorder is characterized by magical thinking, fantastic and grandiose delusions, and confabulation. All this is in stark contrast to the otherwise good contact with reality the person exhibits. This disorder was first described by Ferdinand-Pierre-Louis-Ernest Dupré (1862–1921) in 1910 in an article in the journal *L'Encephale (The Brain)*. This diagnosis is rarely made by French psychiatrists today.

The continuing influence of the chronic delusional states of French psychiatry is reflected in the diagnostic criteria for DELUSIONAL DISORDER in *DSM-IV-TR* (2000) and PERSISTENT DELUSIONAL DISORDERS in *ICD-10* (1992).

See also PARANOIA; PARAPHRENIA.

Magnan, V. "Chronic Delusional Insanity of Systematic Evolution," trans. A. Marie and J. MacPherson, *American Journal of Insanity* 51 (1895): 37–57; 175–198; 524–538; 52 (1896): 397–415.

Pichot, P. "The Diagnosis and Classification of Mental Disorders in the French-speaking Countries: Background, Current Values and Comparison with other Classifications." In *Sources and Traditions of Classification in Psychiatry,* edited by N. Sartorius, et al. Toronto: Hofgrete and Huber, 1990.

chronic schizophrenia The idea that some forms of SCHIZOPHRENIA seem to follow a chronic lifetime course without improvement is as old as the concept of schizophrenia itself. It has always been observed throughout the history of PSYCHIATRY that there were some psychotic disorders that improved and some that ended in permanent deterioration or "dementia." Indeed, KRAEPELIN's concept of "DEMENTIA PRAECOX," which he formed in 1893, was based entirely on the idea that it was a progressively degenerative disorder with a poor prognosis. He called this mental deterioration the *Verblodungs-process*. However, his 1899 definition of the MANIC-DEPRESSIVE PSYCHOSES (see also BIPOLAR DISORDER) was of a group of psychotic disorders with a relatively good prognosis for improvement. Eugen BLEULER produced the still prevalent picture of schizophrenia as having acute and chronic forms in his 1911 *Dementia Praecox, Or the Group of Schizophrenias.*

Schizophrenia has long been conceptualized as pairs of opposites across many different dimensions. The acute/chronic distinction and the reactive/process distinction are essentially equivalent, expressing the idea that there is a form of schizophrenia with a sudden onset and a better prognosis (acute or reactive) and a form that has an insidious onset that gradually develops from early in life and does not seem to get any better (chronic or process). In recent years the term *chronic schizophrenia* has been falling out of use in the clinical research literature (although it is still part of the everyday jargon of mental health professionals) due to the appearance of more descriptive terms for this apparent strain of schizophrenia.

The traditional notion of "chronic schizophrenia" is now being redefined. In the psychiatric research literature chronic schizophrenia is characterized by its NEGATIVE SYMPTOMS, such as restricted emotional range, poverty of speech, reduction of curiosity in the immediate environment around a person, an apathetic or diminished sense of "purpose" in the afflicted person, and a reduced need to engage in social interactions. Negative symptoms are based on the idea that something is "taken away" from a person. When they endure, they have been called "deficit symptoms." There is a vast amount of research that also shows that chronic schizophrenics also show certain "soft neurological signs" and sometimes structural and functional abnormalities in the brain.

See also ACUTE-CHRONIC DISTINCTION; COURSE AND OUTCOME OF SCHIZOPHRENIA; CROW'S HYPOTHESIS; DEFICIT SYMPTOMS; DEGENERATION; PINEL-HASLAM SYNDROME; POSITIVE SYMPTOMS.

circular insanity The name given in 1854 by FALRET to what we now call BIPOLAR DISORDER. The term was widely used in English-language literature until KRAEPELIN's new definition of the disorder and invention of the term MANIC-DEPRESSIVE ILLNESS. People stricken with this mental disorder were often referred to as "circulars," much in the same way that we presently refer to them as "manic-depressives."

See also MANIC-DEPRESSIVE ILLNESS.

Ritti, A. "Circular Insanity." In *A Dictionary of Psychological Medicine,* 2 vols., edited by D. H. Tuke. Philadelphia: P. Blakiston & Son, 1892.

circulating swing A form of treatment for the mentally ill that was popular throughout the 18th and into the early 19th centuries in which patients would be rapidly spun around in a circular motion. Although Dutch physician Herman Boerhaave (1668–1738) may have been the first to use such a device, the first working model of a circulating swing is credited to English physician John Mason Cox, who describes the device in his 1806 book, *Practical Observations on Insanity:*

> His *swing* formed by suspending a Windsor chair to a hook in the ceiling, by two ropes to hind legs and two to fore, joined by a sliding knot to regulate elevation: patient in a straight waistcoat, and a leathern strap around his waist, buckled to the bars behind; legs fastened by straps to the front ones of the chair; then turned around.

Reflecting the many mechanical variations of this basic concept by innovative physicians in other asylums, it was also called the "GYRATOR" or "gyrating chair," "rotary machine," "spinning chair," "rotating swing" or "chair" and also "Darwin's chair" or "machine," since it was suggested by Erasmus Darwin (1731–1802), the physician grandfather of Charles Darwin, as a form of treatment for patients with many different types of ailment. The device attributed to Darwin consisted of a boxlike chair (or bed, apparently), which was suspended by an iron rod from the ceiling. The patient would be tightly strapped into this seat. A small wooden platform was built next to the chair on which another person could push another rod back and forth, which generated the rotation of the rod on which the chair was suspended. Psychiatrists Alexander and Selesnick reproduce an 18th-century illustration of this machine in their book on the history of psychiatry.

It is said that the circulating swing could be driven up to 100 rotations per minute, causing considerable disorientation, vomiting, purging, bleeding from the eyes, and eventual unconsciousness in patients. Needless to say, treatment sessions lasted only a matter of minutes. ESQUIROL, who called it "the machine of Darwin" in 1838, was apparently the first to introduce this rotary machine to France, but he discourages its use along with the following report:

> Doctor Martin, physician of the hospital at Antiquaille, where to this day the insane of Lyons are treated, has informed me that he has been frightened at the accidents which the insane had met with, who had been submitted to the influence of this machine. They fall into a state of syncope, and had also copious evacuations both by vomiting and purging, which prostrated them extremely.

Esquirol notes at the bottom of the page of his *Mental Maladies* in 1838 that, "Since the first edition of this article was published, the rotary machine has been every where abandoned."

American psychiatrist Benjamin RUSH was an enthusiastic advocate of his "gyrater," as well as a stationary "coercion chair," which he referred to as his "TRANQUILLIZER." However, he utilized a form of the circulating swing and had suggestions for technical improvements on the machine. The circulating swing was also part of the regimen recommended by 18th-century Englishman John HASLAM (of "Bedlam").

See also HAYNER'S WHEEL; MECHANICAL RESTRAINT.

Alexander, F. G., and S. T. Selesnick. *The History of Psychiatry.* New York: Harper & Row, 1966.

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity,* trans. E. K. Hunt. Philadelphia: Lea and Blanchard, 1845; first published, 1838.

Scull, A. "The Domestication of Madness," *Medical History* 27 (1983): 233–248.

clanging A frequently observed speech anomaly, in persons with psychotic disorders, in which words are spoken for the way they sound, rather than for what they mean. This can sometimes appear like bizarre punning or attempts at rhyming. "I am the needle-nose who knows. Like the rose in his hair, OK?" is an example of the clanging found in psychotic speech patterns. BLEULER

(in 1911) referred to these language anomalies as "clang associations."

See also LANGUAGE ABNORMALITIES IN SCHIZOPHRENIA.

Clérambault-Kandinsky syndrome A syndrome characterized by delusions of being controlled. It was identified by Gaétan Gatian de Clérambault (1872–1934), a French psychiatrist who was prominent in identifying several CHRONIC DELUSIONAL STATES IN FRENCH PSYCHIATRY.

Clérambault's syndrome (or de Clérambault's syndrome) See EROTOMANIA.

climate as a cause of insanity Many early authorities on mental illness claimed that the nature of a particular climate could cause such disorders. Both Benjamin RUSH and J. E. D. ESQUIROL agreed that temperate climates, which had frequent alterations of hot and cold, were the most likely to cause insanity. These ideas exist in a modern form in studies of the EPIDEMIOLOGY of mental disorders, which show that incidence and prevalence rates are different in different parts of the world—particularly for SCHIZOPHRENIA.

See also VIRAL THEORIES OF SCHIZOPHRENIA.

clown syndrome See *FAXENSYNDROM*.

clozapine See ANTIPSYCHOTIC DRUGS.

CNS The acronym for "central nervous system," essentially designating the brain, the spinal cord, and their associated processes. The "peripheral nervous system" refers to the sensory (afferent) and motor (efferent) nerve cells that connect the remainder of the body with the central nervous system.

Cogentin See ANTIPARKINSONIAN DRUGS.

cognitive-behavior therapy See BEHAVIOR THERAPY.

cognitive dysmetria theory of schizophrenia A DISCONNECTION THEORY OF SCHIZOPHRENIA proposed by Nancy Andreasen of the University of Iowa College of Medicine. Relying primarily on functional brain imaging data, Andreasen and her associates have developed a model that implicates the "connectivity" of NEURAL CIRCUITS between the prefrontal region of the frontal lobe of the brain, the subcortical nuclei of the thalamus, and the cerebellum. A disruption in this circuitry produces what Andreasen has called "cognitive dysmetria." Cognitive dysmetria means the person with schizophrenia has difficulties in prioritizing, processing, coordinating, and responding to information. This "poor mental coordination" is a fundamental cognitive deficit in SCHIZOPHRENIA and may account for the broad diversity of its symptoms.

See also ABOULIA.

Andreasen, N. A., et al. "'Cognitive Dysmetria' as an Integrative Theory of Schizophrenia: A Dysfunction in Cortical-Subcortical-Cerebellar Circuitry?" *Schizophrenia Bulletin* 24 (1998): 203–218.

cognitive studies of schizophrenia In the late 1950s a revolution began in the way experimental studies in psychology were conducted. Advances in cybernetics, linguistics (particularly the work of Noam Chomsky), and the computer sciences gave rise to a new type of psychology. Called "cognitive psychology," it borrowed the metaphors of information processing from the computer sciences to approach the study of human thought and experience in a new way—by examining the human mind's processes of encoding, transforming, storing, and using information for regulating behavior. Thought and language abnormalities had long been noted by SCHIZOPHRENIA researchers, but cognitive psychology extended the study of schizophrenia to find patterns of information processing in sensation, perception, memory, motor (movement) processes, and, in particular, the ability to focus one's attention. Studies comparing schizophrenic and normal information processing almost always find significant differences between these two groups. One line of evidence tends to indicate that some schizophrenics

have information processing problems associated with the left hemisphere of the brain when compared to normals. Furthermore, cognitive studies have helped document evidence for distinct subdivisions within schizophrenics, thus giving more suggestive evidence for subtype differences than had hitherto been possible with strictly behavioral or biological approaches. An example of this is the highly successful demonstration across numerous studies that there are distinct differences between the paranoid subtype of schizophrenia and the nonparanoid subtypes. Indeed, a special issue of *Schizophrenia Bulletin,* edited by experimental psychologist Peter Magaro, was devoted to this evidence in 1981. An excellent review of the experimental studies of "schizophrenic cognition" was published by Canadian psychologist Leonard George in 1985.

In the 1990s the rise of the neurodevelopmental model inspired researchers to investigate new aspects of the cognitive deficits that people with schizophrenia exhibit. The cognitive studies of disorders of ATTENTION are now grounded in neurophysiology in studies of SENSORIMOTOR GATING, the idea that the thalamus acts as a "gate" that separates relevant from irrelevant stimuli and then relays this information to the appropriate circuits of neural networks in the brain. In the case of schizophrenia, "gating" breaks down and irrelevant stimuli competes with relevant stimuli in the brain, causing the experiences and behaviors we observe as the symptoms of schizophrenia. Many studies have found deficits in the working memory of schizophrenics, which is the type of short-term memory needed for tasks such as memorizing an unfamiliar telephone number just long enough to be able to dial it before forgetting it. Working memory is often compared to the RAM facility of a computer.

See also NEUROPSYCHOLOGICAL STUDIES OF SCHIZOPHRENIA.

George, L., and R. Neufeld. "Cognition and Symptomatology in Schizophrenia," *Schizophrenia Bulletin* 11 (1985): 264–285.

Knight, R. A., and S. M. Silverstein. "The Role of Cognitive Psychology in Guiding Research on Cognitive Deficits in Schizophrenia." In *Origins and Development of Schizophrenia: Advances in Experimental Psychopathology,* edited by M. F. Lenzenweger and R. H. Dwarkin. Washington, D.C.: American Psychological Association, 1998.

Magaro, P. A., ed. "Special Issue: Paranoia," *Schizophrenia Bulletin* 7 (1981): 4.

collective insanity See FOLIE À DEUX.

Columbia-Greystone Project A PSYCHOSURGERY research project initiated in 1947 combining the psychiatric research scientists of Columbia University Medical Center in New York City and the psychiatric patients of the New Jersey State Hospital at Greystone Park. The goal was to refine the methods of psychosurgery as a treatment for mental disorders, specifically to find the critical locations in the frontal lobes where more limited incisions could maximize the benefits and minimize the sometimes terrible after-effects. A review of this research was published in 1949. The group called itself the "Columbia-Greystone Associates" and was co-led by Fred Mettler, a professor of anatomy at Columbia University, and Marcus Currey, the medical superintendent and CEO of the Greystone Park State Hospital. Mettler was also a board member of the NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH) at the time, and his influence led to the large supporting grant from the NIMH, totaling hundreds of thousands of dollars, that funded the project.

The project had two phases: a 1947–48 study and a 1951–52 study. In the first study, the more important of the two, a series of 19 patients underwent a psychosurgical procedure known as a TOPECTOMY, a more localized and focal procedure than the traditional "ice pick" lobotomies performed by Walter FREEMAN, the world's leading authority on psychosurgery. They also explored other "open" methods (i.e., procedures that required the surgical opening of the skull), but their results were all rather inconclusive. Realizing the less than spectacular results they were getting with their methods, the associates then invited Freeman to perform a series of his famous TRANSORBITAL LOBOTOMIES on a series of patients at Greystone Park in October 1948. Of this tragic failure, which

led him to abandon the hope of an assembly-line approach to treating chronic psychiatric patients (largely schizophrenics) with transorbital lobotomies, Freeman later wrote:

> Of the 18 patients operated upon . . . there was not a single one that I would have chosen from my own practice. The results were as bad as I anticipated. Furthermore, in one patient the icepick broke, leaving a small bit embedded in the base of the brain. Fortunately, there was no unfavorable effects, but the embarrassment was mine [cited in Shutts, 1982].

Mettler, F. A., ed. *Selective Partial Ablation of the Frontal Cortex.* New York: Hoeber, 1949.

coma therapy In the 20th century, several biological treatments were developed for SCHIZOPHRENIA that were based on the deliberate induction of a comatose state in the patient, with the assumption that the patient would reawaken in a much improved state. The most famous variety of coma therapy was INSULIN COMA THERAPY, developed by psychiatrist Manfred SAKEL and his associates in Austria in 1936, in which a deep hypoglycemic coma was induced in schizophrenics as a sort of "shock" to their system. While coma therapy was widely used (along with PSYCHOSURGERY and ELECTROSHOCK THERAPY) throughout the 1940s and 1950s, it disappeared after the introduction of ANTIPSYCHOTIC DRUGS for the treatment of schizophrenia. Other forms of coma therapy for schizophrenia involved inducing a comatose state through inhaling pure nitrogen or by injections of atropine, but neither of these forms were widely utilized. No rational theory explaining why coma therapy worked for some patients was ever formulated.

See also NITROGEN INHALATION THERAPY.

command hallucination Despite media depictions of "psychotic killers" who carry out murderous crimes "because God told me to," the phenomenon of command hallucinations is relatively uncommon in psychotics. When such hallucinations are present, they tend to be in the form of a "voice" telling the person to do various acts, some of which may be harmful to self or others. Many patients resist the commands and experience great fear and anxiety because of them. For example, a patient once cried out to the author in the middle of a conversation, "They're trying to get me to kill myself, but I won't do it!" He apparently had just then experienced a command-type AUDITORY HALLUCINATION urging him to commit suicide. Sometimes, however, psychotic individuals *do* give in to the commands, and suicide and/or acts of violence can be carried out against others.

Commissioners in Lunacy Commissioned by the British government in 1845, this committee of 15 individuals was endowed with the power to inspect existing madhouses and asylums and refuse or approve the licensure of new ones. The commissioners' jurisdiction extended over England and Wales, unlike previous regulatory boards, which had jurisdiction just over London and a seven mile radius around it. The direct precursors to the Commissioners in Lunacy were the committee of five medical commissioners from the College of Physicians empowered in 1774, and its successor, the Metropolitan Commissioners in Lunacy, established in 1828.

commitment One of the most frightening experiences anyone can imagine is being involuntarily committed to a MENTAL HOSPITAL. The many autobiographical accounts of such traumatic events by ex-mental patients have served only to stimulate the public's imagination, and they have been depicted frequently in fictional accounts in literature, motion pictures and on television. There have been many critics of the role of psychiatrists, which gives them extraordinary power over others usually granted only to judges or the police, and many of these critics have been psychiatrists themselves, notably Thomas Szaz and R. D. LAING (1927–89). Szaz caused a stir in 1963 with his book *Law, Liberty and Psychiatry* because he called for eliminating all forms of involuntary commitment. In his 1985

autobiography, Laing bluntly expresses his view of the powers of psychiatry when he writes:

> Thus, society expects psychiatry to perform two very special functions. To lock certain people up, and to stop and, if possible, change certain states of mind and types of conduct in the name of curing mental illnesses . . . These two tasks are placed on psychiatry. It is ensured that psychiatrists carry out these tasks by giving them the *power* to do so, a power *they* can't refuse, if they want to practice psychiatry.

In the United States, each state is responsible for making its own commitment laws. In most cases, they are understandably vague (given the great variety of symptoms and behaviors exhibited in persons with severe mental disorders), but since the 1970s states have generally focused narrowly on the issue of dangerousness, specifically whether the person is a danger to himself or others. Generally it takes the written approval of only one or two psychiatrists to commit someone involuntarily to a mental hospital. That such a process is needed in the treatment of severe mental illness is largely unquestioned, since in floridly psychotic states of mind people can—and do—engage in harmful acts against themselves or others. Judgment is impaired during such episodes, and a person who is indeed suffering from a severe mental illness may not know that he or she requires help. This is known as lack of INSIGHT.

Most of the laws governing commitment have been transformed over the years to become more humane, largely due to the lobbying efforts of patient advocacy groups since the end of the 1800s. It has become progressively more difficult to commit someone to a psychiatric hospital, and laws have been changed to require frequent psychiatric and judicial review to expedite the earliest possible release.

One of the abuses of the power of commitment held by psychiatrists was the commitment of married women to "insane asylums" at their husband's request even though they were not truly insane. Such power was granted to the superintendents of asylums by some state legislatures, notably in Illinois, whose 1851 commitment law declared: "married women . . . may be entered or detained in the hospital (the state asylum at Jacksonville, Illinois) at the request of the husband of the woman . . . without evidence of insanity required in other cases." These laws were eventually changed after the intense lobbying efforts of one such woman, Elizabeth Parsons Ware Packard, who in 1860 was committed by her husband (the Reverend Theophilus Packard) to the Illinois State Asylum at Jacksonville and was incarcerated there for three years. She apparently drew her husband's ire for expressing philosophical differences on religious matters. The commitment was carried out by two doctors who were members of her husband's church and judged her insane by merely feeling her pulse. She kept a diary while in the asylum and produced many publications based on it over the years. An 1867 investigation of the Jacksonville asylum found 148 such women committed there. Packard persuaded the Illinois state legislature to change the commitment law that year, and she persuaded Iowa to do the same in 1872. Efforts by groups in the MENTAL HYGIENE MOVEMENT working with the AMERICAN PSYCHIATRIC ASSOCIATION helped to abolish such inhumane laws in the United States by the 1930s.

See also LUNACY TRIALS.

Laing, R. D. *Wisdom, Madness, and Folly: The Making of a Psychiatrist.* New York: McGraw-Hill, 1985.

Packard, E. P. W. *Marital Power Exemplified in Mrs. Packard's Trial, and Self-Defense from the Charge of Insanity; or, Three Year's Imprisonment for Religious Belief, by the Arbitrary Will of a Husband, with an Appeal to the Government to so Change the Laws so as to Afford Legal Protection to Married Women.* Hartford: Case, Lockwood, 1866.

Szaz, T. *Law, Liberty and Psychiatry.* New York: Macmillan, 1963.

communicated insanity See FOLIE À DEUX.

community mental health centers Following the pattern of the DEINSTITUTIONALIZATION of the mentally ill from psychiatric institutions in the United States in the 1950s, it soon became clear that these discharged patients were not receiving the proper

care in the community. In a 1961 report entitled *Action for Mental Health,* the Joint Commission on Mental Illness and Health recommended the establishment of federally funded community-based mental health centers so that seriously ill patients could be treated closer to home and be kept out of psychiatric hospitals. In a special message to Congress in February 1963, President John F. Kennedy proposed a system of "Community Mental Health Centers" to be set up around the United States. President Kennedy optimistically argued that, "when carried out, reliance on the cold mercy of custodial isolation will be supplanted by the open warmth of community concern and capability." Community care was designed to be a replacement for confinement in state hospitals.

Unfortunately, as many studies have shown, right from the start CMHCs have treated only a small percentage of discharged psychiatric patients—at most, only 10 to 15 percent of the new cases admitted to the CMHCs were for people with serious psychiatric diagnoses such as SCHIZOPHRENIA. Instead of providing services to the seriously mentally ill—as was the idea behind the plan—CMHCs have overwhelmingly provided counseling and psychotherapy for people with marital problems, family problems, relationship problems, and other interpersonal problems. In many settings valuable treatment resources are being drained by court-mandated "therapy" for individuals as a form of "pretrial intervention" so that they do not have to schedule full trials and be sent to already overcrowded jails. Such individuals often include sociopaths (especially juveniles) who are poorly motivated to change their behavior and see their weekly appointments with a therapist at the local CMHC as merely a way of staying out of jail.

It was estimated that, by 1987, more than 800 CMHCs were granted more than $3 billion in federal funds to maintain this system but without any appreciable improvement in the care of the seriously mentally ill. An illuminating critique of the CMHC system in the United States and its almost exclusive treatment of the "worried well" is provided by psychiatrist E. Fuller Torrey in his section on "The Failure of the Community Health Centers" in his book, *Surviving Schizophrenia.*

Goldman, H. H., et al. "Community Mental Health Centers and the Treatment of Severe Mental Disorder," *American Journal of Psychiatry* 137 (1980): 83–86.

Torrey, E. F. *Surviving Schizophrenia: A Family Manual.* 2nd ed. New York: Harper & Row, 1988.

comorbidity Comorbidity refers to the simultaneous presence in an individual of two or more distinctly different diseases or mental disorders. Their simultaneous presence may be due entirely to coincidence. In epidemiology, comorbidity is studied to see if there is a correlation between the two or more diseases or disorders arising in the same persons at the same time, implying perhaps a deeper, causal relationship. Correlations can be positive, meaning that when one disease is present there is a higher than expected rate of another specific disease also being present. In situations of negative comorbidity, there is a lower than expected rate of the occurrence of another specific disease.

It has long been noted that persons with SCHIZOPHRENIA suffer from a variety of physical diseases that are due to poor self-care or neglect within the medical system. It has been estimated that between 46 percent and 80 percent of inpatients and between 20 percent and 40 percent of outpatients with schizophrenia have been found to have ongoing physical diseases. In about half these cases the medical condition was thought to make schizophrenic symptoms worse. The true rates of comorbidity of schizophrenia with other diseases or disorders is unknown because such persons are deliberately left out of research studies on schizophrenia in order to eliminate possible confounding variables in the interpretation of results.

Comorbidity with other diseases and disorders Persons with schizophrenia have higher-than-expected rates of infection (particularly pulmonary tuberculosis), diabetes, arteriosclerotic disease and myocardial infarction, middle ear disease, irritable bowel syndrome, and HIV infection. In the United States, it is estimated that approximately 5 percent to 7 percent of persons with schizophrenia are infected with HIV.

On the other hand, schizophrenia is negatively comorbid with rheumatoid arthritis and cancer,

particularly lung cancer in men with schizophrenia. This finding is in stark contrast to everyday clinical experience with schizophrenia as it is apparent many persons with schizophrenia are heavy smokers. Indeed, the best estimates based on research are that 73 percent of males and 53 percent of females who are schizophrenic smoke cigarettes. No one knows the reasons behind this negative comorbidity of schizophrenia and lung cancer, but some have suggested that ANTIPSYCHOTIC DRUGS may provide some sort of long-term anticancer protection.

Substance abuse is the most common comorbid disorder associated with schizophrenia. Use of alcohol, cannabis (marijuana), cocaine, methamphetamine and a whole host of other substances, legal and illegal, are known to be contributing factors in relapse and may be involved in triggering the first psychotic episode. In a 10-country study conducted by the WORLD HEALTH ORGANIZATION (WHO) it was found that 57 percent of males with schizophrenia abused alcohol, and another 24 to 41 percent of all persons with schizophrenia abused street drugs, primarily cannabis and cocaine. The WHO singled out cannabis use (smoking marijuana) as a significant predictor of poor outcome, indicating that it is associated with relapse.

Jablensky, A. "The Epidemiological Horizon." In *Schizophrenia.* 2nd ed., edited by S. R. Hirsch and D. Weinberger. Cambridge: Blackwell, 2003.

Compazine See ANTIPSYCHOTIC DRUGS.

complex A term used by C. G. JUNG to describe organized clusters of feelings that take on a life of their own and that exist in all of us. The term was first used by the German philosopher and psychiatrist Theodor Ziehen (1862–1950) as "emotionally charged complex of representations" (*gefühlsbetonter Vorstellungskomplex*) to explain the underlying cluster of feelings that caused delayed reactions in the course of his experiments with the word association test, later made famous by Jung. Jung thought that the mind's basic structure is made up of autonomous "feeling-toned complexes" (*gefühlsbetonter Komplex*), nodal points, or clusters of affect whose dynamics are observed in the phenomenon we call "personality." Jung felt that the "ego" was essentially a complex, and although it was the most important one, it was only one among many. The ego could be influenced and even paralyzed by other such clusters of feelings, which we experience when we suddenly feel we are losing control when mad, joyful, etc., in everyday life. Everyone has complexes, but in normals they work together within a functional system that is adaptive for the survival of the individual. In mental disorders, particularly severe ones such as schizophrenia or multiple personality disorder, their strength is greater and their autonomy from the ego more extreme due to DISSOCIATION, thus disabling the personality, as Jung observes, with "a multiplication of its centers of gravity."

In schizophrenia, Jung thought that the disturbances in the will of the individual, and his or her hallucinations and delusions, represented the pathological work of complexes. In his famous monograph *The Psychology of Dementia Praecox* (1907), he demonstrated how the nature of complexes in schizophrenia fits in with descriptions of similar phenomena in the psychoanalytic theories of Sigmund FREUD. Although Jung recognized that dementia praecox was caused by a "toxin" that led to an irreversible disease process in the brain, he was largely under the influence of the psychological approach of Freud at this time and felt that it was possible for the "feeling-toned complex" to make the changes in the chemistry of the brain to produce the toxin. In this respect he differed significantly from his supervisor, Eugen BLEULER, who felt that the organic disease process in the brain came first and that the complexes only gave the psychotic symptoms their form but did not cause them. In 1908 Bleuler and Jung published a paper together that contrasted their views on this issue. After his break with Freud, Jung returned much later to a more organic view of the causes of schizophrenia.

Jung thought that ancient reports of demoniacal possession (see DEMONOMANIA) were simply due to the work of complexes that had become too strong and had begun to form alternate egos in the personality of the afflicted. Jung's "complex

theory" is at the center of his entire psychology, which was briefly referred to as "complex psychology" but is now more widely known as "analytical psychology."

See also ABAISSEMENT DU NIVEAU MENTAL; MULTIPLE PERSONALITY AND SCHIZOPHRENIA.

Bleuler, E., and C. G. Jung. "Komplexe und Krankheitsursachen bei Dementia Praecox," *Zentralblatt für Nervenheilkunde und Psychiatrie* 31:19 (1908): 220–227.

Jung, C. G. "The Psychogenesis of Schizophrenia," *Journal of Mental Science* 85 (1939): 999–1,011.

———. "The Psychology of Dementia Praecox," in *The Collected Works of C. G. Jung,* Vol. 3. 1907. Reprint, Princeton, N.J.: Princeton University Press, 1960.

compos mentis A Latin term for "sanity" that has found its way into jurisprudence over the centuries. *Non compos mentis* is its opposite, meaning "not in full possession of mental faculties." The expression apparently is derived from the Roman author Tacitus, who uses it in his *Annals.*

See also INSANITY.

concordance rate The rate of agreement, association, or correlation between two individuals (or types of individuals) and a given trait. Concordance rates are most often encountered in discussions of twins studies of SCHIZOPHRENIA and BIPOLAR DISORDER that have sought evidence for the genetic transmission of these diseases. For example, since we known that MONOZYGOTIC TWINS (also known as identical twins) share all the same genes, we known that they must be highly concordant for traits like eye and hair color, blood type, and most physical characteristics. DIZYGOTIC TWINS, on the other hand, who have on the average only half their genes in common, will resemble each other no more than other siblings, making them discordant across many traits. Concordance rates are often presented as decimaled numbers that represent a correlation coefficient, and the closer the number is to 1.0 the more concordant two individuals or groups are for a given trait. If schizophrenia (or bipolar disorder) is the result of genetic inheritance, then the assumption in research studies is that monozygotic twins should *both* develop the disease at higher rates (that is, with concordance rates closer to 1.0) than dizygotic twins, where perhaps only one member is likely to develop the disorder.

Almost all research studies have shown that monozygotic twins do indeed have a higher concordance for schizophrenia and for bipolar disorder than dizygotic twins. On the average, most studies show that the concordance rate for schizophrenia is three times higher in monozygotic twins than in dizygotic twins. Furthermore, the risk for schizophrenia is 40 to 60 times higher in monozygotic twins than in the general population. In patients with bipolar disorder, the concordance rate is approximately .43 for monozygotic twins.

Also supporting the hypothesis of the genetic transmission of schizophrenia are recent re-analyses of these twin studies data, in which it is found not only that monozygotic twins are more concordant for schizophrenia than dizygotic twins, but also that within these pairs of monozygotic twins, those that have a greater presence of NEGATIVE SYMPTOMS (which have been associated with a more degenerative, more "genetic" variety of schizophrenia) have a higher concordance rate (.52) than those monozygotic twins who have a lesser presence of such symptoms (.36).

After decades of research on monozygotic (identical) twins, it has been found that the concordance rate for schizophrenia among identical twins is close to 50 percent, which means that a large portion of whatever it is that causes schizophrenia is not due to genetic factors.

See also CHRONIC SCHIZOPHRENIA; CONSANGUINITY METHOD; CROW'S HYPOTHESIS; DEFICIT SYMPTOMS; GENETICS STUDIES; TWINS METHOD AND STUDIES.

Moldin, S. O., and I. I. Gottesman. "Genes, Experience and Chance in Schizophrenia: Positioning for the 21st Century," *Schizophrenia Bulletin* 23 (1997): 547–561.

concretization An aspect of schizophrenic thought patterns in which abstract thoughts or feelings are "concretized," usually in bizarre ways. For example, during an exacerbation of the psychosis a schizophrenic may feel a loss of control, which causes considerable anxiety. If paranoid, the individual may

attribute this distress to the effect of a particular facial expression someone in his immediate environment may just have manifested—perhaps without any awareness of or conscious interaction with the paranoid patient. The notion that humans tend to think in two broad modes—the concrete and the abstract—was first proposed by the psychologist Kurt GOLDSTEIN in 1939. Goldstein noticed that concrete thinking was particularly found in brain-damaged patients and, to a lesser degree, in schizophrenics. Psychologist and psychoanalyst Silvano ARIETI picked up on this idea and asserted that the "process of active concretization" formed the essential basis of the way in which the thinking of people is changed by SCHIZOPHRENIA when compared to normal thinking processes.

Arieti, S. *Interpretation of Schizophrenia.* 2nd ed. New York: Basic Books, 1974.
Goldstein, K. *The Organism.* New York: American Books, 1939.

confabulation This is the unconcious fabrication of facts or events that is often noted in brain-damaged individuals and in those persons with amnestic disorders. They confabulate due to gaps in memory, and the fabricated response to questions are facile attempts to fill in these gaps, but without any awareness of the person that he or she is confabulating. This is different than lying or DELUSIONS, which are found in the psychotic disorders and are not the response to memory impairment.

confidentiality Individuals have the right to privacy. Special relationships between a person and certain specific medical, mental health, or legal representatives are protected by this right of privacy, and many statutes have established the privileged nature of communications made during the course of professional relationships. A breach of confidentiality by a practitioner is a basis of malpractice actions against that person. Patients of mental health professionals should expect that what is discussed or included as part of treatment is private information, to be released to others only by the patient's (ideally, written) consent.

See also LEGAL ISSUES IN SCHIZOPHRENIA.

confusion A psychological state of disorientation that is found across many different types of MENTAL DISORDERS (including ORGANIC MENTAL DISORDERS) but in particular is evident in the psychotic disorders. It is usually evident during exacerbations of a PSYCHOSIS.

conjugal insanity See FOLIE À DEUX.

Conolly, John (1794–1866) An English psychiatrist and reformer. After graduating from Edinburgh University, Conolly studied in France, where he was influenced by the "moral treatment" of Philippe PINEL. Returning to England, in 1839 he became the chief physician to the Hanwell Asylum in Middlesex and there began to practice his own moral treatment of the mentally ill, including the abolition of MECHANICAL RESTRAINTS. He remained there for four years. He wrote many books on his philosophy of treatment; although they were controversial for their time, they were also highly influential. As the guiding leader of the NONRESTRAINT MOVEMENT, Conolly's ideas spread throughout Europe and America. Indeed, his ideas were held in very high regard in the United States and were partially the inspiration that brought together the 13 founders of the AMERICAN PSYCHIATRIC ASSOCIATION in 1844.

Conolly, J. *An Inquiry Concerning the Indications of Insanity with Suggestions for the Better Protection and Cure of the Insane.* London: 1830.
———. *The Treatment of the Insane without the Use of Mechanical Restraints.* London: Smith, Elder, 1856.

consanguinity method One of the methods of conducting GENETICS STUDIES of SCHIZOPHRENIA and other MENTAL DISORDERS (such as BIPOLAR DISORDER), which are assumed to have a genetic basis. The consanguinity method is based on a simple idea: If a particular disease is assumed to be genetic in origin, then the disease will be more prevalent in relatives of an afflicted person than in the general population as a whole. The afflicted person is known in these studies as the INDEX CASE. The

assumption in consanguinity studies is that the closer a relative is biologically to the index case, the more likely he or she is to develop the disorder. Twins studies are based on this principle but for many reasons are considered more scientifically powerful evidence than traditional consanguinity studies.

The very first published study on the genetics of schizophrenia was the consanguinity study conducted by Ernst Rüdin in 1916. He apparently carried out this study at the urging of Emil KRAEPELIN. Rüdin, as expected, found a significant increase in the prevalence rate of schizophrenia in the biological relatives of his index cases. He also recognized that the gene seemed to be passed on in NON-MENDELIAN PATTERNS OF TRANSMISSION. Further studies were conducted in Europe by Schultz in 1932 and in the United States by KALLMANN in 1938.

Rüdin, E. *Zur Vererburg und Neuentstehung der Dementia Praecox.* Berlin: Springer-Verlag, 1916.

Slater, E. "A Review of Earlier Evidence on Genetic Factors in Schizophrenia." In *The Transmission of Schizophrenia,* edited by D. Rosenthal and S. Kety. Oxford: Pergamon Press, 1968.

Zerbin-Rüdin, E., and K. S. Kendler. "Ernst Rüdin and His Geneologic-Demographic Department in Munich: An Introduction to Their Family Studies of Schizophrenia," *American Journal of Medical Genetics* 67 (1996): 332–337.

contagious insanity See FOLIE À DEUX.

continuous sleep therapy Swiss psychiatrist Jakob Kläsi developed this form of therapy for schizophrenics in the early 1920s. Kläsi induced a prolonged sleep in his patients with the use of barbiturates. These periods of sleep lasted a week or more, and the patient was only allowed to eat or perform bodily functions upon wakings, after which more barbiturates would be administered and the patient would be put back to sleep. His only theory to rationalize this treatment was that SCHIZOPHRENIA was the result of a pathological excitement that resulted from an inflammatory process in the brain that could be alleviated through rest, as other inflammatory conditions could be. However, the complications of the procedure (toxicity, the development of respiratory problems and pneumonia) outweighed the apparent therapeutic benefits, and thus the treatment was not widely used.

See also SLEEP TREATMENT.

Diethelm, O. "An Historical View of Somatic Treatment in Psychiatry," *American Journal of Psychiatry* 95 (1938): 1,165–1,179.

Kläsi, J. "Über die therapeutische Anwendung der 'Dauernarkose' mittels sominifens bei Schizophrenen," *Z. Neurol. Psychiatr.* 74 (1922): 557–592.

continuum of psychosis See *EINHEITSPSYCHOSE*.

convulsive therapies Although no sound scientific theories have ever supported their use, the convulsive therapies were among the most widely used somatic treatments for SCHIZOPHRENIA in the 20th century. The basic idea is that deliberately inducing a convulsion or seizure—either by drugs or electricity—somehow has a therapeutic effect in schizophrenia.

The first report of a convulsive therapy was by the Hungarian psychiatrist L. von MEDUNA in 1935. von Meduna apparently believed (without any supporting scientific evidence) that epilepsy and schizophrenia were biologically incompatible and that, therefore, inducing a convulsive seizure in schizophrenics would be therapeutic. He used camphor and metrazol to induce these convulsions and reported successful results. However, his relapse rate was high, and his "convulsive therapy" was found to be more effective with patients with AFFECTIVE DISORDERS (such as DEPRESSION) than with schizophrenics. This similar beneficial result with people with severe affective disorders has also been found to be true for ELECTROSHOCK THERAPY (now commonly referred to as ECT, or "electroconvulsive therapy"), which was first used by CERLETTI and Bini in 1938. Since the 1970s ECT has been infrequently used for schizophrenia in the United States.

See also METRAZOL SHOCK THERAPY.

Fink, M. "Convulsive Therapy: A Review of the First 55 Years," *Journal of Affective Disorders* 63 (2001): 1–15.

copro-psychiatrie A 19th-century "school" of PSYCHIATRY that claimed that mental illnesses, and particularly the psychotic disorders, were caused by diseases of the digestive tract, particularly the intestines and bowels. These physicians primarily studied the feces, urine, and other bodily "secretions of the insane." In the second (1861) edition of his famous textbook, *Die Pathologie und Therapie der Psychische Krankheit* (the first was in 1845), German psychiatrist Wilhelm GRIESINGER notes that this "peculiar bud from the stem of the 'Somatic School' has . . . gone out of fashion."

See also AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX.

cortical pruning as a cause of schizophrenia This is a theory that proposes a developmental process ("cortical" or "axonal pruning") that is extended past its normal point of termination (at about age 16) and goes on to cause SCHIZOPHRENIA. In the brain, neurons ("brain cells") pass messages back and forth to one another through a vast web of interconnections. From the nucleus of the neuron, a "message" travels down a branchlike structure called the "axon." The point at which information from one cell passes to another is a gap separating the axons called a "synapse." Biochemical NEUROTRANSMITTERS such as DOPAMINE, serotonin, and norepinepherine all cross this gap to affect the adjoining neuron.

Starting with the postmortem studies of P. R. Huttenlocher, published in 1979, it was discovered that there are major changes in the number of synapses (especially in the prefrontal cortex) throughout childhood and adolescence. "Synaptic density" (think of this as the thick branches of a tree or bush—the axons—intercrossing one another) increases in this cortical area until about ages five to seven, and then it begins a gradual decline until about age 16, when the density of synapses seems to level off to average adult levels. It is estimated that as much as 30 percent to 40 percent of these interconnections between brain cells disappear or "fall off" or are "pruned" (as one would a tree or shrub), and as a result the brain is measured to be less "active" or have less "energy" ("reduced cerebral metabolism"), particularly in the prefrontal cortical regions. This process is called axonal pruning.

A theory for a possible contributing cause of schizophrenia based on this normal process of "cortical" or "axonal pruning" was first put forth by Irving Feinberg in 1982, and developed by researchers Ralph Hoffman and Steven Dobscha in a paper published in 1989. In that paper, they hypothesized that the normal developmental process of cortical pruning that happens to us all in childhood and adolescence, and especially its measured reduction of cerebral metabolism in the prefrontal cortex, may actually cause schizophrenia if the process continues into late adolescence and early adulthood.

A computer model simulation of what the effect of cortical pruning would be in normals was conducted by Hoffman and Dobscha, and it was found that such experiences as DELUSIONS and HALLUCINATIONS and other psychotic symptoms might be experienced by humans. Another prominent schizophrenia researcher, Letten Saugstad of Norway, proposed that the cortical pruning process is implicated in the development of manic-depressive psychosis as well, with the hypothesis being that very early puberty is the necessary factor in the development of manic-depressive psychosis, and extremely late puberty the necessary factor in the development of schizophrenia. If the onset of puberty is viewed as coinciding with the last major step in brain development (the end of the cortical pruning process), then manic-depressiveness may result from the earlier than normal termination of the cortical pruning process.

Cortical pruning theories of mental illness have not been supported. As of 2005, such a theory of schizophrenia has been rejected.

Feinberg, I. "Schizophrenia and Late Maturational Brain Changes in Man," *Psychopharmacology Bulletin,* 18 (1982): 29–31.

———. "Schizophrenia: Caused by a Fault in Programmed Synaptic Elimination during Adolescence?" *Journal of Psychiatric Research* 4 (1982/1983): 319–334.

Hoffman, R. E., and S. K. Dobscha. "Cortical Pruning and the Development of Schizophrenia: A Computer Model," *Schizophrenia Bulletin* 15 (1989): 477–490.

Huttenlocher, P. R. "Synaptic Density in Human Frontal Cortex—Evidence for Synaptic Elimination during

Normal Development," *Neuro-science Letters* 33 (1979), 247–252.
Saugstad, L. F. "Social Class, Marriage, and Fertility in Schizophrenia," *Schizophrenia Bulletin* 15 (1989): 9–43.

Cotard's syndrome A relatively uncommon delusional syndrome, usually found in people with a psychotic disorder (usually, PARANOID SCHIZOPHRENIA) or with an ORGANIC MENTAL DISORDER, in which he or she denies his or her own existence or the existence of the external world. For this reason, French psychiatrist Jules Cotard (1840–89) introduced this idea in 1880 at a meeting in Paris of the Societé Médico-Psychologique by calling it *le délire de négation* (delusions of negation). Cotard first published his ideas on this newly identified syndrome in 1882. Another French psychiatrist, Séglas, named this condition the Cotard Syndrome in 1897. Schizophrenics who exhibit Cotard's syndrome may make statements such as "I'm dead" or "I'm not here or anywhere. I'm a ghost." Nonpsychotic conditions that are probably related to Cotard's syndrome are feelings of DEREALIZATION or DEPERSONALIZATION.

Cotard, J. "Du délire des négations," *Archives de Neurologie* 11 (1882): 152–170: and 12: 282–296.
Séglas, J. *La Délire de Négation.* Vol. 1. Paris: Masson, 1897.

cottage system Another name for the centuries-old system of caring for the mentally ill in which they are maintained in the community rather than in institutions. Belgium's GHEEL COLONY, which is almost 1,000 years old, is an example of how long this system has been maintained.

Cotton, Henry A. See FOCAL INFECTION AS CAUSE OF PSYCHOTIC DISORDERS.

course and outcome of schizophrenia From antiquity until the second half of the 1800s, all insanities were thought to fall within two broad categories, MANIA and MELANCHOLIA. These two terms did not have the meaning they have today until the end of the 1800s. Speculation as to the course and outcome of the multitude of mental disorders forced to fit into these two ancient categories was varied and not based on any scientific study. For example, Benedict Morel in France speculated in 1857 that both mania and melancholia were the result of hereditary DEGENERATION and, over successive generations, ended in idiocy and death. Therefore, all mental disturbances were ultimately signs of degeneration and doomed an individual or his or her children to dementia and death.

With the efforts of German psychiatrists such as Karl Ludwig KAHLBAUM (beginning in 1863) and Emil KRAEPELIN (beginning in 1883) to identify and classify syndromes of MENTAL DISORDERS, it soon became apparent that one way of distinguishing seemingly similar mental disorders from one another was by course and outcome. Some mental disorders could be temporary and result in full recovery; others seemed to flare up occasionally and leave lasting deficits that became worse over the course of a person's life.

The importance of course and outcome proved to be crucial in the history of PSYCHIATRY beginning with the publication of the sixth edition of Kraepelin's textbook, *Psychiatrie.* In the 1899 edition, Kraepelin divided and reclassified all the known "insanities" (psychotic disorders) into two main categories: DEMENTIA PRAECOX and MANIC-DEPRESSIVE ILLNESS. His main criterion for dividing the insanities this way was prognosis. Manic-depressive illness was characterized by exacerbating and remitting episodes, many full recoveries, no cognitive deterioration (dementia), and an excellent prognosis. Persons with manic-depressive illness could often return to full intellectual, social, and occupational functioning between episodes. On the other hand, dementia praecox in its three main forms (paranoid, hebephrenic, and catatonic) was a degenerative disease characterized by a progressive deteriorating course and outcome. From the time he introduced the concept of dementia praecox in 1893, he had largely viewed dementia praecox in this unforgiving way, but by 1920 he had admitted the existence of cases of partial or full recovery (the existence of which Eugen BLEULER had insisted upon from the first description of SCHIZOPHRENIA in 1908).

Kraepelin identified two main patterns across the life spans of people with dementia praecox: "simple" (insidious, slow, and chronic) and "undulating" (episodic, with psychotic symptoms flaring up and subsiding at times, yet leaving a core deficit in cognitive functioning that worsens until death). Since Kraepelin's time there has been much interest in the "natural history of schizophrenia," that is, the typical pattern or patterns the disorder demonstrates over long periods of time. Wilhelm Meyer-Gross of Heidelburg University in Germany was the first to conduct a long-term follow-up study of 294 patients diagnosed with schizophrenia. In his 1932 publication of his results, Mayer-Gross reported that 17 years after first being diagnosed with schizophrenia, approximately 30 percent were found to be "practically cured, living at home, socially adjusted," 19 percent were in institutions, 5 percent were "living at home, employed, but poorly socially adjusted," and 3.5 percent were "living at home, but manifestly ill." Strikingly, 42.5 percent were dead, most having died in MENTAL HOSPITALS. In 1941 Manfred BLEULER, son of Eugen Bleuler, published early data on the possible course types of schizophrenia and devoted most of his career to long-term follow-up studies of persons with chronic mental disorders.

Longitudinal or long-term follow-up studies have examined the types of onset (sudden or insidious), patterns of exacerbations and remissions of psychotic symptoms, changes in cognitive functioning (attention, working memory, episodic or autobiographical memory, executive functions) over time, and the end state (full recovery to mild, moderate, or severe deterioration by the end of the time period of study).

There have been five major longitudinal studies of the course and outcome in schizophrenia since 1972, and all five have rejected Kraepelin's fatalistic definition of dementia praecox as always ending in a state of chronic dementia. All of them also reject Kraepelin's early division of the course of dementia praecox into two patterns, simple and undulating, with one outcome, dementia. In fact, the number of different courses of schizophrenia is not known for certain. Estimates based on research have varied widely from four to 79 different possible patterns that combine course and outcome.

Results from the five major longitudinal studies have been appearing in print since 1972. Two were conducted in Switzerland: The BURGHÖLZLI HOSPITAL Study (1972) conducted by Manfred Bleuler and his colleagues (designated in the chart below by "B"), and the Lausanne Investigations (1976) conducted by Luc Ciompi and colleagues (L). Two additional studies were conducted in the United States: the Vermont Longitudinal Research Project (1987) conducted by Courtenay Harding and colleagues at Vermont's only state hospital (V), and the Chicago study (1991) conducted by J. T. Marengo and colleagues (C). A worldwide study of 14 different geographical locations in developing and developed countries was conducted by the WORLD HEALTH ORGANIZATION in its collaborative International Study of Schizophrenia (ISoS) project (2001). Since Switzerland and the United States are developed or First World countries, the ISoS results are particularly interesting because of the addition of data from developing countries and reflect the much better outcome for persons with schizophrenia in those parts of the world.

The common patterns found in the five major longitudinal studies are generally divided into eight course types for schizophrenia. In the chart below, adapted from a chart prepared by H. Haefner and W. An der Heiden and published in 2003, the numbers represent the percentage of persons with schizophrenia that fit each of the eight course and outcome combinations:

Based on these five major longitudinal studies, 10 North American long-term follow-up studies that lasted a minimum of 10 years, and the genetic, biochemical, psychopharmacological, neuropathological, neuroimaging, and neuropsychological picture of schizophrenia as it now stands, the following conclusions about the course and outcome of schizophrenia may be drawn from our present state of scientific knowledge:

1. In developed countries, schizophrenia is a chronic disease, causing impairment (neurocognitive, social, and occupational) that lasts a lifetime. In developing countries, schizophrenia follows a less severe course and has a better outcome. No one knows why this is so.

	Onset	Course type	End state	L	B	V	C	ISoS
1	Acute	Undulating	Recovery/Mild	25.4	30–40/25–35	7	10.8	29.4
2	Chronic	Simple	Moderate/Severe	24.1	10–20	4	36.5	14.4
3	Acute	Undulating	Moderate/Severe	11.9	5	4	9.5	4.9
4	Chronic	Simple	Recovery/Mild	10.1	5–10	12	4.1	10.4
5	Chronic	Undulating	Recovery/Mild	9.6	–	38	6.8	22.6
6	Acute	Simple	Moderate/Severe	8.3	5–15	3	13.5	9.1
7	Chronic	Undulating	Moderate/Severe	5.3	–	27	12.2	4
8	Acute	Simple	Recovery/Mild	5.3	5	5	6.8	5.3

2. When compared to other mental disorders, such as BIPOLAR DISORDER, the outcome for schizophrenia is worse.
3. Schizophrenia is not a neurodegenerative disease that begins after puberty, as Kraepelin believed. Negative symptoms and cognitive impairment are present in the prodromal phase, years before the first episode of schizophrenia. Cognitive impairment does not ever improve over the course of schizophrenia, but it also does not significantly worsen either. Measurable brain abnormalities, such as enlarged ventricles (when present, which is in a minority of persons with schizophrenia), do not worsen over time. Most of the destructive impact of schizophrenia occurs early in the process, during the years-long prodromal phase or around the time of the first psychotic episode. Antipsychotic drugs do not improve most negative symptoms and they do not improve cognitive functioning (attention, working memory, autobiographical memory, executive functioning). "Full recovery" unfortunately implies some residual cognitive impairment will remain.
4. The underlying disease processes in schizophrenia, while mostly disabling and chronic, do not get progressively worse over the life span. In fact, people with schizophrenia suffer most of their loss of functioning early in the disease process. After five to 10 years their symptoms reach a "plateau" and either do not get worse or go into partial remission. This again argues against a view of schizophrenia as a neurodegenerative disease.
5. There is no firm scientific evidence, from these longitudinal studies, biological research, or GENETICS STUDIES, to support the clinical subtypes of schizophrenia found in *DSM-IV-TR* (paranoid, disorganized, catatonic, undifferentiated, residual) or *ICD-10* (paranoid, hebephrenic, catatonic, undifferentiated, residual, or simple). Therefore, although in practice clinicians believe that the paranoid subtypes have a better prognosis than the nonparanoid subtypes, this is not supported by longitudinal studies. Clinicians have no scientific basis for making a prognosis based on the presenting clinical subtype. The only firm scientific evidence for possible subtypes of schizophrenia is for forms of the disorder with an acute onset or an insidious onset, and these are associated with good prognosis and poor prognosis, respectively.
6. Primary negative symptoms are stable over time and are not affected by environmental factors. Positive symptoms (HALLUCINATIONS and DELUSIONS) are unstable over time and are influenced by environmental factors. The stability of negative symptoms contradicts the hypothesis that schizophrenia is a progressive neurodegenerative disease, as Kraepelin believed.
7. Schizophrenia is associated with an increased risk of suicide, physical illness, and an average life span that is 10 to 15 years less than the general population.
8. ANTIPSYCHOTIC DRUGS do not work in as many as one-third of all persons with schizophrenia. Antipsychotic drugs do not prevent brain damage in schizophrenia. Antipsychotic drugs do not directly work on the underlying causes of schizophrenia and therefore do not alter the natural course of the disease process.
9. The causes of schizophrenia are unknown.
10. In individual cases, it is impossible to predict the course or outcome of schizophrenia.

Bleuler, M. *Krankheitsverlauf, Persoenlichkeit, und Verwandtschaft der Schizophrener und Ihrer Gegenseitigen Beziehungen.* Leipzig: George Thieme, 1941.

Haefner, H., and W. An der Heiden. "Course and Outcome of Schizophrenia." In *Schizophrenia. 2nd ed.,* edited by S. R. Hirsch and D. Weinberger. Cambridge: Blackwell, 2003.

Mayer-Gross, W. "Die Klinik (der Schizophrenie)." In *Handbuch der Geisteskrankheiten. Band IX. Spezieller Teil V: Die Schizophrenie,* edited by O. Bumke. Berlin: Springer, 1932.

McGlashan, T. H. "A Selective Review of Recent North American Studies of Schizophrenia," *Schizophrenia Bulletin* 14 (1988): 515-542.

creativity and psychosis Is there a relationship between "madness" and creativity? Thousands of years of popular speculation have thought so. The first of the now familiar "pathographies" of famous creative individuals began to appear in the mid-1800s, led by the works of French alienist J. J. Moreau de Tours (1804–84) and German psychiatrist P. J. Möbius (1853–1907), who wrote psychiatric interpretations of the creative lives of Rousseau, Goethe, Schopenhauer, and Nietzsche. In the 20th century, psychologists have tried to answer this question experimentally by comparing the thought processes of schizophrenics with those of highly creative nonschizophrenic individuals. It has long been reported that when highly creative nonschizophrenics are given traditional diagnostic tests, they tend to score higher on psychopathology than "normals." However, there is no evidence that these people or other highly creative individuals are more susceptible to SCHIZOPHRENIA than the general population.

A review of these studies on creativity and schizophrenia was published by J. A. Keefe and P. A. Magaro in 1980. Although there was no direct evidence of a link between the two, schizophrenics and creative nonschizophrenics did share several qualities in the styles of their thinking: both used language in very unusual ways, both had deviant, idiosyncratic views of reality when compared to other people, and both tended to be perceived as "eccentric" by others. An important distinction to be made is that one of the hallmarks of a schizophrenic is the inability to focus attention in a normal, sustained manner, and such attention is necessary for planning and carrying out all activities of life—including creative ones. Thus, being "schizophrenic" does not make one creative, nor vice versa.

However, there has been much speculation that many highly creative people throughout history may have been afflicted (or blessed, as the case may be) with BIPOLAR DISORDER. The thought disorder of schizophrenia is generally absent in manic-depressives, but there is an incredible rush of energy due to the manic phase of the illness that can keep creative people working on projects literally for days with little or no sleep. Such persons may have been Vincent Van Gogh, Edgar Allan Poe, Handel, Berlioz, F. Scott Fitzgerald, Eugene O'Neill, and Virginia Woolf. The anecdotal evidence for a connection between MANIC-DEPRESSIVE ILLNESS and creativity is quite strong.

Alcoholism, either in connection with bipolar illness or alone, is prominently represented in creative individuals. Writers in particular seem to be prone to alcoholism, and the first five American Nobel laureates for literature (Lewis, O'Neill, Faulkner, Hemingway, and Steinbeck) were all alcoholics.

There has also been some speculation, based on anecdotal evidence, that relatives of highly creative people are often schizophrenic or manic-depressives. For example, Albert Einstein's son Edward (born in 1910) was afflicted with schizophrenia. James Joyce's daughter Lucia was a diagnosed schizophrenic who spent most of her life in mental institutions. British horror writer Ramsey Campbell's mother was schizophrenic, and Jane Fonda's mother (Frances Seymour Brokow) committed suicide in a mental hospital in 1950 by slitting her own throat. The exact nature of her severe illness is not known. Even famous psychiatrists have not been exempt, for the mothers of both Harry Stack Sullivan and C. G. JUNG are known to have had serious MENTAL DISORDERS that may have resulted in psychiatric hospitalization. Indeed, both Stack and Jung themselves are known to have had periods in their lives when psychotic-like symptoms and a general functional breakdown were known to occur. Thus, the question of madness and creativity

is an intriguing one that will continue to generate endless speculation.

See also ART, SCHIZOPHRENIC.

Dykes, M., and A. McGhie. "A Comparative Study of Attentional Strategies of Schizophrenic and Highly Creative Normal Subjects," *British Journal of Psychiatry* 128 (1976): 50–56.

Jamison, K. R. *Touched with Fire: Manic-Depressive Illness and Temperament.* New York: Free Press, 1993.

Keefe, J. A., and P. A. Magaro. "Creativity and Schizophrenia: An Equivalence of Cognitive Processing," *Journal of Abnormal Psychology* 89 (1980): 390–398.

Croatia Some parts of Croatia have some of the highest prevalence rates for SCHIZOPHRENIA in the world; the northwestern coastal area has a prevalence rate twice as high as that of other areas. Rates for manic depression are also high in Croatia. The Istrian Peninsula in Croatia has a particularly high rate (about 7.4 per 1,000) when compared to other areas of Croatia (from 2.9 to 4.2 per 1,000).

Lemkau, P. V. "Selected Aspects of the Epidemiology of Psychoses in Croatia," *American Journal of Epidemiology* 94 (1971): 112–117.

cross-cultural studies It has long been reported that severe MENTAL DISORDERS such as SCHIZOPHRENIA and MANIC-DEPRESSIVE ILLNESS seem to be more prevalent in technologically developed Western countries than in developing countries in the Third World. This is a very old observation. As early as 1835 British psychiatrist J. C. Prichard (1786–1848) noted in his text *A Treatise on Insanity* that "insanity belongs almost exclusively to civilized races of man: it scarcely exists among savages, and is rare in barbarous countries." Other prominent figures in psychiatry in the 19th century who expressed these views were Isaac RAY, Dorothea DIX, Edward Jarvis, and Pliny EARLE.

In the 19th and early 20th centuries, many anecdotal reports by psychiatrists and anthropologists about mental disorders in "primitive" societies supported the view that schizophrenia in particular seemed to be uncommon. The more scientific epidemiological studies of the prevalence of schizophrenia show that it is found in different amounts in different parts of the world. In reviewing all this data, psychiatrist E. Fuller Torrey published a fascinating book in 1980 on *Schizophrenia and Civilization* in which he argued that "schizophrenia appears to be a disease of civilization, with a close correlation between its prevalence and the degree of civilization."

However, diagnostic criteria can be very different from culture to culture, and many diseases that look like schizophrenia (such as manic-depressive psychosis in its earliest stage, certain metabolic disorders, or ORGANIC MENTAL DISORDERS caused by strokes, tumors, or lesions induced by head trauma) may not in fact be so. To correct these problems and to construct a true picture of schizophrenia worldwide, many rigorous, scientific, long-term follow-up studies have been conducted in many areas of the world. The three most important studies have been major projects of the WORLD HEALTH ORGANIZATION: the International Pilot Study of Schizophrenia (IPSS), which was carried out in nine countries (Denmark, India, Colombia, Nigeria, United Kingdom, Soviet Union, Czechoslovakia, Taiwan, and the United States) between 1968 and the early 1970s; the Determinants of Outcome Study, conducted between 1983 and 1985 in 10 countries, using methods that were improvements over the IPSS study of a decade earlier; and the International Study of Schizophrenia (ISoS) and its follow-up studies, completed in 1997. The ISoS looked at 14 different geographical locations in both developed and developing countries. All these studies have shown that schizophrenic patients in less-industrialized societies (as in the Third World) have a significantly better outcome than do those schizophrenics in industrialized nations. However, these studies also show a core of "worst outcome" schizophrenics, and these groups seem to match the familiar descriptions of CHRONIC SCHIZOPHRENIA known in Western societies, where it is thought to be more genetically based and more "organic" and degenerative in nature than the "acute-onset" types. "Acute onset psychoses" were found, instead, to predominate in the non-Western world.

Whether these cross-cultural differences are due to sociocultural differences (Third World countries being more "sociocentric," Western societies more "egocentric") or to the prevalence of different, less chronic strains of schizophrenia in Third World countries is presently unknown.

Jablensky, A., et al. "Schizophrenia: Manifestations, Incidence and Course in Different Cultures. A World Health Organization Ten-Country Study," *Psychological Medicine Monographs Supplement* 20 (1992): 1–97.

Lin, K. M., and A. M. Kleinman. "Psychopathology and Clinical Course of Schizophrenia: A Cross-Cultural Perspective," *Schizophrenia Bulletin* 14 (1988): 555–567.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

Crow's hypothesis For many years, researchers sought to combine all the highly diversified studies of SCHIZOPHRENIA into a single theory that could account for all the new findings that advances in technology had brought. In essence, the desire was for a theory that could account for the symptoms of schizophrenia and relate them to specific biological processes. Furthermore, such a theory would have to be testable. In 1980 psychiatrist T. J. Crow did just that. He published his concept of schizophrenia as essentially a "two-syndrome" disease and connected findings on the symptomatology of schizophrenia with the biochemical and neurophysiological qualities of the disease. He named these two subtypes of schizophrenia Type I and Type II; because it has been so popular with those who carry out schizophrenia research, the theory is commonly referred to as Crow's hypothesis or two-syndrome paradigm.

Type I schizophrenia is thought by Crow to be characterized by an acute onset, generally normal intellectual functioning, no discernible abnormalities in the structure of the brain, and a good response to ANTIPSYCHOTIC DRUGS. It is thought to be caused by an excess of dopamine production in the brain and is generally associated with POSITIVE SYMPTOMS (symptoms that seem to be additions to the personality, such as hallucinations and delusions). Most important, it is associated with the absence of NEGATIVE SYMPTOMS (those symptoms that represent something taken away from the personality, such as poverty of speech, poverty of content of speech, restricted affect, psychomotor retardation, reduced desire for social interaction, and constricted thought process).

In Type II schizophrenia, characteristics include insidious onset (i.e., it develops slowly, like a chronic illness), intellectual deterioration, enlarged ventricles in the brain, poor response to antipsychotic drugs, and prominent negative symptoms. Thus, the difference in Type I versus Type II schizophrenia is based not only on the predominance of unrelated symptoms (positive versus negative) but also the fact that Type II schizophrenia is clearly characterized by structural BRAIN ABNORMALITIES. Type II, therefore, is the subtype of schizophrenia that most resembles traditional brain diseases.

Although Crow's hypothesis generated considerable research, it did not stand the test of time. By the 1990s his "two-syndrome" concept had been replaced by new research schemes derived from statistical studies of the symptoms of schizophrenia. These factor-analytic studies rejected the notion of "syndromes" and "diagnostic subtypes" and instead replaced them with various "dimensions" of psychopathology. Instead of Crow's two syndromes, proposals for three and four dimensional alternatives have been offered by Nancy Andreasen (3), Peter Liddle (3), and Mark Lenzenweger and Robert Dworkin (4).

Crow, T. J. "Molecular Pathology of Schizophrenia: More Than One Disease Process?" *British Medical Journal* 280 (1980): 66–86.

———. "The Two-syndrome Concept: Origins and Current Status," *Schizophrenia Bulletin* 11 (1985): 471–486.

Lenzenweger, M. F., and R. H. Dworkin. "The Dimensions of Schizophrenia Phenomenology? Not One or Not Two, At Least Three, Perhaps Four," *British Journal of Psychiatry* 168 (1996): 432–440.

Crowther, Bryan (1765–1814) A surgeon of the BETHLEM ROYAL HOSPITAL who wrote a book in 1811 of his observations made during the dissections of the brains of deceased "Bedlam" patients. He

was assisted by apothecary John HASLAM in these autopsies, who also incorporated his observations in a book. He is thus one of the early investigators to use neuropathological methods to look for BRAIN ABNORMALITIES in the severely mentally ill. In his book, Crowther also mentioned that, as surgeon to the Bethlem Royal Hospital, he routinely practiced the BLEEDING of patients every spring regardless of the type or severity of their illness.

When John Haslam was interrogated in 1815 by a committee of the House of Commons about alleged abuses at "Bedlam," it came up in his testimony that Crowther was a raging alcoholic who needed to be put in MECHANICAL RESTRAINT at times. Haslam told the committee: "Mr. Crowther was generally insane, and mostly drunk. He was so insane as to have a straight-waistcoat." Haslam and the superintendent of Bethlem, Thomas Monro, were dismissed as a result of the committee's findings, but Crowther died shortly before the committee opened its hearings—escaping, no doubt, a similar fate.

Crowther, B. *Practical Remarks on Insanity, to Which Is Added a Commentary on the Dissection of the Brains of Maniacs, with Some Account of Diseases Incident to the Insane.* London: 1811.

Report of the Committee for Better Regulation of Madhouses. London: Baldwin, Craddock, & Joy, 1815.

cruciform stance A form of MECHANICAL RESTRAINT in which a disobedient patient was harnessed and tied in a standing position to a cross-shaped metal structure. Patients were then left on this structure for many hours or days at a time. An eminent 19th-century German psychiatrist, Heinrich Wilhelm Neumann (1814–84), recommended the cruciform stance or harness as "the best possible punishment for the worst transgressions of the insane." The horizontal form of this mode of mechanical restraint was known as the BED SADDLE and survived into the 20th century.

Kreapelin, E. *One Hundred Years of Psychiatry,* trans. W. Baskin. 1917. Reprint, New York: Philosophical Library, 1962.

CT scan Abbreviation for "computed tomography," in BRAIN IMAGING STUDIES used to image the structure of the brain. It is the same as the more commonly known term CAT scan or computerized axial tomography. Information is gathered from the body in cross-sectional planes, as if examining the body with X-rays slice by slice. An image is created by a computer synthesis of X-ray transmission data obtained from many different directions through each plane. Image by image (or "slice" by "slice") the body is studied, and abnormalities are searched for in the computer-generated images. CT scans and other brain-imaging techniques are now commonly being used to study brain abnormalities in schizophrenia and have led to discoveries about how the brains of people with SCHIZOPHRENIA are different from the brains of normals. It is the first of the many new brain-imaging techniques developed since the first published report of the use of a CT scan in 1973; its first use in schizophrenia research was reported in 1976.

See also BRAIN IMAGING STUDIES OF SCHIZOPHRENIA.

Cullen, William (1710–1790) A noted British physician and one of the influential instructors of Benjamin RUSH. He is remembered for founding the Glasgow Medical School in Scotland and for a system of classifying mental disorders that influenced later psychiatrists, notably Philippe PINEL and RUSH. Cullen is also remembered for coining the term *NEUROSIS,* a class of diseases with a physiological basis in the nervous system. One of these, Vesania, was an ancient Latin term for "insanity," used until the end of the 18th century. His treatment recommendations for mental illness were largely those also used for other physical disorders: BLEEDING, PURGING, bathing, and changes in diet.

Cullen, William. *First Lines of the Practice of Physic, with Practical and Explanatory Notes by John Rotheram.* Edinburgh: Bell, Bradfute, etc., 1796.

"Cure-Awl, Dr." This was the derisive nickname of physician William AWL, the first superintendent

(in 1838) of the Ohio State Asylum for the Insane and one of the 13 founders of the AMERICAN PSYCHIATRIC ASSOCIATION. The nickname derives from his incredible claim in 1842 that under his direction the Ohio Asylum had achieved a 100 percent cure rate for insanity.

Exaggerated claims of the curability of severe mental illness were not uncommon in the mid-19th century in the young United States, and such claims were considered a source of national pride. In fact, the preponderance of such claims in the 1830s and 1840s led to a "cult of the asylum" in the United States, led by Dorothea DIX, who cited this evidence in her lobbying efforts to state legislators to build more asylums. Without evidence to the contrary, state after state mandated the construction of state asylums for the insane, and Dix was credited for being personally responsible for 32 of them. It wasn't until 1877 that these fabricated statistics were finally shown to be false in an influential book by Pliny EARLE, another of the 13 founders of the American Psychiatric Association.

Earle, P. *The Curability of the Insane.* Philadelphia: Blakiston, 1877.

Rothman. D. J. *The Discovery of the Asylum: Social Order and Disorder in the New Republic.* Boston: Little, Brown, 1971.

cycloid psychoses A variety of BRIEF PSYCHOTIC DISORDERS that have played an influential role in German and Scandinavian psychiatry. The term first appears in the work of German psychiatrist Karl Kleist (1879–1960) in 1926 in the *Archiv fuer Psychiatrie und Nervenkrankheiten (Archives for Psychiatry and Nervous Disease)* as "cycloid degeneration psychoses" to refer to two types of transient psychotic disorders: the confusional psychoses that alternated between agitated confusion and stupor, and the motility psychoses that alternated between hyperkinesis and akinesis. The term "cycloid psychoses" replaced a term used by Kleist for the same disorders in a 1921 publication, "sudden, fully-formed, constitutional psychoses (*autochthone konstitutionelle Psychosen*)." The cycloid psychoses have a sudden onset and a brief duration with full recovery, though in some instances they may reoccur. Kleist was a major critic of Emil KRAEPELIN's 1899 division of the psychotic disorders into two main categories, DEMENTIA PRAECOX and MANIC-DEPRESSIVE ILLNESS, and believed there were many psychotic disorders that fell between these two but that could not be reduced to either. Kleist, following his teacher Carl Wernicke (1848–1905), believed in the possibility of localizing these MENTAL DISORDERS in functionally unstable areas of the brain and classifying them according to their underlying neurological impairment. This was in opposition to SCHIZOPHRENIA, which Kleist believed was caused by the degenerative progressive atrophying of nerve cells in the brain.

Kleist and Karl Leonhard (1904–88), his colleague in Frankfurt, Germany, in the mid-1930s, eventually identified at least 26 cycloid psychoses that were schizophrenia-like and cyclical (like manic depression). In 1953 Kleist introduced the terms *unipolar* and *bipolar* to differentiate the cycloid psychoses in an article published in the *Monatsschrift fuer Psychiatrie und Neurologie.* In 1957, in *Die Aufteilung der endogenen Psychosen (The Classification of Endogenous Psychoses),* Leonhard grouped psychotic disorders into three large categories of "endogenous psychoses": one, the affective, or phasic psychoses (with "bipolar" distinguished from "monopolar" types); two, the cycloid psychoses; and three the schizophrenia psychoses, which he broke down into "systematic" (stable symptoms picture, systematized delusions) and "nonsystematic" psychoses (fluctuating or polymorphic symptom picture, fluctuating severity). In his book, Leonhard insisted that "Cycloid psychoses are completely cured in every phase. Should it be otherwise in a particular case, we deal with misdiagnosis." The concept of cycloid psychoses is still popular in German psychiatry.

See also DYSPHRENIA.

Beckmann, H., and E. Franzek. "Cycloid Psychoses and Their Differentiations from Affective and Schizophrenia Psychoses." In *Contemporary Psychiatry,* edited by F. Henn, N. Sartorius, H. Helmchen, and H. Lauter. Heidelberg: Springer, 2001.

Beckmann, H., and K.-J. Neumarker, eds. *Endogenous Psychoses: Leonhard's Impact on Psychiatry.* Berlin: Ullstein Mosby, 1995.

Kleist, K. "Autochthone Degenerationspsychosen," *Zeitschrift fuer gesamte Neurologieund Psychiatrie* 69 (1921): 1–11.

cytogenetics This is the area of specialization within genetics that is concerned with the study of the structure and function of the cell, and especially the study of the CHROMOSOMES.

D

Darwin's chair (or machine) See CIRCULATING SWING.

Daseinanalyse Literally, the "analysis of existence," a method and mode of treatment formulated by Ludwig Binswanger (1881–1966) in the 1950s that was based on understanding the experiential structures of the inner worlds of mentally ill persons. Binswanger had worked at the BURGHÖLZI HOSPITAL under Eugen BLEULER and C. G. JUNG in the first years of the 20th century. He constructed this revision of FREUD's psychoanalysis with the ideas of phenomenological philosophers Heidegger and Husserl. His emphasis on carefully describing the inner experiences of schizophrenics (the phenomenology of schizophrenic experience) had great influence on subsequent studies of the afflicted individual's experience of his or her own disease process. It influenced British PSYCHIATRY, in particular in the 1950s and 1960s, and especially the work of R. D. LAING.

Binswanger thought that the experiential world of schizophrenics was characterized by four qualities:

1. A breakdown in the consistency of natural experience. To get out of this situation, they construct DELUSIONS to minimize the anxiety felt about the inner chaos and to reestablish order in the world.
2. A splitting-off of experiential consistency into rigid pairs of alternatives. The world is seen as good/bad, pure/evil, yes/no. These alternatives are often grandiose, inflated, "exaggerated ideals." When choices in the world are limited in this dualistic way, the schizophrenic cannot help but sometimes to fall into the darkness of making the negative choice, therefore viewing him- or herself only in terms of deficiency, imperfection, or "sin."
3. A process of "covering." The schizophrenic tries to "cover-up" through thoughts, words, and behaviors the awful negative aspect of existence (the *Dasein,* in Binswanger's terminology) that is unbearable to the schizophrenic. This naturally leads to an inflated notion of the preferred alternative for viewing existence.
4. An experience of existence as being "worn away," as though by friction. No longer can the person find a way in or out of his way of being, and this eventually fatigues him and leads to a renunciation or resignation of the world, what Binswanger calls an "existential retreat."

In 1957 Binswanger published a series of five case histories of schizophrenics that he treated using his *daseinanalyse.* Despite a significant amount of interest in its philosophy and its phenomenological approach to clinical situations, daseinanalysis never was a widely accepted treatment for schizophrenics and is today an uncommon treatment mode in general.

Binswanger, L. *Being-in the-World: Selected Papers of Ludwig Binswanger.* Translated and edited by J. Neddleman. New York: Basic Books, 1963.

———. *Schizophrenie.* Pfullingen: Gunther Neske Verlag, 1957.

day hospitals An alternative to commitment to psychiatric institutions, day hospitals provide care for severely mentally ill people during the day, after which they are allowed to go home at night. This is generally viewed as a cheaper and more humane alternative to full-time care in institutions, which

are usually the sponsors of such programs. A rarer version of this idea involves "night hospitals," where patients return at night after spending the day in a community setting. Both are forms of what is commonly referred to as "partial hospitalization." The earliest recorded operating day hospital was opened in the Soviet Union in the 1930s. It was not until 1946 that the movement began in Britain with the opening of a day hospital in London by a British psychiatrist by the name of Bierer. Day hospitals were introduced in North America in 1947 by Donald Cameron, a psychiatrist from McGill University in Montreal, Canada.

See also COMMUNITY MENTAL HEALTH CENTERS.

Vaughan, P. J. "Developments in Psychiatric Day Care," *British Journal of Psychiatry* 147 (1985): 1–4.

deficit symptoms/syndrome These are the primary, enduring NEGATIVE SYMPTOMS of SCHIZOPHRENIA that are not considered secondary to other factors (e.g., DEPRESSION or ANXIETY, the effects of ANTIPSYCHOTIC DRUGS, or the environmental deprivation found in institutions). These terms were first proposed in a 1985 paper by W. T. Carpenter and his colleagues on deficit and nondeficit forms of schizophrenia. They are intended as a clarification and an alternative to CROW'S HYPOTHESIS of "Type I" and "Type II" schizophrenia. In Crow's two subtypes, POSITIVE SYMPTOMS (such as delusions and hallucinations) predominate in Type I but can also appear on a transient basis in Type II schizophrenia. The negative symptoms in Type II schizophrenia (restricted affect, diminished social drive, anhedonia, diminished intellectual ability) can also be transient in some cases, due to the secondary factors listed above. Carpenter and his coworkers wish to restrict more closely the two proposed subtypes of schizophrenia to one displaying a "primary enduring core of deficit symptoms" and one that does not. This proposed diagnostic category of "schizophrenia with deficit syndrome" would then most clearly be related to the variety of the disease most associated with neurological deterioration and a chronic course.

See also CHRONIC SCHIZOPHRENIA; COURSE AND OUTCOME OF SCHIZOPHRENIA.

Carpenter, W. T., D. W. Heinrichs, and A. M. Wagman. "Deficit and Nondeficit Forms of Schizophrenia: The Concept," *American Journal of Psychiatry* 145 (1988): 578–583.

Defoe, Daniel (1661–1736) Best remembered as the author of *Robinson Crusoe* (1719), Defoe was prolific writer and social critic who took a particularly keen interest in the humane treatment of the mentally ill. He wrote many articles on the abusive conditions in private madhouses, arguing that they should be inspected and licensed, which they eventually were. He published his own journal, known as the *Review,* and from time to time included articles of his own with themes like the 1706 "Scheme for the Management of Mad-houses."

degeneration theory In his *Traité des dégénérescences physiques, intellectuelles et morales de l'espece humaine* (Treatise on the Physical, Intellectual and Moral Degeneration of the Human Species) of 1857, the French alienist Benedict-Augustin Morel proposed the theory that physical and mental diseases were caused by immorality, substance abuse, masturbation, and living in unsanitary urban centers. These experiences in the life of an individual led to the hereditary transmission of a these physical, mental, and moral weaknesses to one's children. Each generation would thus pass along this hereditary taint, making each less and less fit to survive. It was believed (without statistical evidence until the end of the 1800s) that this process of DEGENERATION from an original healthy "type" would end family lines when the last generations were populated with persons who were too physically ill, insane, demented, or mentally retarded ("idiocy," "cretinism," or "feeble-mindedness") to survive and reproduce. This notion of "hereditary taint" or "bad blood" was akin to the notion of "original sin in the germ plasm"—that is, one was born burdened by the sins of the fathers (previous generations). Degeneration theory was an important influence in PSYCHIATRY in the latter half of the 19th century, particularly in France with the work of Valentin Magnan, in England with the work of Henry Mausdley, and in Germany in the work of Emil KRAEPELIN.

After its introduction by Emil Kraepelin in 1893, DEMENTIA PRAECOX (or *demence precoce,* a term first used by Morel in 1860) was viewed within this context as evidence of a "blood line" nearing the end of its degeneration process because it was a form of dementia arising in young people that is usually only seen in old age. Forms of insanity such as dementia praecox (SCHIZOPHRENIA) were thought to have an earlier AGE OF ONSET and a more severe course in each new generation. Today this phenomenon is known as genetic ANTICIPATION. It has been observed to occur in some neurodegenerative diseases and is being studied for its possible connection to schizophrenia. Degeneration theory became a dominant medical theory and a major source of PARANOIA among the public by the end of the 19th century, fueled in no small part by the popular hysteria provoked by the 1892 book *Entartung* (published in English as *Degeneration* in 1895). As an accepted theory in medicine, degeneration theory finally subsided in importance in the 1920s.

Backed by the authority of Francis Galton (1822–1911) in England, in the first half of the 20th century programs of EUGENICS (a term Galton coined) led to the promotion of selective breeding among humans to produce stronger blood lines of healthy human beings, forced sterilization of the insane, the immoral, and the criminal, and, in Nazi Germany, the murder of individuals (such as persons with dementia praecox/schizophrenia) who were deemed too biologically "unfit" to live and reproduce. The geneticist Eolf Axl Carlson traced the tragic history of eugenics in his 2001 volume, *The Unfit: A History of a Bad Idea.*

Emil Kraepelin, dementia praecox and degeneration It has long been asserted that Emil Kraepelin considered dementia praecox as evidence of the correctness of degeneration theory. We know from his autobiographical "self-assessment" that he wrote in 1920, and which remained unpublished until almost 80 years after his death, that he personally believed in degeneration theory and advocated eugenic programs to stop the "deterioration of the race" of the German people (*Volk*). But "degeneration" was more often used in his psychiatric publications to refer to the processes of progressive intellectual (dementia), physical, and social deterioration that occurred in an individual as part of a disease process that, in most persons, began only after puberty. For example, he originally introduced dementia praecox in 1893 as one of the insanities in the category of "psychic degenerative processes." In 1896 Emil Kraepelin estimated that in approximately 70 percent of the cases of dementia praecox he had observed, "hereditary predisposition" was present and "the so-called signs of degeneration were frequently observed" (*Psychiatrie,* 6th ed., p. 97) However, this hereditary predisposition did not lead directly to dementia praecox but instead to a metabolic self-poisoning of the body, or AUTOINTOXICATION (*Selbstvergiftung*), probably arising from the sex glands, which eventually affected the brain and produced psychotic symptoms (HALLUCINATIONS and DELUSIONS) and dementia. This belief was shared by another prominent German psychiatrist, Wilhelm Weygandt (1870–1939), who speculated in 1907 that "I should like to put forward a tentative explanation of dementia precox of my own. . . . I would suggest that so far as the organic side is concerned the most plausible concept is one of autotoxic damage affecting genetically predisposed brains." Kraepelin's use of the concept of degeneration should thus be viewed from these two perspectives: first, and most important, as a description of the course and outcome of a disease process, and only secondarily as evidence supporting the grander medical, social, cultural, and political claims of degeneration theory.

See also CHRONIC DELUSIONAL STATES IN FRENCH PSYCHIATRY; GENETICS STUDIES.

Carlson, E. A. *The Unfit: A History of a Bad Idea.* Cold Spring Harbor, N.Y.: Cold Spring Harbor Laboratory Press, 2001.

Engstrom, E., W. Burgmair, and M. M. Weber. "Emil Kraepelin's 'Self-Assessment': Clinical Autobiography in Historical Context," *History of Psychiatry* 13 (2002): 89–119.

Genil-Perrin, G. *Historie des origines et de l'évolution de l'idée de dégénérescence en médecine mentale.* Paris: 1913.

Morel, B. A. *Traité des dégénérescences physiques, intellectuelles et morales de l'espèce humaine.* Paris: 1857.

Weygandt, W. "Kritische Bemerkungen zur Psychologie der Dementia Praecox," *Monatsschrift für Psychiatrie und Neurologie* 22 (1907): 289–301.

deinstitutionalization With the advent of ANTIPSYCHOTIC DRUGS in the mid-1950s, and with the growing concern over the costs of institutionalizing large numbers of people and the harmful effects such living conditions might have, starting in 1955 literally hundreds of thousands of psychiatric patients were released—all too often to the streets—with little or no support services available to them. In 1955 there were approximately 559,000 patients in public psychiatric facilities in the United States, but by the mid-1980s that number had dwindled to about 110,000. The greatest number were released between 1965 and 1980, when an estimated 358,000 patients were sent back into the community to live. This process, although initially well-intentioned, led to the alarming problem of the homeless mentally ill, the "street people," that characterizes the last quarter of the 20th century.

Talbott, J. A. "Deinstitutionalization: Avoiding the Disasters of the Past," *Hospital and Community Psychiatry* 30 (1979): 621–624.

Torrey, E. F. *Nowhere to Go: The Tragic Odyssey of the Homeless Mentally Ill.* New York: Harper/Perennial, 1989.

délire de négation See COTARD'S SYNDROME.

délire d' énormité Literally the "delusion of enormity," a psychotic delusion that a person has undergone a massive increase in size. Such a person may insist that he or she fills up the entire room or is as large as the earth or perhaps even the entire universe. In some cases, it has been known to alternate with COTARD'S SYNDROME (the "delusion of negation"), and in fact it has been referred to as a "manic" form of Cotard's syndrome.

Enoch, M. D., and W. H. Trethowan. "Cotard's Syndrome." In *Uncommon Psychiatric Syndromes,* 2nd ed., edited by Enoch and Trethowan. Bristol: John Wright & Sons, 1979.

delirium An acute, reversible mental state characterized by clouded consciousness, confusion, extreme mental and motor excitement, defective perception, impaired memory, and a rapid flow of disconnected ideas. DELUSIONS and HALLUCINATIONS can accompany delirious states. Delirium is a symptom of an organic brain disorder, for it has a physiological basis (fevers, toxic effects from drugs or alcohol, exhaustion, etc.). Delirium is reversible, which distinguishes it from dementia, which is not.

From the time of ancient Greece and Rome, "delirium" has referred to a disturbance in the train of thinking, associated with physical disease. In 19th-century France, the term began to be used in reference to such a disturbance in thinking but without any connection to physical disease. For example Philippe PINEL uses the term *délire* to refer both to disturbances in logical reasoning and judgment (delusions) as well as to organic brain disease. In Great Britain and Germany, the distinction between "delusion" and "delirium" was largely maintained throughout the 19th century and is the basis of our modern definitions of these terms.

Berrios, G. E. "Delirium and Confusion in the 19th Century: A Conceptual History," *British Journal of Psychiatry* 139 (1981): 439–449.

delusion Historically, one of the primary symptoms of a psychotic disorder. The German psychiatrist Karl Jaspers once wrote that "Since time immemorial Delusion has been taken as the basic characteristic of madness." Although there is disagreement in the many different theories and definitions of what exactly a delusion is, a delusion is defined "a false personal belief based on incorrect inference about external reality" and is firmly maintained despite the consensually accepted beliefs of most others. Individuals with delusions will generally hold on to their beliefs even when confronted with strong evidence that contradicts their beliefs. In this sense, delusions are said to be "fixed," as if unchangeably cemented into the mind. Delusions are sometimes referred to as "ideational symptoms," because they involve a disturbance in ideas or cognition, whereas HALLUCINATIONS are sometimes called "perceptual" or "sensational symptoms," since they represent a disturbance in the processes of sensation and perception.

The first use of the word *delusion* in the English language in reference to mental disorder was in 1552, and the word's derivation can be traced back to a form of the Latin verb meaning "to play false." In Great Britain in the first half of the 19th century, the word *delusion* was used in a medical sense to refer to perceptual disorders (similar to our present use of the word *illusion*), but after 1850 it appears to have taken on its present meaning of "wrong belief."

See also CHRONIC DELUSIONAL STATES IN FRENCH PSYCHIATRY.

Arthur, A. Z. "Theories and Explanations of Delusions: A Review," *American Journal of Psychiatry* 121 (1964): 105–115.

Garety, P. "Delusions: Problems in Definition and Measurement," *British Journal of Medical Psychology* 58 (1985): 25–34.

Schmidt, G. "A Review of the German Literature on Delusion Between 1914 and 1939." In *The Clinical Roots of the Schizophrenia Concept,* edited by J. Cutting and M. Shepherd. Cambridge: Cambridge University Press, 1987.

delusional disorder A classification of psychotic disorders that first appeared in the 1987 *DSM-III-R*. The essential characteristic of delusional disorder is the persistent presence of a DELUSION that is not "bizarre" and is not due to any other psychotic disorder (such as SCHIZOPHRENIA, SCHIZOPHRENIFORM DISORDER, or a mood disorder such as bipolar illness). Persons with this disorder do not have obviously odd or peculiar behavior. As *DSM-III-R* stated, "A common characteristic of people with Delusional Disorder is the apparent normality of their behavior and appearance when their delusional ideas are not being discussed or acted upon." Yet they secretly (or in some cases, not so secretly) harbor a delusion that profoundly disagrees with reality. Formerly, this type of disorder was called paranoid disorder, but there are many different types of delusions that have nothing to do with "PARANOIA" (which is commonly interpreted as unfounded suspiciousness). The disorder rarely causes interruptions in intellectual or occupational functioning, and in most studies the average age of onset seems to be between 40 and 55.

There are seven different subtypes of delusional disorder: *erotomanic* (more traditionally known as Clérambault's syndrome), in which the delusion is that another person, usually of a higher social status, is in love with the subject; the *grandiose,* in which a person is convinced that he or she is "special" due to an inflated sense of power, identity, wealth, or special relationship to a deity or a special person (such as a celebrity); the *jealous,* in which the delusion is that one's sexual partner is unfaithful; the *persecutory,* in which the delusion involves a convincing belief that one is being purposely maligned or singled out for harassment in some way; the *somatic,* in which the person is convinced that he or she has some disease, mental disorder, or physical defect; the mixed type, in which delusions characteristic of one or more of the above types are present, but no one these predominates; and finally, a category of unspecified type for delusions that do not fit in the above categories.

In *ICD-10* (1992), this category of psychotic disorders is divided into *delusional disorder, other persistent delusional disorder,* and *unspecified persistent delusional disorder.* Delusions that are not related to schizophrenic delusions (that is, those that are "other than completely impossible or culturally inappropriate") must be present for at least three months. No hallucinations in any modality can be in evidence. The subtypes of persistent delusions are as follows: persecutory, litiginous, self-referential, grandiose, hypochondriacal (somatic), jealous, and erotomanic.

Delusional disorder has its roots in a long tradition in French psychiatry that identified a class of psychotic disorders that do not fall within the categories of schizophrenia (DEMENTIA PRAECOX) or a mood disorder (MANIC-DEPRESSIVE ILLNESS).

See also CHRONIC DELUSIONAL STATES IN FRENCH PSYCHIATRY; PARANOIA; PARAPHRENIA.

Dowbiggin, I. "Delusional Disorder." In *A History of Clinical Psychiatry: The Origin and History of Psychiatric Disorders,* edited by G. E. Berrios and R. Porter. London and New Brunswick, N.J.: Athlone Press, 1995.

delusional jealousy The false belief that one's sexual partner is engaging in sexual activities with others. This DELUSION of infidelity is also known

as the OTHELLO SYNDROME. Delusional jealousy is considered a psychotic disorder, whereas "obsessional jealousy" is the term used for persons with neurotic disorders. "Pathological jealousy" was first described by Karl Jaspers in 1910.

delusional perception A term for a phenomenon noticed in certain psychotic disorders in which the distinction between a DELUSION and an HALLUCINATION is not clear. It almost appears as if those individuals who are delusional are also caught in a process that changes their perceptual processes. Thus, when asked about their experiences, it is often difficult to distinguish whether the events described are simply delusions (bizarre ideas) or actual hallucinatory experiences that were "perceived" with the senses. This term (also called "perceptual delusions") is more often described in the German and French psychiatric literature than in the English-language literature.

Matussek, P. "Studies in Delusional Perception." In *The Clinical Roots of the Schizophrenia Concept: Translations of Seminal European Contributions on Schizophrenia,* edited by J. Cutting and M. Shepherd. Cambridge: Cambridge University Press, 1987.

delusions, bizarre A totally implausible idea or belief that is idiosyncratic and would not be believed as true by anyone. For example, a psychotic individual may believe that singer Diana Ross is the "Antichrist" or that singer Madonna is the biblical "Whore of Babylon."

delusions, grandiose A common psychotic delusion found particularly in PARANOID SCHIZOPHRENIA and in manic-depressive psychosis, in which a person has a highly exaggerated sense of his or her importance, identity, knowledge, or influence. For example, a psychotic individual may claim to own IBM and generously offer to write a hospital staff member a check for $5 million if they would only help that person escape or be discharged from the hospital. Many religious delusions are grandiose (e.g., "I'm Jesus Christ").

delusions, mood-congruent A delusion whose content matches the particular manic or depressed mood state that a person is in. For example, the delusion that one has AIDS or cancer when, in fact, one does not is consistent with a depressed mood in an individual. If in a manic mood state, grandiose delusions in particular may be mood-congruent (e.g., claims of owning millions of dollars or of being the most brilliant writer in the world).

delusions, mood-incongruent A delusion whose content does not match the particular mood state that a person is experiencing. These are the opposite of MOOD-CONGRUENT DELUSIONS.

delusions, nihilistic Commonly found in schizophrenia, these delusions involve the conviction that one does not exist, or that external reality does not exist. This is also referred to as COTARD'S SYNDROME.

delusions, persecutory One of the most common types of DELUSION found in PARANOID SCHIZOPHRENIA, and occasionally in other psychotic disorders as well. It is the delusion that the psychotic individual is being singled out, and even pursued for special abuse, by persons or "forces," and that this places the mentally disordered person in a constant state of danger. Delusions of being poisoned are common. Although known since antiquity, and included in ESQUIROL's descriptions of "monomania," the earliest comprehensive treatment of persecutory delusions was perhaps given by German psychiatrist Carl Wilhelm Ideler (1795–1860) in 1948. These delusions were also referred to as "persecutory delirium" by French psychiatrist Ernest Charles Lasègue in 1852.

Ideler, C. W. *Der Wahnsinn.* Bremen: 1848.

delusions, somatic A delusional belief about the structure of functioning of one's body. For example, a male schizophrenic patient may fully believe that he is pregnant, or a psychotic woman may believe

that a team of doctors kidnapped her during the night and removed her uterus and genitalia.

delusions, systematized An organized system of delusions that all refer to a similar theme and that form the basis for a psychotic individual's incorrect interpretation of new experiences. For example, a psychotic person who has failed a psychology licensing examination may believe that the members of the licensing board in that state are involved in a conspiracy against the afflicted person and, furthermore, that these board members are responsible for the person's inability to find a parking space. The term *systematic* or *systematized delusions* originated in the work of French psychiatrist Valentin Magnan of Paris. The idea was first put forth in a series of articles published in 1888 in *Le Progrès médical*, then in a monograph published in 1892 with his colleague Paul Sérieu (1864–1947), entitled *Le délire chronique à évolution systématique*. Such systematized delusions were not only organized but persistent, unlike the disorganized and transient delusions found in other psychotic disorders.

See also BOUFFÉE DÉLIRANTE; CHRONIC DELUSIONAL STATES IN FRENCH PSYCHIATRY.

delusions of being controlled One of the most common types of delusion found in SCHIZOPHRENIA, it involves the idea that a person's thought, feeling, and behavior are controlled by some external force (e.g., "Kate is controlling my thoughts"). This is also known as the Clérambault-Kandinsky syndrome.

delusions of passion See EROTOMANIA.

delusions of poverty The delusion that a person is totally devoid of any material possessions, or that such possessions will soon be taken away from the person, rendering him or her poverty-stricken.

delusions of reference The delusions that people, objects, or events in an individual's immediate environment have an unusual or "special" significance. This significance is usually of a negative or threatening quality, but not always. For example, a psychotic individual may believe that the expression on television newsman Dan Rather's face is a secret message that is intended just for that person.

demence A term used by both Philippe PINEL in 1801 and Benjamin RUSH in 1812 to describe what we would now call THOUGHT DISORDER—disconnected and disorganized thoughts that are strung together without any logical order. Pinel describes the "special character of dementia" that is still observed in schizophrenics today:

> Rapid succession or uninterrupted alternation of undulated ideas, and evanescent and unconnected emotions. Continually repeated acts of extravagance; complete forgetfulness of every previous state; diminished sensibility to external impressions; abolition of the faculty of judgment; perceptual activity.

Benjamin Rush preferred to rename this condition "dissociation," as he believed that this constituted its primary symptom. However, Rush's use of this term is different than the more commonly accepted definition of DISSOCIATION by Pierre JANET (1859–1947). Dissociation was "an association of unrelated perceptions, or ideas, from the inability of the mind to perform the operations of judgement and reason." Furthermore, "ideas, collected together without order, frequently constitute a paroxysm of the disease." Rush's emphasis on ASSOCIATION DISTURBANCES was later also emphasized by Eugen BLEULER in 1911 as one of the four PRIMARY SYMPTOMS OF SCHIZOPHRENIA.

Pinel, P. *A Treatise on Insanity* 1801. Reprint, Sheffield: W. Todd, 1806.

Rush, B. *Medical Inquiries and Observations upon Diseases of the Mind*. Philadelphia: Kimber & Richardson, 1812.

dementia Dementia is an ORGANIC MENTAL SYNDROME that is characterized by impairment in short- and long-term memory, disturbances in the ability to think abstractly, impaired judgment,

and personality changes; there is also evidence of other abnormal brain functioning. In personality changes, a person may not seem himself or herself, may become withdrawn, and a once lively personality may become flat. A once neat person may start to appear sloppy and apathetic. When social judgment is impaired by the organic brain disease process that produced the dementia, some people may become irritable, impulsive, or paranoid. They may wander about and become lost. Alzheimer's disease (primary degenerative dementia of the Alzheimer's type) is the picture of extreme dementia that most of us are familiar with.

According to modern definition, dementia may not necessarily be progressively degenerative, and actually may go into remission in some circumstances. However, in the 19th century the older idea of dementia was that it referred to chronic insanity or that it was a progressively degenerative brain disease that led to death (see DEGENERATION). With advances in the science of neurology in the second half of the 19th century, specific chronic brain disorders were identified that involved dementia, although conditions that could not be conclusively identified as "organic" were also recognized as "vesanic dementias." The idea of vesanic dementias contributed to the formation of the idea of PSYCHOSIS in the latter half of the 19th century.

Berrios, G. E. "Dementia during the 17th and 18th Centuries," *Psychological Medicine* (1987).

dementia infantalis A term first used in 1930 by Austrian psychiatrist Theodore Heller to describe CHILDHOOD ONSET SCHIZOPHRENIA. He thought that dementia infantalis was present in children before the age of four. It is sometimes referred to as "Heller's disease."

See also AUTISM, INFANTILE.

dementia paralytica See GENERAL PARALYSIS OF THE INSANE.

dementia paranoides A term coined by Emil KRAEPELIN in the fourth edition of his textbook, *Psychiatrie,* to characterize a psychotic disorder with a sudden onset and disorganized delusions, which progresses rapidly into DEMENTIA. Dementia paranoides was one of the "psychic processes of degeneration" in this 1893 textbook, along with DEMENTIA PRAECOX and CATATONIA. However, in the fifth edition of 1896, Kraepelin placed these three disorders under the category of "metabolic disorders leading to dementia." In 1899 dementia praecox ballooned into one of the two great insanities (along with MANIC-DEPRESSIVE ILLNESS), and dementia paranoides, catatonia, and HEBEPHRENIA were now merely forms of dementia praecox. Sigmund FREUD's famous interpretation of the autobiography of the psychotic Daniel Paul Schreber, formerly a presiding judge on Saxony's highest court, is where this term figures most prominently in his writings. Since Schreber was a homosexual, this helped support Freud's theory that homosexual panic was at the root of paranoia.

See also PARANOID SCHIZOPHRENIA.

Freud, S. "Psycho-analytic Notes on an Autobiographical Account of a Case of Paranoia (Dementia Paranoides)." In *The Standard Edition of the Complete Psychological Works of Sigmund Freud,* edited by J. Strachey. 1911. Reprint, New York: Macmillan, 1964.

dementia praecocissima This term was first used in 1905 by Italian psychiatrist Sante De Sanctis (1862–1935) to describe a form of dementia praecox that had its onset before puberty. De Sanctis is generally credited for being the first to describe what later become known as CHILDHOOD SCHIZOPHRENIA.

De Sanctis, S. *Neuropsichiatria infantile. Patalogia e diagnostica.* Turin: Lattes, 1925.

———. "On Some Varieties of Dementia Praecox," tr. M. Osborn. In *Modern Perspectives in International Child Psychiatry,* edited by J. G. Howells. 1906. Reprint, Edinburgh: Oliver & Boyd, 1969.

dementia praecox A term that referred to a psychotic disorder marked by rapid cognitive disintegration beginning soon after the clear onset of

the disease, usually in the years following puberty. Cognitive disintegration did not mean an impairment of intelligence but instead referred to a disruption in the various mental functions that we now commonly refer to as attention, memory, and goal-directed thinking (executive functions). DEMENTIA in this older sense meant "incoherence." The primary disturbance in dementia praecox was not one of mood (as was the case in MANIC-DEPRESSIVE ILLNESS), but of cognition. From the outset, dementia praecox was viewed as a progressively degenerating disease from which no one recovered.

Démence précoce (1853, 1860) This psychotic disorder was first mentioned by the French alienist Benedict-Augustin Morel in 1853, but later described in his 1860 textbook, *Traité des maladies mentales.* Morel introduced this term to define a disorder striking primarily men in their teenage or young adult years. Following the first clear disruption in their lives, their intellectual functioning rapidly declined. Morel placed this insanity within the larger context of his DEGENERATION THEORY. These young men were beginning a rapid intellectual deterioration that would result in total disability and possible death. Morel, however, did not conduct any long-term or quantitative research on the course and outcome of *démence précoce* (KRAEPELIN would be the first in history to do that), so this prognosis was based on speculation.

The contributions of Karl Kahlbaum and Ewald Hecker (1863–1874) In 1863 Karl KAHLBAUM (1828–99) of Prussia published his Habilitation (the equivalent of a second doctoral dissertation in Germany, necessary for becoming a university professor), *Die Gruppirung der psychischen Krankheiten* (The Classification of Psychiatric Diseases). In this book, Kahlbaum described a class of progressively degenerating psychotic disorders that he grouped under the term *Vesania typical* (typical insanity). In 1866 Kahlbaum became the director of a private psychiatric clinic in Görlitz, Prussia, a small town near Dresden. He was accompanied by his younger assistant, Ewald Hecker (1843–1909), and together they conducted a series of research studies on young psychotic patients that would eventuate in a major influence on the development of modern PSYCHIATRY. Together Kahlbaum and Hecker were the first to describe and name such syndromes as dysthymia, cyclothymia, PARANOIA, CATATONIA, and HEBEPHRENIA.

Perhaps their most lasting contribution to psychiatry was the introduction of the "clinical method" from medicine to the study of mental diseases, a method which is now known as psychopathology. Other than Morel's claims about his degeneration theory, the element of time had largely been missing from definitions of mental disorders. Psychiatrists made pronouncements about prognosis that were not based on careful observations of the changing symptoms of patients over time. MAD-DOCTORS, ALIENISTS, and other physicians who wrote about the insane arbitrarily invented names for insanities and described their characteristic signs and symptoms based on a short-term, cross-sectional observation period of their lunatic patients. When the element of time was added to the concept of diagnosis, a diagnosis became more than just a description of a collection of symptoms: diagnosis now also defined prognosis (course and outcome). An additional feature of the clinical method was that the characteristic symptoms that define syndromes should be described without any prior assumption of brain pathology (although such links could be made later as scientific knowledge progressed). Karl Kahlbaum first made his appeal for the adoption of the clinical method in psychiatry in his 1874 book on catatonia. Without Kahlbaum and Hecker there would be no dementia praecox.

Emil Kraepelin and dementia praecox (1893) In 1891 Emil Kraepelin left his position at the university in Dorpat (now Tartu, Estonia) to become a professor and director of the psychiatric clinic at the university in Heidelberg, Germany. Convinced of the value of Kahlbaum's suggestions for a more exact qualitative clinical method in psychiatry (which Kahlbaum never applied himself), Kraeplin realized that by adding a quantitative component to such a research program he could place psychiatry on a more scientific foundation. Quantification helped to eliminate any subjective biases on the part of the researcher. He began the first such research program of this nature in the history of psychiatry at Heidelberg in 1891, collecting data about every new patient that was admitted to the clinic (and not just "interesting cases," as had been

the case in the past) and summarizing them on specially prepared index cards, his famous *Zählkarten.* He had been keeping data on such cards since 1887. In his posthumously published *Memoirs* (which was first published in German 61 years after his death), Kraepelin described his method:

> . . . after the first thorough examination of a new patient, each of us had to throw in a note [in a "diagnosis box"] with his diagnosis written on it. After a while, the notes were taken out of the box, the diagnoses were listed, and the case was closed, the final interpretation of the disease was added to the original diagnosis. In this way, we were able to see what kind of mistakes had been made and were able to follow-up the reasons for the wrong original diagnosis (p. 61).

Kraepelin was obsessed with finding patterns in the data on these cards, taking them home with him or on vacation at times. In 1893, two years after starting his more rigorous research program in Heidelberg, the fourth edition of Kraepelin's textbook, *Psychiatrie,* reflected some preliminary impressions derived from the analysis of his cards. Clinical syndromes involved not only a diagnosis according to signs and symptoms, but one which also included course and outcome. In that edition, he introduced a class of psychotic disorders he called psychic degenerative processes. Three of these came directly from the work of Kahlbaum and Hecker: DEMENTIA PARANOIDES (a sudden-onset, degenerative form of Kahlbaum's paranoia; catatonia (directly from Kahlbaum's 1874 monograph on the subject; and dementia praecox, which was essentially Hecker's hebephrenia (as described in 1871). Dementia praecox was hebephrenia and would remain so in Kraepelin's thinking for six more years.

In March 1896 the fifth edition of Kraepelin's textbook appeared. In it, Kraepelin stated that he was confident of the value of his clinical method of using qualitative and quantitative data collected over a long period of observation of patients as a way of developing a diagnosis that included prognosis (course and outcome):

> What convinced me of the superiority of the clinical method of diagnosis (followed here) over the traditional one, was the *certainty with which we could predict (in conjunction with our new concept of disease) the future course of events.* Thanks to it the student can now find his way more easily in the difficult subject of psychiatry.

In the 1896 fifth edition, dementia praecox (still essentially hebephrenia), dementia paranoides, and catatonia are separate psychotic disorders included among "metabolic disorders leading to dementia."

In the sixth edition of *Psychiatrie* of 1899, Kraepelin reordered the psychiatric cosmos for the next century by grouping most of the insanities into two large categories, dementia praecox and manic-depressive illness. They were distinguished by the following characteristics: dementia praecox was primarily a disorder of intellectual functioning, whereas manic-depressive illness was primarily a disorder of affects or mood, dementia praecox had a uniformly deteriorating course and a poor prognosis, whereas manic-depressive insanity had a course of acute exacerbations followed by complete remissions with no lasting deterioration of intellectual functioning, and there were no recoveries from dementia praecox, whereas in manic-depressive illness there were many complete recoveries. In 1899 dementia praecox took its now-familiar form as a heterogenous class of psychotic disorders comprised of hebephrenic, catatonic, and paranoid forms. These forms have persisted until today through Eugen BLEULER'S SCHIZOPHRENIA of 1908 (to which he added a fourth form, dementia simplex, or simple schizophrenia), and the main types of schizophrenia in *DSM-IV-TR* (the paranoid, catatonic, and disorganized types, with the latter retaining its historical designation as the hebephrenic type in *ICD-10* [1992]).

In the seventh edition of 1904, there was little change in the description of dementia praecox, but Kraepelin does admit for the first time that in a small number of cases recovery from dementia praecox might occur.

The eighth edition of Kraepelin's *Psychiatrie* was a four-volume opus, each of which appeared in different years between 1909 and 1915. In this edition, dementia praecox became one of the "endogenous dementias." It is in the 1913 third

volume (second part) of this edition that Kraepelin adjusts his concept of prognosis to admit that a partial remisison of symptoms occurred in approximately 26 percent of his patients. This brought dementia praecox in line with Eugen Bleuler's claims about schizophrenia, which he had insisted from the start (in 1908) that (a) in many cases there was no fateful progressive deterioration, (b) in some cases the symptoms did indeed remit for periods of time, and (c) there were cases of complete recovery.

The eighth edition of 1913 is also notable for the fact that Kraepelin increased the number of forms of dementia to 11. However, the three classical original subtypes would remain as the most influential description of this disorder for the century that followed.

The eighth edition of *Psychiatrie* was the last Kraepelin would produce in his lifetime. He was working on a ninth edition with Johannes Lange (1891–1938) but died in 1926 before it could be completed. Lange finished the bulk of it and published it in 1927.

Etiology Kraepelin realized that the state of scientific knowledge was such that definitive claims about the cause of dementia praecox could not be made. Heredity clearly played a role, as Kraepelin and his research associates had demonstrated this in quantitative research. As a result of following the clinical method suggested by Kahlbaum, Kraepelin set aside claims about underlying brain disease or specific neuropathology in the diagnostic descriptions of his mental disorders. However, from the fifth edition of 1896 to the third volume of the eighth edition of 1913, it was clear that Kraepelin believed that dementia praecox was caused by a poisoning of the brain and "autointoxication," probably arising from the sex glands after puberty. Kraepelin's ideas about AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX is covered in depth in a separate entry in this volume.

Dementia praecox is a universal human disease Kraepelin believed that dementia praecox was not a culture-bound syndrome and that it represented a disease process that could be found all over the world. Kraepelin himself loved to travel, and in Asia he observed that dementia praecox was similar to the European form of the illness in Chinese, Japanese, Tamil, and Malay patients, leading him to suggest in the eighth edition of *Psychiatrie* that "we must therefore seek the real cause of dementia praecox in conditions which are spread all over the world, which thus do not lie in race or in climate, in food or in any other general circumstance of life. . . ."

Treatment Without knowing the cause of dementia praecox or manic-depressive illness, Kraepelin repeatedly stated that there could be no treatments specific to these conditions. Treatment for these insanities was the same for any institutionalized patient with any diagnosis: the occasional use of drugs (opiates, barbiturates, and so on) to alleviate acute episodes of distress, prolonged baths (greatly admired by Kraepelin as a humane method of calming patients), and occupational activities (if possible). Kraepelin himself had experimented with hypnosis early in his career and found it lacking. Psychotherapy as such was not part of the medical cognition of Kraepelin. In fact, Kraepelin detested both FREUD and JUNG for introducing diagnostic terms and forms of treatment that had no empirical basis.

The reception of dementia praecox By 1899 Kraepelin himself had counted almost 20 German-language publications that made reference to his new diagnostic term, dementia praecox. In the decade after 1899, the number of German-language publications using Kraepelin's categories of dementia praecox and manic-depressive illness as a basis for clinical speculation and experimental research exploded. German-language psychiatric concepts were always introduced much faster in America (than, say, Britain) where émigré German, Swiss, and Austrian physicians essentially created American psychiatry. Swiss-emigree Adolf MEYER, arguably the most influential psychiatrist in America for the first half of the 20th century, published the first critique of dementia praecox in an 1896 book review of the fifth edition of Kraepelin's textbook. But it was not until 1900 that the first three American publications regarding dementia praecox appeared, one of which was a translation of a few sections of Kraepelin's sixth edition of 1899 on dementia praecox. Because so many influential American physicians began to take psychoanalysis seriously after Freud and Jung attended a conference at Clark University in 1909, dementia

praecox and, after 1911, Bleuler's schizophrenia were openly accepted. Until 1910 Bleuler had been peripherally connected through Jung to Freud's psychoanalytic movement, and this eased the adoption of his broader version of dementia praecox (schizophrenia) in America over Kraepelin's more narrow and prognostically more negative one. Until the late 1950s the terms dementia praecox and schizophrenia were used interchangeably in American psychiatry. The reception of dementia praecox as an accepted diagnosis in British psychiatry came much slower, perhaps taking hold only around the time of the First World War. In France an older psychiatric tradition regarding the psychotic disorders (see the entry for CHRONIC DELUSIONAL DISORDERS IN FRENCH PSYCHIATRY) predated Kraepelin, and the French never fully adopted Kraepelin's classification system. Instead the French maintained an independent classification system throughout the 20th century. After 1980, when *DSM-III* totally reshaped psychiatric diagnosis, French psychiatry began finally to alter its views of diagnosis to converge with the North American system. Kraepelin thus finally conquered France via America.

The "neo-Kraepelinians" and DSM-III (1980) Editions of the *Diagnostic and Statistic Manual of Mental Disorders* since the first one in 1952 had reflected views of schizophrenia as "reactions" or "psychogenic" (*DSM-I*), or as manifesting Freudian notions of "defense mechanisms" (as in *DSM-II* of 1968, in which the symptoms of schizophrenia were interpreted as "psychologically self-protected). The diagnostic criteria were wide, including either concepts that no longer exist or that are now labeled as personality disorders (for example, SCHIZOTYPAL PERSONALITY DISORDER). There was also no mention of the dire prognosis Kraepelin had made. Schizophrenia seemed to be more prevalent and more treatable than either Kraepelin or Bleuler would have allowed.

As a direct result of the effort to construct RESEARCH DIAGNOSTIC CRITERIA in the 1970s that were independent of any clinical diagnostic manual, Kraepelin's ideas began to return in prominence. For research purposes, the definition of schizophrenia returned to the narrow range allowed by Kraepelin's dementia praecox. Furthermore, the disorder was a progressively deteriorating one once again, with the notion that recovery, if it happened at all, was rare. This revision of schizophrenia became the basis of the diagnostic criteria in *DSM-III*. Some of the psychiatrists who worked to bring about this revision referred to themselves as the neo-Kraepelinians.

Berrios, G. E., and R. Hauser. "The Early Development of Kraepelin's Ideas on Classification," *Psychological Medicine* 18 (1988): 813–822.

Diem, O. "Die einfach demente Form der Dementia praecox," *Archiv für Psychiatrie und Nervenkrankheiten* 37 (1903): 111–187.

Hecker, E. "Die Hebephrenie," *Virchows Archiv für pathologische Anatomie* 52 (1871): 392–449.

Jablensky, A., et al. "Kraepelin Revisited: A Reassessment and Statistical Analysis of Dementia Praecox and Manic-Depressive Insanity in 1980," *Psychological Medicine* 23 (1993): 843–858.

Kahlbaum, K. *Die Gruppierung der psychischen Krankheiten und die Eintheilung der Seelenstorungen.* Danzig, 1863.

———, K. *Die Katatonie oder das Spannungsirresein.* Berlin: Hirschwald, 1874.

Kraepelin, E. "Dementia praecox." In *The Clinical Roots of the Schizophrenia Concept: Translations of Seminal European Contributions On Schizophrenia,* edited by J. Cutting and M. Shepherd. 1896. Reprint (5th ed.), Cambridge: Cambridge University Press, 1987.

Kraepelin, E. *Memoirs,* Berlin: Springer-Verlag, 1987.

Dementia Praecox Studies The first scientific or medical journal in any language to be named after a psychiatric disorder. During its short life (1918 to 1922), *Dementia Praecox Studies* not only provided extensive bibliographic essays and reviews of published laboratory reports from several nations but also provided translations of selected experimental studies of unpublished doctoral theses from the original German or French. Perhaps most important, *Dementia Praecox Studies* served as the primary place of publication for the experimental reports of the Research Laboratory of the Psychopathic Hospital of Cook County (Illinois) and the editorials of its director, the noted Chicago surgeon and, in 1895, the unsuccessful Socialist candidate for mayor of Chicago, Bayard Taylor HOLMES, M.D. (1852–1924).

Dementia Praecox Studies was the only journal ever produced by the handful of Kraepelinian physicians in the United States. Like Emil KRAEPELIN, they believed that MENTAL DISORDERS were first and foremost brain diseases with neuropathological, biochemical, infectious, and genetic causes. But from the 1890s until the late 1960s, American psychiatry was dominated by the followers of Adolf MEYER's "psychosocial reaction" theory and Sigmund FREUD's pseudoscience of PSYCHOANALYSIS. These traditions of "mind twist men" were suspicious of laboratory science and rejected biological and genetic causes for mental disorders. The premature death from pneumonia of Harvard Medical School pathologist Elmer Ernest Southard (1876–1920) left the "brain spot men" without a prominent spokesman. The death of Bayard Holmes in 1924 essentially ended the Kraepelinian movement in America for decades.

The opening pages of the January 1918 edition contain the following invitation from Herman Campbell Stevens for the submission of laboratory research reports: "The purpose of this publication is to arouse interest in the subject of dementia praecox. . . . How little is known about the disease is apparent from a reading of the standard treaties on psychiatry and from the current literature. It is the purpose of this journal to serve as a clearing-house for scientifically established facts with regard to dementia praecox. Any competent and contentious study of a morphological, biochemical or psychiatric nature will be accepted. It is the aim of the editors to encourage research in the hope that a rational therapy and prophylaxis will result." Bayard Holmes unabashedly expressed his "faith" in the hypothesis that "disease of the mind is the result of organic disease of the body," and as "in spite of the magnitude of this problem there is a great scarcity of books and monographs dealing with the physical, chemical and biologic conditions of the unfortunate victims of this disease," he urges "the publication of a journal devoted exclusively to the study from the organic point of view, of one part of the field of mental disease, viz., dementia praecox."

Holmes, B. "Prospectus of *Dementia Praecox Studies*," *Dementia Praecox Studies* 1 (January 1918), unnumbered appendix to the first issue.

Stevens, H. C. "Our Point of View," *Dementia Praecox Studies* 1 (January 1918): 1–2.

demoniac A person who is "possessed" by demons or evil spirits. In all cultures, whether simple or complex and technological, there is usually a belief that mental illness was caused by such discarnate entities.

See also CACODEMONOMANIA; POSSESSION SYNDROME.

demonomania A 19th-century term for a type of mental disorder in which a person believes his or her thoughts, feelings, or behaviors are due to the direct influence of, or communication with, "spiritual" entities. ESQUIROL devoted an entire chapter in this disorder in his 1838 *Mental Maladies,* which he said is composed of "all those forms of delirium which have reference to religious beliefs." He identifies two distinct subtypes of demonomania, depending on whether the person believes he or she is influenced by "good" or "bad" spirits. The first of these, *theomania,* "would have designated that class of the insane, who believe that they are God, who imagine that they have conversations and intimate communications with the Holy Spirit, angels and saints, and who pretend to be inspired, and to have received a commission from heaven to convert men." The second type of demonomania, CACODEMONOMANIA, involves such imagined contact with evil spirits or the Devil. Esquirol uses the word *demonomania* to refer to both "good" and "evil" spiritual influences rather than just evil ones since, as he correctly points out, "The word demon among the ancients was not understood in a bad sense. It signified the Divinity, a tutelary Genius, a guardian Spirit. . . ." Esquirol suggests he is thus "preserving the primitive significance of this word."

See also POSSESSION SYNDROME.

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity,* trans. E. K. Hunt. Philadelphia: Lea & Blanchard, 1845; first published, 1838.

Noll, R. *Vampires, Werewolves, and Demons: Twentieth Century Reports in the Psychiatric Literature.* New York: Brunner/Mazel, 1991.

denial A type of defense mechanism in which a person does not seem to be aware of some aspect of external reality or of himself that is obvious to others. This type of behavior is commonly observed in people with psychotic disorders, and in its extreme forms denial can give an individual's statements an almost delusional quality.

See also DELUSION.

Denmark See SCANDINAVIA.

depersonalization An aberration of the sense or experience of oneself in which the feeling of the "reality" of one's experience is missing. People experiencing depersonalization claim that they feel distant from their own experience, that it is "dreamlike," or that reality has an uncanny "strangeness" to it. They may feel that they are automatons, or that their experience is "automatic" and not "spontaneous" in any way. Feelings that one's extremities have changed in size sometimes accompany this syndrome. Depersonalization can occur in normals for temporary periods of time (particularly in adolescents, with estimates that as many as 70 percent of them experience it at one time or another), but it is also experienced by those individuals who are diagnosed with SCHIZOTYPAL PERSONALITY DISORDER, SCHIZOPHRENIA, or, when not psychotic, depersonalization disorder, which is one of the DISSOCIATIVE DISORDERS.

depression When depression is present in an individual afflicted with one of the psychotic disorders it is considered a dangerous sign. Suicide is far more likely to result from depression in psychotic individuals. Studies have shown that for SCHIZOPHRENIA, an individual is most likely to commit suicide within the first 10 years of the onset of the disease.

Depression has always been a type of AFFECTIVE DISORDER, but there has been more recognition that many people who are diagnosed with schizophrenia suffer from depression. This depression may be caused by the underlying schizophrenic disease process, the realization by the person that his or her mental capacities are deteriorating, or as a side effect of antipsychotic medication. Many schizophrenics are thus also given ANTIDEPRESSANT DRUGS along with their antipsychotic medication. Sometimes people who are suffering from a severe depression can hear AUDITORY HALLUCINATIONS and, in many ways, appear to be schizophrenic. However, clinicians must make the sometimes difficult differential diagnosis between this depression with psychotic features and true schizophrenia.

See also ANTIPSYCHOTIC DRUGS.

DeLisi, L. E. *Depression in Schizophrenia.* Washington, D.C.: American Psychiatric Press, 1990.

Sands, J. R., and M. Harrow. "Depression during the Longitudinal Course of Schizophrenia," Schizophrenia Bulletin 25 (1999): 157–171.

derealization This is the component of DEPERSONALIZATION in which one's sense of the reality of one's world is disturbed. Depersonalization includes alterations in the sense of identity (e.g., the feeling of being an automaton), in addition to derealization.

dereistic thinking A word coined by Eugen BLEULER in 1912 to describe a type of intense fantasy activity that totally ignores any contradictions with reality and that may seem quite realistic. Bleuler constructed the term "dereistic" from two Latin words meaning "away from reality." Dereistic thinking sometimes occurs in the daydreams of normal people, but it is found in its clearest (and most reality-free) forms in dreams, the hallucinations and delusions of schizophrenics, and in mythology. Bleuler's concept of dereistic thinking resembles a similar process later referred to by his colleague at the BURGHÖLZI HOSPITAL in Zurich, C. G. JUNG, as "active imagination." Dereistic thinking also resembles the descriptions of REGRESSION or of "regression in the service of the ego" by Sigmund FREUD and his followers.

Bleuler, E. *Textbook of Psychiatry.* 4th ed. Translated by A. A. Brill. 1916. Reprint, New York: Macmillan, 1924.

De Sanctis, Sante (1862–1935) An Italian physician and a professor of psychiatry at the University of Rome who is perhaps best remembered for his 1905 description of DEMENTIA PRAECOCISSIMA, a childhood form of DEMENTIA PRAECOX. He wrote on a wide variety of topics, including dreams, experimental psychiatry, and forensic psychiatry. In 1932 he published an autobiography of his life and career in PSYCHIATRY.

deteriorating psychoses A 19th-century term for psychotic disorders marked by their DEGENERATION, such as DEMENTIA PRAECOX.

developmental insanity See ADOLESCENT INSANITY.

diagnosis, differential One of the most important determinants of treatment is the diagnosis of the disorder. This is extremely important when it comes to severe MENTAL DISORDERS such as SCHIZOPHRENIA or BIPOLAR DISORDER, which often require different classes of drugs and which have different courses. Often one of the first diagnostic decisions that a clinician must make is whether the patient is psychotic (out of touch with reality) or not. If so, then: Are the symptoms due to one of the psychotic disorders, or are they due to an organic mental disorder (such as an underlying neurological disease or intoxication)? If a known organic brain disease, or intoxication, can be ruled out, then the clinician must decide which among the various psychotic disorders best fits the history of the person's illness and the type of symptoms that person is displaying. Often a difficult differential diagnosis must be made between schizophrenia (particularly the paranoid subtype) and a manic episode with psychotic features.

The two most commonly used diagnostic system are the AMERICAN PSYCHIATRIC ASSOCIATION'S *DSM-IV-TR* (2000) and the WORLD HEALTH ORGANIZATION'S *ICD-10* (1992).

American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders.* 4th ed, text revision. Washington, D.C.: American Psychiatric Association, 2000.

World Health Organization, *Mental Disorders: Glossary and Guide to Their Classification in Accordance with the Tenth Revision of the International Classification of Diseases.* Geneva, Switzerland: World Health Organization, 1992.

diathesis-stress theories One of the main categories of genetic theories of SCHIZOPHRENIA. Diathesis-stress theories all posit that it is the interaction between genetic heritage (the "diathesis" or "inherited predisposition," which places the person at "high-risk" for the development of the disease) and stressors in the environment that causes the disease. Diathesis-stress theories are polygenetic ones. The diathesis is often assumed to involve the additive effect of the operation of a large number of genes, sometimes called schizophrenic polygenes. These theories hold that the more schizophrenic polygenes an individual inherits, the more vulnerable that person is to stressors in the environment that can induce the onset of schizophrenia.

A famous theory of the diathesis-stress causes of schizophrenia was put forth by clinical psychologist Paul Meehl in 1962. Meehl proposed that a genetic predisposition for particular kinds of neurological defects, which he called SCHIZOTAXIA, must interact with the experiences of environmental social learning to produce a type of person that may be called a schizotype. If the schizotype is subjected to certain stressors that are severe enough, that person will develop schizophrenia. Meehl's theory fits in with the other polygenetic diathesis-stress theories because it accounts for the interaction of heredity and the environment in the production of schizophrenia, and it allows for a wide range of schizophrenia-like disorders that the schizotype can exhibit without experiencing the extreme stressors that could cause schizophrenia. Furthermore, it assumes that the environment may be the source of the development of one over the other type of schizophrenic subtype.

Diathesis-stress theories based on polygenetic assumptions are still among the most widely accepted theories with researchers who are trying to learn the causes of severe MENTAL DISORDERS such as schizophrenia and BIPOLAR DISORDER. These theories are the latest battleground in the longstanding "nature v. nurture" debate in science.

Yet, with increases in our knowledge of the causes of diseases, it is becoming clearer and clearer that the nature-nurture distinction is becoming more and more blurred. Epidemiologist Brian McMahon succinctly lists the problems in understanding the complexity of gene-environment interactions:

1. It has become clear that there is no disease that is determined entirely by genetic or environmental factors.
2. There is, evidently, more overlap in the time of operation of genetic and environmental factors than was previously suspected.
3. Just as the environment may exert its effect through the genetic mechanism of mutation, so may genetic factors operate by changing the environment.
4. The roles of genes and environment, and the nature of the specific factors involved, may be quite different in individuals with identical manifestations.

See also GENETIC TRANSMISSION; HIGH-RISK STUDIES.

MacMahon, B. "Gene-environment Interaction in Human Disease." In *The Transmission of Schizophrenia,* edited by D. Rosenthal and S. Kety. Oxford: Pergamon Press, 1968.

Meehl, P. "Schizotaxia, Schizotypy, Schizophrenia," *American Psychologist* 17 (1962): 827–828.

dibenzodiazepine See ANTIPSYCHOTIC DRUGS.

dibenzoxazepine See ANTIPSYCHOTIC DRUGS.

dihydroindolone See ANTIPSYCHOTIC DRUGS.

dimensions of schizophrenia SCHIZOPHRENIA has always been characterized as a "heterogeneous" disorder made up of several different clinical "subtypes" or, perhaps, several different diseases. Emil KRAEPELIN posited three forms for his DEMENTIA PRAECOX (1899): PARANOIA, HEBEPHRENIA, and CATATONIA. Eugen BLEULER added a fourth to his schizophrenia concept (1908), a subtype called "simple schizophrenia." Both of the current major diagnostic manuals of mental disorders, *DSM-IV* (1994) and *ICD-10* (1992), base their diagnostic criteria for schizophrenia on Kraepelin's and Bleuler's clinical subtypes.

"Subtype" models of schizophrenia were based on clinical observation of symptoms and the grouping and classification of those symptoms by individual researchers. By the 1970s a movement arose to reexamine these traditional subtypes using the new findings in neuropathology, genetics neuroimaging, and neuropsychology as a basis for a new model of schizophrenia. In 1980 T. J. Crow proposed the first of these new models, his "two-syndrome concept" of schizophrenia involving Type I (positive symptoms, later onset, better prognosis) and Type II (negative symptoms, earlier onset, and poorer prognosis). CROW'S HYPOTHESIS generated a great deal of additional research and, by 1987, its claims were being challenged by new statistical studies of the symptoms of schizophrenia using factor analysis that led to new "dimensional models" of schizophrenia.

Factor analysis is a statistical technique that, when used in studies of schizophrenic symptoms quantified with the use of structured interviews, identified groups of related symptoms that tend to coexist in an individual. Closely related symptoms "load" onto a single "factor" or "dimension." Factor analysis does not identify discrete clusters of patients (which is what subtype models like those of Kraepelin, Bleuler, or *DSM-IV-TR* claim to do). However, it does identify clusters of symptoms that may be related to ongoing findings on the biological processes in schizophrenia. Proponents of dimensional models claim that this is indeed the case, and that statistically created, quantitative dimensional models are better indicators of possible underlying neuropathology in schizophrenia.

The first dimensional model of schizophrenia using factor analysis was proposed by Peter F. Liddle in 1987. Liddle's factor analytic studies came up with four dimensions for three newly proposed syndromes for schizophrenia: (1) a psychomotor poverty syndrome, (2) a disorganization syndrome, and (3) a reality distortion syndrome.

According to Liddle, there is a disconnection of the neuronal networks in the brain that serve supervisory mental functions (the executive mental functions, usually associated with the frontal lobe).

Most factor analytic studies of schizophrenic symptoms come up with three or four dimensions. Most recently, Mark Lenzenweger has proposed a four-dimension model of schizophrenia: (1) reality distortion (HALLUCINATIONS, DELUSIONS), (2) disorganization (positive formal thought disorder, bizarre behavior), (3) negative symptoms (flattened affect, AVOLITION, ALOGIA, asociality), and (4) premorbid social functioning.

Whether the traditional clinical subtypes of schizophrenia or the new dimensional models will prevail in the future is presently unknown.

Liddle, P. F. "Inner Connections within the Domain of Dementia Praecox: Role of Supervisory Processes in Schizophrenia," *European Archives of Psychiatry and Clinical Neuroscience* 245 (1995): 210–215.

———. "The Symptoms of Chronic Schizophrenia: A Re-Examination of the Positive-Negative Dichotomy," *British Journal of Psychiatry* 151 (1987): 145–151.

Lenzenweger, M. F. "Schizophrenia: Refining the Phenotype, Resolving Endophenotypes," *Behaviour Research and Therapy* 37 (1999): 281–295.

diminished responsibility A legal term in England that has been used since the 13th century as an argument to plea the innocence of mentally ill offenders. Prior to this time insanity was viewed as an affliction from God to punish sinfulness, and therefore criminal activities by such individuals were not viewed with compassion. The concept of "guilty, but insane" was introduced only in 1843.

See also INSANITY DEFENSE; M'NAUGHTEN RULES.

diphenhydramine See ANTIPARKINSONIAN DRUGS.

disconnection theories of schizophrenia It has long been known that specialized NEURAL CIRCUITS in the human brain connect disparate regions of the cortex and subcortical structures to perform specific types of tasks. There are many such neural networks in the brain, and much research has been done to learn how these functionally specialized "systems" or "populations of neurons" work in normal human brains as they perform very simple tasks (for example, a simple memory or spatial task). There is much about the functioning of the normal human brain that we still do not understand.

The problem is therefore compounded when we try to understand the "connectivity" of different regions of the human brain when these same simple tasks are performed by persons with SCHIZOPHRENIA. A growing class of theories of schizophrenia claim there is an abnormal connection in the circuitry between different regions of the brain and that these regions do not cooperate on specific tasks the way they would in a brain belonging to a person who does not have schizophrenia. These disconnection theories, as they are called, are now a major focus of investigation in schizophrenia research. A primary source of data supporting these various complementary theories comes from functional BRAIN IMAGING studies. Although some theories compete with one another, most complement one another and overlap to a greater or lesser degree.

The major disconnection theories are as follows: (1) Schizophrenia is a deficit of neuronal connectivity between the frontal lobe and the temporal lobe of the brain. This theory is associated with the studies of Daniel Weinberger, K. J. Friston, C. D. Frith, and Peter Liddle. (2) The positive symptoms of schizophrenia are due to a dysfunction of the temporolimbic cortex. This is a theory associated with the work of the German neuropathologist B. Bogerts. (3) Schizophrenia is due to a deficit in the connectivity between the thalamus (a major relay center for messages throughout the brain). This is a theory proposed by E. G. Jones. (4) Schizophrenia is due to a dysfunction in cortical-subcortical-cerebellar circuitry. This theory, known as the "cognitive dysmetria" theory, is proposed by Nancy Andreasen.

Friston, K. J. "Schizophrenia and the Disconnection Hypothesis," *Acta Scandinavica Psychiatrica* 99 (1999): 68–79.

Friston, K. J., and C. D. Frith. "Schizophrenia: A Disconnection Syndrome?" *Clinical Neurosciences* 3 (1995), 89–97.

disorganized type One of the classic subtypes of SCHIZOPHRENIA in *DSM-IV-TR* (2000), better known throughout the history of psychiatry as HEBEPHRENIA (first described by Ewald Hecker in 1871). In *ICD-10* (1992), this form of schizophrenia is still known as the "hebephrenic type." This syndrome is marked by incoherence (disorganized speech), disorganized behavior, an obvious LOOSENING OF ASSSOCIATIONS, and FLAT AFFECT. Affect is also often inappropriate. Sometimes there can be a "silliness" to it, including giggling, strange mannerisms, frequent somatic (hypochondriacal) complaints, and unusual facial grimaces or other odd behavior. There may be AUDITORY HALLUCINATIONS of voices or DELUSIONS, but the delusions are unsystematic and grossly illogical.

Hebephrenia was Emil KRAEPELIN's model for DEMENTIA PRAECOX in the 1893 and 1896 editions of his textbook, *Psychiatrie*. In those editions, dementia praecox (hebephrenia), DEMENTIA PARANOIDES, and CATATONIA were grouped together as three separate but related psychotic disorders. It was only in the 1899 edition that hebephrenia becomes only one of three forms of dementia praecox, along with catatonia and the paranoid form. The hebephrenic (disorganized), catatonic, and paranoid forms of schizophrenia are still recognized in current diagnostic manuals. The disorganized type (hebephrenia) is still regarded as the most chronic. NEGATIVE SYMPTOMS (constricted emotional range and intellectual abilities, ALOGIA, AVOLITION, and so on) seem to predominate over POSITIVE SYMPTOMS (HALLUCINATIONS and delusions). In clinical lore it is also associated with earlier age of onset and afflicts males far more than females. However, the scientific basis of dividing schizophrenia into these subtypes is currently questionable. Clinical experience and research studies indicate that most persons with schizophrenia have symptoms of one or more of the subtypes during their lives (hence the category UNDIFFERENTIATED TYPE for these persons), and there is no current biological or genetic basis for discriminating schizophrenia into various types. The disorganized type, however, is "classical" schizophrenia.

disorientation This is the clinical term most often used for people who have an obvious organic mental syndrome (such as DELIRIUM or DEMENTIA) and who are confused about who they are, where they are, or what day of the week, month, or even year it is. A common shorthand notation for this, often seen in clinical progress notes, is "disoriented X 3" (i.e., disoriented in three spheres of normal experience).

dissociation This is literally a splitting of the normally coherent and integrated functions of consciousness, particularly identity and memory. It is the defining characteristic of the DISSOCIATIVE DISORDERS, which include dissociative identity disorder, psychogenic fugue, psychogenic amnesia, and depersonalization disorder.

The concept of dissociation was apparently introduced by French ALIENIST J. J. Moreau de Tours in 1845. Pierre JANET (1859–1947) provided the first extensive psychological elaboration of this concept in his classic work, *L'Automatisme Psychologique,* in 1889 to describe systems of associated ideas that have been split off from consciousness and exist in a parallel life along with the dominant stream of consciousness. Janet referred to dissociation as *"dèsagrègation."* As this "disaggregation" or "dissociation" (as became the customary translation and use of this word in English) strengthens around its thematic core, referred to by Janet as "subconscious fixed ideas," the gap between these parallel streams of consciousness are widened, and *existences secondes,* or "secondary existences," are then created. Janet felt that this was a pathological—not a normal—psychological process and was to be found in hysteria, hypnosis, and in instances of "dual consciousness" or multiple personality.

Joseph Breuer (1842–1925) and Sigmund FREUD (1856–1939) also contributed to the study of dissociative phenomena with their interpretation of the famous case of "Anna O." reported in 1895 in their book, *Studies On Hysteria,* Anna O. was treated by Breuer from 1880 to 1882 for a series of psychosomatic problems and peculiar dissociative absences. However, Breuer and Freud disagreed as to the fundamental nature of these absences, with Breuer interpreting these phenomena as a form of "autohypnosis" and Freud insisting that their basic reason for existing was to serve as a DEFENSE

MECHANISM. It is Freud's basic claim that has been accepted by generations of clinicians, although Breuer's autohypnotic hypothesis has been resurrected recently as a major factor in the early childhood creation of multiple personalities. Only Swiss psychoanalyst and psychiatrist C. G. JUNG (1875–1961) seems to have included a nonpathological interpretation of dissociation as a major part of his psychological theories.

See also COMPLEX; MULTIPLE PERSONALITY.

Bliss, E. L. "A Reexamination of Freud's Basic Concepts from Studies of Multiple Personality Disorder," *Dissociation* 1 (1988): 36–40.

Moreau de Tours, J. J. *Du hachisch et de l'aliénation mentale: Etudes psychologiques.* Paris: Fortin, Masson, & Cie, 1845.

Noll, R. "Multiple Personality, Dissociation, and C. G. Jung's Complex Theory," *Journal of Analytical Psychology* 34 (1989), 353–370.

van der Hart, O., and B. Friedman. "A Reader's Guide to Pierre Janet on Dissociation: A Neglected Intellectual Heritage," *Dissociation,* 2 (1989): 3–16.

dissociative disorders A category of mental disorders first created in 1980 in *DSM-III* whose primary symptom is DISSOCIATION. Disturbances in identity and memory characterize these disorders. The dissociative disorders can often be mistaken for more serious psychotic disorders such as SCHIZOPHRENIA. Since there is no significant break with reality, persons suffering from dissociative disorders are not considered psychotic. This concept is recognized even by the legal system in the United States, where there have been instances of individuals with multiple personality disorder who have committed serious crimes but who have not been judged "insane" because they were not technically psychotic. An example of this is the sensational case of convicted rapist Billy Milligan in Ohio in the 1970s; he suffered from multiple personality disorder but was not judged legally insane.

A more traditional clinical term for the dissociative disorders is "hysterical neuroses, dissociative type." In *ICD-9* (1978), these disorders were included among those subtypes listed for "Hysteria."

Keyes, D. *The Minds of Billy Milligan.* New York: Random House, 1981.

Putnam, F. W. "Dissociation as a Response to Extreme Trauma." In *Childhood Antecedents of Multiple Personality,* edited by R. Kluft. Washington, D.C.: American Psychiatric Press, 1985.

distractibility A descriptive clinical term for when a person's attention seems to be easily diverted to unimportant or irrelevant events in the person's immediate environment. This is a characteristic found in many people who do not have diagnosable MENTAL DISORDERS, and such people are often referred to as "dreamy," "spacey," or "spaced-out." However, in certain psychotic disorders such as SCHIZOPHRENIA this distractibility can be extreme, and such disturbances in the processes of attention are often said to be one of the primary characteristics of schizophrenia.

See also ATTENTION, DISORDERS IN; COGNITIVE STUDIES OF SCHIZOPHRENIA.

Dix, Dorothea Lynde (1802–1887) It is said by historian of psychiatry Gregory Zilboorg in his 1941 classic, *A History of Medical Psychology,* that "The history of medical psychology in America during the nineteenth century is the history of the AMERICAN PSYCHIATRIC ASSOCIATION and the life of Dorothea Dix." Dix was a retired schoolteacher who, starting in 1841, became one of the most noted reformers of the care of the mentally ill in the 19th century. Her investigations of the terrible conditions suffered by the mentally ill and the poor in ALMSHOUSES, prisons, and the few institutions that existed fueled her energetic campaign of petitions to state legislatures and the Congress of the United States, and to the Parliament in England, to allocate funds to build more humane institutions for the care of the mentally ill. It is estimated that between the 1840s and 1880s she was directly responsible for the building of 32 new state asylums for the insane in the United States.

In an 1848 "Memorial" address to Congress in Washington, D.C., Dix reported that during her investigations she had seen "more than 9000 idiots, epileptics and insane in the United States, destitute

of appropriate care and protection . . . bound with galling chains, bowed beneath fetters and heavy iron balls attached to drag-chains, lacerated with ropes, scourged with rods and terrified beneath storms of execration and cruel blows; now subject to jibes and scorn and torturing tricks; now abandoned to the most outrageous violations."

Dix remained a reformer until late in her life. As repayment for her achievements in the care-taking of others, she was given a permanent apartment on the grounds of the New Jersey State Hospital at Trenton, where she lived out most of her remaining years.

See also ABUSE OF PSYCHIATRIC PATIENTS; ASYLUMS; BEERS, CLIFFORD W.

Deutsch, A. *The Mentally Ill in America.* Garden City, N.Y.: Doubleday, 1937, chapter 9.

Tiffany, F. *The Life of Dorothea Lynde Dix.* Boston: 1891.

Zilboorg, G. *A History of Medical Psychology.* New York: W. W. Norton, 1941.

dizygotic twins "Fraternal" or "nonidentical" twins. Dizygotic twins are thought to share about 50 percent of their genes in common, compared to the nearly 100 percent shared by MONOZYGOTIC TWINS. This makes for an interesting comparison between these two types of twin-pairs in GENETICS STUDIES of SCHIZOPHRENIA and BIPOLAR DISORDER, and some of the most suggestive evidence that these MENTAL DISORDERS have a genetic basis is the fact that a particular disease is much more likely to appear in both monozygotic twins than in both dizygotic twins.

See also CONCORDANCE RATE; CONSANGUINITY METHOD; TWINS METHOD AND STUDIES.

DMPEA The acronym for dimethoxphenethylamine, once thought to be one of the BIOLOGICAL MARKERS OF SCHIZOPHRENIA. DMPEA is a product of a chemical process known as transmethylation (in biochemistry, the transference of a methyl group from one compound to another). In 1963 scientists Friedhoff and Van Winkle found increased concentrations (when compared to normal controls) of DMPEA in the urine of 60 percent of acute schizophrenics who were not treated with ANTIPSYCHOTIC DRUGS. Furthermore, they found the even more suggestive evidence of higher than normal concentrations of DMPEA in the urine of 71 percent of male paranoid schizophrenics and in 75 percent of female paranoid schizophrenics. However, further research on the role of this and other compounds produced by the biochemical process of transmethylation found in the body fluids of schizophrenics, has not indicated a specific relationship to this or any other mental disorder.

See also BIOCHEMICAL THEORIES; TRANSMETHYLATION HYPOTHESIS.

Friedhoff, J. J., and E. Van Winkle. "Conversion of Dopamine to 3,4-dimethoxyphenylacetic Acid in Schizophrenia Patients," *Nature* 199 (1963): 1,271–1,272.

Luchins, D., T. A. Ban, and H. E. Lehmann. "A Review of Nicotinic Acid, N-methylated Indolamines and Schizophrenia," *International Journal of Pharmacopsychiatry* 13 (1978): 16–33.

DNA marker See MOLECULAR MARKER.

Dollhaus An old German term for "madhouse."

dominant In genetics, a trait observable in an individual (called the PHENOTYPE) and caused by one ALLELE (the term for an alternative form of a gene) is said to be dominant with respect to another trait known to be caused by a second allele, if the individual carrying both alleles shows signs only of the first trait and not the second.

dopamine A chemical substance in the brain that functions as a NEUROTRANSMITTER, that is, it is involved in the communication between neurons in the brain. Dopamine is one of the CATECHOLAMINES. For the most part, dopamine is thought to play the role of an inhibitor of functions. It has been found to be implicated in the motor (movement) control systems of the brain, and especially in SCHIZOPHRENIA.

See also DOPAMINE HYPOTHESIS.

dopamine hypothesis A NEUROTRANSMITTER theory of the cause (ETIOLOGY) of SCHIZOPHRENIA that was popular in the 1970s and 1980s but which is now regarded as too simplistic. Interestingly, this theory of the cause of schizophrenia arose from studying how its main form of treatment, ANTIPSYCHOTIC DRUGS, worked in the cortex of the brain to eliminate HALLUCINATIONS and DELUSIONS (POSITIVE SYMPTOMS). Antipsychotic drugs were found to do so by blocking dopamine at its receptor sites. This led to the hypothesis that the brain was producing dopamine in excess of normal levels—although then, as today, there is no way to know exactly what "normal" levels of dopamine in the brain may be. This hypothesized overproduction of dopamine was evidence of a neurological dysfunction, so therefore there must be a dysfunction of the dopaminergic system, and that dysfunction causes schizophrenia. The dopamine hypothesis replaced another of the BIOCHEMICAL THEORIES OF SCHIZOPHRENIA, the various forms of the TRANSMETHYLATION HYPOTHESIS, which, other than genetics, had been the dominant biological theory of the cause of schizophrenia since the 1950s. The dopamine hypothesis of schizophrenia in its fully articulated form was first proposed by Solomon Snyder and his colleagues in an article published in the *American Journal of Psychiatry* in 1976. However, the evolution of the dopamine hypothesis has a much longer history.

In 1957 the Swedish neuroscientist Arvid Carlsson (1923–) discovered that dopamine acted as a neurotransmitter in the brain. His research report was published the following year in the journal *Science*. His work on DOPAMINE and the role of the CATECHOLAMINES as neurotransmitters eventually led to Carlsson sharing the Nobel Prize in medicine in 2000.

Although antipsychotic drugs had been used since 1952, no one was sure exactly how they worked on the brain to reduce psychotic symptoms. The first suggestion that a neurotransmitter may be implicated not only in the pharmacodynamics of antipsychotic drugs, but that there may be a link to the cause of MENTAL DISORDERS such as schizophrenia, was put forth in 1954 in a paper by David Wolley and Edward Shaw. They suggested a role for the newly discovered (1953) neurotransmitter serotonin (5HT), but their paper had virtually no impact on fellow researchers.

In 1963 Arvid Carlsson and his colleague Margit Lindqvist published a famous paper reporting that they had demonstrated that CHLORPROMAZINE and haloperidol worked on the catecholamine systems in the brain, reducing activity by acting on the postsynaptic neurons. Although this 1963 paper is cited in many publications by schizophrenia researchers as the first place the dopamine hypothesis of schizophrenia is mentioned, in fact, dopamine is not specifically mentioned at all in the paper. Three years later, pharmacologist Jacques van Rossum, a professor of pharmacology at the medical faculty of the University of Nijmegen in the Netherlands, published a paper that specified dopamine as the catecholamine system that was blocked at the postsynaptic neuron by antipsychotic drugs. This 1966 paper contained the first mention of the term *dopamine hypothesis* and the first formal description of its connection to schizophrenia:

> When the hypothesis of dopamine blockade by neuroleptic agents can be further substantiated it may have fargoing consequences for the pathophysiology of schizophrenia. Overstimulation of dopamine receptors could then be part of the etiology. Obviously, such an overstimulation may be caused by overproduction of dopamine, production of substances with dopamine actions (methoxy derivatives), abnormal susceptibility of the receptors, etc.

Van Rossum's paper is also sometimes cited as the first description of how dopamine is blocked at its "receptor sites" by antipsychotic drugs, but the idea of "receptors" had not been defined in the mid-1960s. In fact, the first neurotransmitter receptor (for acetylcholine) was not discovered until 1970. The development of radio-labeling techniques for research on neurotransmitter systems in the nervous system led to an explosion of interest in research on receptors by 1972.

In 1974 Solomon Snyder of Johns Hopkins University reported the discovery of dopamine receptors. He and his colleagues discovered two types: D_{-1} and D_{-2} receptors. Furthermore, they discovered that antipsychotic drugs worked by binding

selectively to D_{-2} receptors and not D_{-1} receptors. Since all antipsychotic drugs worked by binding to the D_{-2} receptor, it was thought that there must be a dysfunction or abnormality in the D_{-2} receptor that caused PSYCHOSIS. This was the basis of the DOPAMINE HYPOTHESIS of schizophrenia put forth by Solomon Snyder in 1976. Since van Rossum's 1966 article had not made much of an impact on his contemporaries, Snyder's did, and it is Snyder who gets the credit for initiating a new phase of research in schizophrenia. However, by the 1980s Snyder backed off from this single-system theory of a neurotransmitter dysfunction cause of schizophrenia and criticized this logic. In the 1980s Arvid Carlsson also became a critic of this single-system dopamine hypothesis of schizophrenia.

The dopamine hypothesis of schizophrenia, although discarded in its original form as a causal theory, still exerts its influence on the pharmaceutical industry. The idea that selected neurotransmitter receptors can be targeted (for blockade or activation) by specific drugs, and that psychiatric symptoms would lessen from this action, has until recently pushed psychopharmacological research and marketing to cling to single-transmitter theories of the causes of mental illnesses (e.g., dopamine for schizophrenia, serotonin for depression, and so on). Such specificity is attractive not only to researchers, but also to those marketing new drugs: single-transmitter drugs are easier to comprehend by a largely science-blind public. Pharmaceutical companies make use of ancient metaphors from the humoral theory of medicine to explain how these drugs work: DEPRESSION or schizophrenia is caused by an "imbalance" of a specific "chemical." Therefore, the way to restore health is by restoring the balance of the chemical (humor) in the brain by the use of a drug.

There are known to be more than 100 neurotransmitter systems in the brain, and if one system is altered by drugs, it is still not understood how this affects other neurotransmitter systems. Newer generations of psychoactive drugs work on multiple receptors of two or more neurotransmitters, and the effect on the rest of the brain may be correspondingly more complicated to discern. However, although a dysfunction in the dopaminergic system is no longer posited as the single cause of schizophrenia, there is no doubt that dopamine plays a role in the pathophysiology of positive symptoms such as delusions and hallucinations.

The "revised" dopamine hypothesis of schizophrenia As a part of the new NEURODEVELOPMENTAL THEORY OF SCHIZOPHRENIA proposed by Daniel Weinberger of The NATIONAL INSTITUTE OF MENTAL HEALTH in Bethesda, Maryland, a "revised" version of the dopamine hypothesis has been proposed. The "revised" dopamine hypothesis is an attempt to account for NEGATIVE SYMPTOMS and cognitive impairment, serious features of schizophrenia that cannot be explained by the original dopamine theory that only accounts for positive symptoms. In the revised view, schizophrenia is associated with (but not necessarily caused by) a dopamine imbalance involving an excess of dopamine production in the subcortical structures of the brain (the mesolimbic system) and an underproduction of dopamine production in the prefrontal cortex. Subcortical dopamine projections might be hyperactive, hyperstimulating D_{-2} receptors and producing hallucinations and delusions. Dopamine projections to the prefrontal cortex might be hypoactive, resulting in the hyperstimulation of D_{-1} receptors, negative symptoms, and cognitive impairment.

Both dopamine hypotheses have little experimental support. To date, there is still no compelling evidence that documents abnormalities of dopamine functioning in schizophrenia. Postmortem neuropathological studies of the brains of persons with schizophrenia have been inconclusive. Brain imaging studies using PET (positron emission tomography) or SPECT (single photon emission computerized tomography) have been used for receptor imaging in living subjects, particularly the D_{-2} receptor. While the hyperactivity of subcortical transmission at D_{-2} receptors has been supported, other aspects of the revised dopamine hypothesis have not. Speculations about dopamine dysfunction and the production of negative symptoms and cognitive impairment, and the claim that positive symptoms become independent of the dopamine system and "take on a life of their own" in chronic, treatment-resistant schizophrenia, are unsupported with hard evidence. The revised dopamine hypothesis, like its predecessor, will probably have a short shelf life in science.

In fact, as any practicing clinician can tell the researchers, there is strong evidence against both dopamine hypotheses: antipsychotic drugs do not always alleviate hallucinations and delusions, and in fact may not do so in up to a third of all persons experiencing these psychotic symptoms. Corroboration of this clinical observation can be found in studies that, in some persons, hallucinations and delusions are present when, in fact, there seems to be measurably normal levels of synaptic dopamine. Blocking the D_{-2} receptors of these persons with antipsychotic drugs has little or no effect on their psychotic symptoms. This may mean that other neurotransmitter systems acting independently of the dopaminergic system may also produce positive symptoms.

Baumeister, A. A., and J. L. Francis. "Historical Development of the Dopamine Hypothesis of Schizophrenia," *Journal of the History of the Neurosciences* 11 (2002): 265–277.

Carlsson, A. "The Current Status of the Dopamine Hypothesis," *Neuropsychopharmacology* 1 (1988): 179–186.

Carlsson, A., and M. Lindqvist. "The Effect of Chlorpromazine on the Formation of 3-Methoxytyramine and Normetanephrine in Mouse Brain," *Acta Pharmacologica* 20 (1963): 140–144.

Healy, D. *The Creation of Psychopharmacology.* Cambridge, Mass.: Harvard University Press, 2002.

Laruelle, M. "Dopamine Transmission in the Schizophrenic Brain." In *Schizophrenia.* 2nd ed., edited by S. R. Hirsch and D. Weinberger. Cambridge: Blackwell, 2003.

Snyder, S. "The Dopamine Hypothesis of Schizophrenia: Focus on the Dopamine Receptor," *American Journal of Psychiatry* 133 (1976): 197–202.

Van Rossum, J. M. "The Significance of Dopamine Receptor Blockade in the Mechanism of Action of Neuroleptic Drugs," *Archives of International Pharmacodynamics and Therapeutics* 60 (1966): 492–494.

Wolley, D. W., and E. Shaw. "A Biochemical and Pharmacological Suggestion about Certain Mental Disorders," *Proceedings of the National Academy of Sciences of the United States of America* 40 (1954): 228–231.

double-bind theory One of the most widely discussed theories of the cause of SCHIZOPHRENIA, from the 1950s to the 1970s, although it is now generally regarded as of little scientific significance. This theory was derived from communications and cybernetics research and was first put forth by Gregory BATESON and his colleagues in 1956. Essentially, it places the cause of schizophrenia in the interaction patterns of the family, and this theory was the basis of much later family interaction research.

Essentially, the double-bind theory centers on the incongruence between the basic content of primary communications and the underlying meaning (expressed by tone of voice, gestures or context of the communication), which incongruence is called metacommunications. Bateson and his colleagues purported to find that, in the families of schizophrenics, the schizophrenic member is caught in a double-bind when incongruent messages are communicated and the recipient must respond to the incongruent message without being given the opportunity to clarify the incongruence in the message. For example, the parent of a schizophrenic may say, "Of course I love you," while wearing a facial expression of disgust or while doing something intrusive or harmful to the afflicted person. A lifetime of such aberrant communications since early childhood is thus thought to produce schizophrenia. The double-bind theory has remained just that, with no carefully controlled scientific study to validate its claims.

See also FAMILY INTERACTION THEORIES.

Bateson, G., et al. "Towards a Theory of Schizophrenia," *Behavioral Science* 1 (1956): 251–264.

double conscience or consciousness These are 19th-century terms that refer to multiple personality disorder, in which one or more alternate personalities would coexist with the ego of the "birth personality." The very first complete medical case history of a person with multiple personalities was that of the young American woman Mary Reynolds, first reported in 1817.

Mitchell, S. L. "A Double Consciousness or a Duality of Person, in the Same Individual," *Medical Repository* 3 (1817): 185–186.

Mitchell, S. W. "Mary Reynolds: A Case of Double Consciousness," *Transactions of the College of Physicians of Philadelphia* 10 (1888): 366–389.

double insanity See FOLIE À DEUX.

douche One of the primary modes of alleviating the active symptoms of mental illness since antiquity; in particular, in mental institutions in the 18th and 19th centuries the patient would be forced under a shower of (usually) ice-cold water. This was done in many fashions, including: by physically restraining the patient and pouring buckets of cold water over his or her head (as in the SPREAD-EAGLE CURE), or by using a "douching machine" in which a patient would be strapped in a chair beneath an apparatus that forced strong jets of cold water down onto his or her head. The reproduction of a design drawing of such an apparatus from the 1820s is provided in the first volume of Howells and Osborn's *A Reference Companion to the History of Abnormal Psychology.*

ESQUIROL describes the use of the douche on the mentally ill in his 1838 textbook, *Mental Maladies:*

> The douche consists in pouring water upon the head from a greater or less height. It was known to the ancients; and is administered in different ways. . . . The patient received the douche, seated in an arm chair; or better, plunged into a bath of tepid or cold water.
>
> The douche produces its effects, both by the action of the cold, and the percussion. It exercises a sympathetic influence upon the epigastrium. It causes cardialgia, and desires to vomit. After its action ceases, the patients are pale, and sometimes sallow. It also acts morally, as a means of repression; a douche often sufficing to calm a raging excitement, to break up dangerous resolutions, or force a patient to obedience. . . . The douche ought to be applied with discretion, and never immediately after a repast. . . . Its employment ought to be continued but a few minutes at a time, and its administration never left to servants. They may abuse it, and we ought not to be ignorant that the douche is not exempt from grave accidents.

In describing the douche method of BATHS for the mentally ill included in Tuke's *A Dictionary of Psychological Medicine,* 14 other means of administering baths are discussed in detail. One of them sounds like the "Chinese water-torture" of motion picture fame:

> Schneider and Morel shaved their patients' heads, and placed them under an intermittent stream of water, which fell drop by drop on the back of the scalp . . .

See also HYDROTHERAPY.

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity,* trans. E. K. Hunt. Philadelphia: Lea & Blanchard, 1845; first published, 1838.

Howells, J. G., and M. L. Osborn. *A Reference Companion to the History of Abnormal Psychology.* 2 vols. Westport, Conn.: Greenwood Press, 1984.

Williams, D. "Baths." In *A Dictionary of Psychological Medicine.* Vol. 1, edited by D. H. Tuke. London: J. & A. Churchill, 1892.

dreams in schizophrenia There is no scientific evidence to suggest that the dream content of persons with SCHIZOPHRENIA (or any other mental disorder) are markedly different from "normals." Throughout the 20th century, psychoanalysts, including FREUD and JUNG, made such erroneous claims, and the misconception that schizophrenic dreams are somehow different from those of nonschizophrenics is widespread in the public. All these claims were based on clinical anecdotes and not from more rigorously designed quantitative studies of dream content. It is now the conventional wisdom in cognitive neuroscience that psychoanalysis was merely a pseudoscience (like phrenology or astrology) with no scientific support for any of its claims. The speculations of Freud and Jung and their devotees about dreams and the "unconscious mind" have only historical, not scientific, significance. The only consistent finding in quantitative dream research studies is that "patient populations" (not just persons suffering from schizophrenia, but people suffering from depression and a whole host of other disorders)

have fewer "friends" appearing in their dreams. Instead, when contrasted with the dream content of "normals," the characters in their dreams tend to be family members or strangers. There are also fewer "friendly interactions" with people in their dreams. None of this points to some special status for the dreams of schizophrenics, but instead points to the generally accepted theory that there is more in common between our waking and dreaming lives than there is discontinuity (as Freud and Jung would have us believe).

An ongoing quantitative study of dreams is being conducted by G. William Domhoff of the University of California, Santa Cruz.

Domhoff, G. W. "New Rationales and Methods for Quantitative Dream Research Outside the Laboratory," *Sleep* 21 (1998): 398–404.

Maharaj, N. *An Investigation into the Structure of Schizophrenic Dreams,* Doctoral Dissertation, Leiden University, The Netherlands, 1997.

drug holiday A "vacation" from taking ANTIPSYCHOTIC DRUGS that is necessary from time to time so that the psychiatrist can assess the further need of medication for a patient.

drug psychoses A category of organic psychotic conditions, listed in *ICD-10* (1992), for those psychoses induced by the ingestion of various drugs (e.g., amphetamines, barbiturates, opiates, and hallucinogens). There is a break with reality, and HALLUCINATIONS and DELUSIONS may be present. They can be due to the active intoxicating effects of the substances, or to the effects of withdrawal.

See also AMPHETAMINE PSYCHOSIS; SUBSTANCE-INDUCED PSYCHOTIC DISORDER.

DSM-IV *The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* appeared in 1994 as the latest in a series of major revisions of the "Bible" of psychiatrists. The earlier editions were *DSM-I* (1952), *DSM-II* (1968), *DSM-III* (1980), and *DSM-III-R* (1987). The AMERICAN PSYCHIATRIC ASSOCIATION has periodically updated its diagnostic manuals to be consistent with advances in research on mental disorders. The later editions have attempted to be phenomenologically based (i.e., focused on descriptions of behaviors in various MENTAL DISORDERS) and have attempted to be free of pejorative theoretical assumptions. For example, the word *NEUROSIS* was no longer included when *DSM-III* came out in 1980, since it referred to a concept from psychoanalytic theory that did not always match current research on the various disorders. Teams of psychiatrists are continually working in committees to collect research information and to revise, eliminate, or create new diagnostic categories for each revision of the manual. *DSM-IV-TR* (2000) is just such a revision.

Originally designed for use in the United States, it is now one of the most widely used diagnostic manuals for mental disorders in the world.

The diagnostic criteria have changed considerably over the many editions of the *DSM*s. This is especially true for SCHIZOPHRENIA. Although Emil KRAEPELIN's narrowly defined view of schizophrenia dominated the early part of the century, by the 1950s BLEULER's more inclusive concept of schizophrenia and the influence of psychoanalytic pseudoscience on American mental health professionals led to a broadening of the definition of what it meant to be a schizophrenic—and often with disastrous consequences for those persons stigmatized with that inappropriate label. The broad definition of schizophrenia and the influence of psychoanalytic language finally disappeared in 1980 with the publication of *DSM-III.* Currently, the narrow "Neo-Kraepelinian" definition of schizophrenia is the accepted standard and continues to find scientific evidence in support of it.

dual diagnosis The presence of two existing mental disorders in a person that requires the granting of two different diagnostic labels. This term is most often used to describe those "dually diagnosed" patients who are mentally retarded as well as schizophrenic (or carry some other psychotic diagnosis). One of the growing problems in the post-psychedelic era of the 1960s is the large number of YOUNG ADULT CHRONIC PATIENTS who are abusers of drugs and alcohol and who also seem to

have a serious (often psychotic) MENTAL DISORDER. These patients are also dually diagnosed and in the United States are sometimes referred to as "double trouble" patients.

ducking See BATH OF SURPRISE; BATHS; HYDROTHERAPY.

duplex personality See DOUBLE CONSCIENCE OR CONSCIOUSNESS.

dysphrenia A BRIEF PSYCHOTIC DISORDER or ACUTE AND TRANSIENT PSYCHOTIC DISORDER described by the German psychiatrist Karl Ludwig KAHLBAUM (1829–99) in his Habilitation thesis, *Die Gruppirung psychicher Krankheiten* (*The Classification of Mental Diseases*) in 1863. Dysphrenia was a severe psychotic disorder of sudden onset and short duration. Symptoms were mixed or "impure" and varied widely from case to case (in modern terms, a syndrome characterized by POLYMORPHIC PSYCHOTIC SYMPTOMS). Kahlbaum assumed that the underlying cause (etiology) of the psychosis involved an underlying disease process of an epileptic, sexual, or rheumatic nature. Persons suffering from dysphrenia recovered in full without any long lasting effect. In his highly influential book, Kahlbaum distinguished dysphrenia from the spectrum of typical psychotic disorders, or *vesania typica,* which were all stages of a single underlying disease process that was progressive in nature. He believed that a different disease process (epileptic, sexual, or rheumatic) provoked an exacerbation of the same underlying disease process found in progressive and chronic psychotic disorders but "without leaving a lasting alteration in the elements that serve its expression" (p. 67).

Kahlbaum's group of chronic and progressively deteriorating psychotic disorders, which he grouped under the *vesania typica* concept, was a major source of inspiration for Emil KRAEPELIN when he proposed his heterogeneous disease concept of DEMENTIA PRAECOX in 1896. Kraepelin was aware of the existence of brief psychotic disorders, but these disorders were difficult to reconcile with his view of dementia praecox as a progressively chronic disease. Starting in 1893, in successive editions of his famous textbook, *Psychiatrie,* Kraepelin placed brief psychotic disorders under the category of "periodic" insanities. In 1899, when he introduced MANIC-DEPRESSIVE ILLNESS as a psychotic disorder that was periodic but continually remitting and manifesting a better prognosis than dementia praecox, Kraepelin considered brief psychotic disorders as subtypes of MANIA.

Kahlbaum, K. L. *Die Gruppirung psychicher Krankheiten.* Danzig, 1863.

E

Earle, Pliny (1809–1892) Earle was a psychiatrist and one of the 13 founders of the AMERICAN PSYCHOLOGICAL ASSOCIATION in 1844. He had traveled widely in Europe and was knowledgeable about European treatments for mental illness. He held several important positions in his lifetime, including that of medical superintendent of the Bloomingdale Asylum in New York in 1844 and the State Lunatic Hospital at Northampton, Massachusetts in 1864, where he remained for the next 21 years. He is perhaps best remembered for pioneering the teaching of PSYCHIATRY in American medical schools, and for his 1887 book, *The Curability of the Insane,* which sharply contradicted the wildly inflated claims of "curability" of the insane that had been made by various superintendents of ASYLUMS in the United States during the previous 40 years.

écho de la pensée Literally, "echo of the thought." This is a characteristic of schizophrenic thought disorder that is commonly called "thought broadcasting." A psychotic individual exhibiting *écho de la pensée* believes that his private thoughts are being sent out into the minds of other people, who may then speak them for him. In more-deteriorated psychotic states, the person may not even recognize these thoughts as his or her own and attribute them entirely to other people.

echolalia The spontaneous (yet persistent) repetition of the words and phrases of others. It is as if the listening person is an "echo" of the speaker's speech. For example, the speaker may ask, "Does that belong to you?" only to be met with the response (usually in a mumbling, mocking, or staccato tone) "Belong to you. Belong to you." Informally, it is sometime called "parroting" after the behavior of parrots. This symptom is found in SCHIZOPHRENIA (particularly the DISORGANIZED TYPE) and especially in autistic children or individuals with certain brain disorders.

See also AUTISM, INFANTILE; LANGUAGE ABNORMALITIES IN SCHIZOPHRENIA.

ECT The acronym for "electroconvulsive therapy" is the most recent attempt to neutralize the negative connotations most people associate with the method's original name, ELECTROSHOCK THERAPY.

EEG studies of schizophrenia German psychiatrist Hans Berger (1873–1941) invented the electroencephalogram in 1924 and first published the results of his studies of the electrical activity of the human brain in 1929. The EEG (as it is still known today) employed electrodes, which were attached to the scalp in strategic locations around the head, to map the electrical activity of the different regions of the brain. In the decade that followed this discovery there was great hope that the EEG could be used in psychiatry as a diagnostic tool, the assumption being that the brain wave patterns of people with particular mental disorders would differ from one another and from the patterns of people without diagnosable disorders. Although applications were found in neurology, PSYCHIATRY eventually found the EEG was of little diagnostic value.

EEG studies of schizophrenics generally showed more abnormalities than those of nonschizophrenic persons, but no specific brain wave abnormality could be linked to SCHIZOPHRENIA. However,

an improvement on the classical EEG methodology has been the use of event-related potentials, also known as ERPs, which have been a much more promising BIOLOGICAL MARKER OF SCHIZOPHRENIA. Whereas most EEG studies are conducted while the subject is at rest, ERPs involve the presentation of a flash of light, a tone or a very mild electrical stimulus to a subject so that the responding electrical activity in the brain can be recorded. ERPs are very useful because they are a nonintrusive way (unlike the surgical implantation of electrodes in the brain) of measuring the neural activity in relation to sensory, motor, and cognitive processes.

A large literature exists of ERP research that has been conducted with people diagnosed with schizophrenia. Three lines of evidence have been considered to be most promising in the search for biological markers: (1) Certain brain wave abnormalities in schizophrenics (technically, amplitude reductions in middle and late positive components) are thought to be related to dysfunctions in attention, which are found in some schizophrenics and in some individuals at high-risk for schizophrenia (2) ERP patterns have been found to differ from those of people diagnosed with other mental disorders and (3) certain aspects of the electrical activity of the brain measured by ERPs seem to be genetically determined (i.e., the brain may be predisposed to react to certain types of stimuli in specific ways).

In the 1990s, the EEG technique was combined with new BRAIN IMAGING technology in studies of the functioning and structure of the brains of persons with schizophrenia. Studies combining EEG activity with PET SCAN measurements have found abnormal functioning in the connections between the left frontal lobe and the temporal lobe. One study combining MAGNETIC RESONANCE IMAGING (MRI) with EEG found that the reduction of volume in the left superior temporal gyrus was strongly correlated with a decrease in the amplitude of the P3 (or P300) peak, which has been a commonly reported phenomenon reported in EEG studies of the brains of schizophrenics. This "latency of the P300 cortical ERP," as this abnormality is called, may be additional evidence that at least one form of schizophrenia resembles diseases like dementia, Alzheimer's disease, multiple sclerosis, Huntington's chorea, and Parkinson's disease. The same P300 latency is found in all these diseases and is also found during normal aging.

See also ATTENTION, DISORDERS IN; HIGH-RISK STUDIES.

Berger, H. "Über das Elektrenkephalogramm des Menschen," *Archiv für Psychiatrie und Nervenkrankheiten* 98 (1933): 231–255.

Erlenmeyer-Kimling, L. "Biological Markers for the Liability to Schizophrenia." In *Biological Perspectives of Schizophrenia,* edited by H. Helmchen and F. A. Henn. New York: Wiley, 1987.

Holzman, P. S. "Recent Studies of Psychophysiology in Schizophrenia," *Schizophrenia Bulletin* 13 (1987): 49–76.

McCarley, R. W., et al. "Auditory P300 Abnormalities and Left Superior Temporal Gyrus Volume Reduction in Schizophrenia," *Archives of General Psychiatry* 50 (1993): 190–197.

Morrison-Stewart, S. L., et al. "Coherence on Electroencephalography and Aberrant Functional Organization of the Brain in Schizophrenic Patients during Activation Tasks," *British Journal of Psychiatry* 159 (1991): 636–644.

O'Donnell, B. F. "Increased Rate of P300 Latency Prolongation with Age in Schizophrenia," *Archives of General Psychiatry* 52 (1995): 544–549.

Egas Moniz, António Caetano de Abreu Freire (1874–1955) A Portuguese neurologist who performed the first PSYCHOSURGERY (a term he coined) on a human being (a LEUCOTOMY) on November 15, 1935. For the invention of this procedure he won a Nobel Prize in physiology and medicine in 1949. Egas Moniz spells out his rationale for the leucotomy in the first book on psychosurgery, *Tentatives Opératoires dans le Traitement de Certaines Psychoses (Experimental Surgery in the Treatment of Certain Psychoses),* which was published in France in the spring of 1936: "To cure these patients it is necessary to destroy the arrangements of cellular connections, more or less fixed, that must exist in the brain and particularly those that are linked with the frontal lobes." Egas Moniz's work inspired Walter FREEMAN to perform the first leucotomy in the United States and to popularize the practice of psychosurgery.

Egas Moniz, A. *Tentatives Opératoires dans le Traitement de Certaines Psychoses.* Paris: Masson, 1936.

egocentricity Individuals with psychotic disorders are sometimes described as being egocentric in the same way that, for example, an infant is egocentric: impulses are expressed without regard to the context of social situation. Thus, psychotic individuals may engage in activities that are socially repugnant, bizarre, or simply inconsiderate. According to psychoanalytic theory, energy ("libido") is withdrawn from the external world and drawn back into the internal world in psychotic individuals. Thus, the person becomes more interested in his or her internal world and its needs rather than the demands of external reality. In this way, the concept of egocentricity is related to descriptions of the autism of some psychotic individuals, particularly schizophrenics.

Einheitspsychose In German, a "unitary psychosis," the idea that all mental illnesses (certainly all of the psychotic disorders) are simply variations of the same underlying disease process (the EINHEITSPSYCHOSE) and are not separate mental disorders with no apparent relationship to one another. This idea was first applied to mental illness by the Belgian ALIENIST Joseph Guislain (1797–1860) in 1833.

The eminent German psychiatrist Wilhelm GRIESINGER describes this idea in the "Form of Mental Disease" chapter in his 1861 classic, *Mental Pathology and Therapeutics.* He proposes that there are "two grand groups" or "fundamental states of mental anomalies": (1) those characterized by disturbances in emotional states (what we would call MOOD DISORDERS), and (2) those characterized by "disorders of the intellect and will" (the "thought disorder" characteristic of SCHIZOPHRENIA and related "spectrum" disorders). Griesinger believed that these types of disorder fit a degenerative pattern, with the mood disorders ("states of depression" then "states of exaltation" or manic states) developing eventually into more serious disorders in which thinking functions deteriorate ("states of mental weakness"), leading to the total degeneration of the mind. Griesinger writes:

> Observation shows, further, that in the great majority of cases, those conditions which form the first leading group *precede* those of the second group; that the latter generally appear only as consequences and *terminations* of the first, when the cerebral affection has not been cured. There is, moreover, again presented within the first group, in a great proportion of cases, a certain definite *succession* of the various forms of emotional states, whence there results a method of viewing insanity which recognizes in the different *forms,* different *stages* of one morbid process; which may, indeed, be modified, interrupted, or transformed by the most varied intercurrent pathological circumstances, but which, on the whole, pursues a constantly progressive course, which may proceed even to complete destruction of the mental life.

The idea of the *Einheitspsychose* returned in a theory by the noted British schizophrenia researcher Timothy J. Crow. He postulated in a 1986 article that all the psychotic disorders are distributed along a continuum that extends from unipolar depression through bipolar (manic-depressive) and schizoaffective psychosis to schizophrenia—a progressive degeneration from bad to worse. This matched Griesinger's observations exactly: that the psychotic disorders characterized by disturbances in emotion degenerate into psychoses characterized by disturbances of will and thought. Crow added a 20th-century twist to this idea by proposing that this spectrum of disorders is caused by a single gene; in other words, there is a single genetic locus where significant variation occurs in defect that predisposes to all these psychotic disorders. In a 1989 article he reviewed the evidence that the defective gene has a locus on the sex chromosomes, particularly the X chromosome. Crow guessed the "psychosis gene" was located somewhere on the X chromosome. He was wrong.

Crow, T. J. "The Continuum of Psychosis and Its Implications for the Structure of the Gene," *British Journal of Psychiatry* 149 (1986): 419–429.

DeLisi, L. E., and T. J. Crow. "Evidence for a Sex Chromosome Locus for Schizophrenia," *Schizophrenia Bulletin* 15 (1989): 431–440.

Griesinger, W. *Mental Pathology and Therapeutics.* Translated by C. L. Robertson and J. Rutherford. 1845. Reprint, New York: William Wood & Co., 1882.
Vleigen, J. *Die Einheitpsychose.* Stuttgart: F. Enke, 1980.

elective mutism A symptom found in some people who are diagnosed with a psychotic disorder who, for whatever reason, simply refuse to talk. This has been described particularly in connection with CATATONIA.

electronarcosis therapy Since at least the 1870s, asylum physicians who were at a loss as to how to treat persons in acute episodes of psychotic disorders experimented with sedative drugs (usually opium derivatives or barbiturates) to induce long periods of sleep. This SLEEP TREATMENT procedure was targeted specifically for SCHIZOPHRENIA by Jakob Kläsi in the 1922 and was used in the United States and Europe from the 1920s to the 1940s. In the Soviet Union a technique was developed for electrically stimulating the brain stem of persons with schizophrenia to induce prolonged sleep without drugs. This electronarcosis therapy was introduced as early as 1936 in the Soviet Union and was used well into the 1960s. Electronarcosis was also used by psychiatrists in the early 1960s in the former German Democratic Republic (communist East Germany). Electronarcosis therapy is no longer used for the treatment of schizophrenia today.

Wortis, J. *Soviet Psychiatry.* Baltimore: Williams and Wilkins, 1950.

electroshock therapy Now more commonly known as electroconvulsive therapy, or "ECT," it is a form of treatment designed by Italian psychiatrist Ugo CERLETTI and his colleagues in Rome to treat severe mental illness by electrically inducing seizures. An alleviation of symptoms followed the deliberate induction of such seizures. It was considered an improvement on other types of CONVULSIVE THERAPIES, which had many toxic side effects associated with the use of drugs to induce such powerful seizures. The very first patient to receive this treatment (a schizophrenic) did so on April 15, 1938. Electroshock therapy then became one of the most widely used forms of treatment for schizophrenia until the 1970s, when it became clear that ANTIPSYCHOTIC DRUGS were a more effective means of controlling psychotic symptoms and that ECT was much more effective with severe depression than with schizophrenia.

Cerletti experimented with pigs before attempting the procedure on humans. Most other psychiatrists were afraid to try this new procedure, but not Cerletti. In a rather macabre account of the very first electroshock treatment ever administered, D. J. Impastato relates the details of this historic (and horrific) event:

> Now came the search for Rome's first patient. For obvious reasons this was not a simple matter. Then, luckily, a patient from North Italy was admitted to the clinic who was a catatonic schizophrenic and who spoke an incomprehensible gibberish. He was unable to give his name or state anything about himself. No one could identify him. Dr. Cerletti decided he should be the historic patient. Following adequate preparations the first treatment was given in 1938. Present were Cerletti, Bini, Longhi, Accornero, Kalinowsky and Fleischer. The patient was brought in, and the machine was set at 1/10 of a second and 70 volts and the shock given. Naturally, the low dosage resulted in a petit mal reaction. After the electric spasm, which lasted a fraction of a second, the patient burst out into song. The Professor suggested that another treatment with a higher voltage be given. The staff objected. They stated that if another treatment were given the patient would probably die and wanted further treatment postponed until the morrow. The Professor knew what that meant. He decided to go ahead right then and there, but before he could say so the patient suddenly sat up and pontifically proclaimed, no longer in a jargon, but in clear Italian: "Non una seconda! Mortifera!" (Not again, it will kill me). This made the Professor think and swallow, but his courage was not lost. He gave the order to proceed at a higher voltage and a longer time: and the first electroconvulsion in man ensued. Thus was

born EST out of one man and over the objection of his assistants.

No scientifically satisfying theory has ever been put forth to justify or explain the use of electroshock therapy for SCHIZOPHRENIA. Like most treatments for mental illness over the last several centuries, as soon as a new scientific discovery is made it is quickly adapted for use on the mentally ill in the hope that a new treatment or cure can finally be found. When it was discovered that blood circulated in the body, BLEEDING and BLOOD TRANSFUSIONS (often using animal blood) were quickly tried on the insane. When Hungarian psychiatrist von MEDUNA put forth the scientifically unsound theory that, since epilepsy and schizophrenia were biologically incompatible, deliberately inducing seizures (by chemical means) in schizophrenics would cure it, such methods were widely tried and efforts were made to improve upon them. Electroshock therapy was such an improvement, despite the fact that the initial theory to explain its beneficial effects was unsound.

Electric shocks that were too weak to produce convulsions were used almost 200 years before Cerletti to treat illness, but it was only around 1804 that a use for psychosis is recorded. A machine that produced electric shocks from weak electric currents was set up in the Middlesex Hospital in England in 1767 to treat various ailments, and shocks were applied to various parts of the body. At about this time American inventor and statesman Benjamin Franklin suffered unconsciousness and retrograde amnesia after a severe electric shock during one of his electricity experiments, and he apparently suggested its use for the treatment of the insane. In the 1790s British surgeon John BIRCH used his machine to "pass shocks through the brain" of depressed patients at London's Saint Thomas Hospital; this may be the first recorded use of electric shocks applied directly to the brain to treat a mental disorder. In 1838 ESQUIROL reviewed the reports of the use of electricity in the treatment of mental illness, including his own experiments with its use:

> Gmelin and Perfect affirm, that they have effected cures by electricity. At the Salpêtrière, during two summers, those of 1823 and 1824, I submitted to the influence of electricity a large number of our insane women. One only was cured, in the course of my experiments. This was a young and very strong girl, who had become a maniac in consequence of a fright, which suppressed her menses. She had been insane for a month, and was electrized for fifteen days. At the menstrual period, the discharge appeared, and she was immediately restored.

Although electroshock therapy is still sometimes used for schizophrenia, this is quickly becoming an outmoded form of treatment for the disease, at least in the United States. Symptomatic relief is often only temporary, and a major review of the bulk of the research published prior to 1980 has concluded that electroshock therapy has not been shown to improve the quality of life of schizophrenic patients.

In June 1985 the NATIONAL INSTITUTE OF MENTAL HEALTH in the United States convened a Consensus Development Conference on Electroconvulsive Therapy and issued a summary statement on the body of scientific evidence about ECT. The panel of experts concluded that "The evidence for the efficacy of ECT in schizophrenia is not compelling but is strongest for those schizophrenic patients with a shorter duration of illness, a more acute onset, and more intense affective symptoms. ECT has not been useful in chronically ill schizophrenic patients." When is ECT indicated? The expert panel found that "The efficacy of ECT has been established most convincingly in the treatment of delusional and severe endogenous depressions, which make up a clinically important minority of depressive disorders." However, the panel warns that there are "significant side effects, especially acute confusional states and persistent memory deficits for events during the months surrounding ECT treatment."

Due in no small part to the supportive studies of Max Fink (1923–) and others, in the early 21st century some researchers and clinicians are advocating a role for ECT in treatment-resistant schizophrenia.

Arndt, R. "Electricity." In *A Dictionary of Psychological Medicine.* Vol. 1, edited by D. H. Tuke. London: J. & A. Churchill, 1892.

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity,* trans. E. K. Hunt. 1838. Reprint, Philadelphia: Lea and Blanchard, 1845.

Harms, E. "Origins and Early History of Electrotherapy and Electroshock," *American Journal of Psychiatry* 12 (1955): 933.

Impastato, D. J. "The Story of the First Electroshock Treatment," *American Journal of Psychiatry* 116 (1960): 1,113–1,114.

National Institutes of Health, *Electroconvulsive Therapy,* Consensus Development Conference Statement, 1985, vol. 5, no. 11. Bethesda, Md.: U.S. Dept. of Health and Human Services, National Institutes of Health, Office of Medical Applications of Research.

Salzman, C. "The Use of ECT in the Treatment of Schizophrenia," *American Journal of Psychiatry* 137 (1980): 1,032–1,041.

EMD An acronym for "eye movement dysfunction," perhaps one of the most promising candidates for a BIOLOGICAL MARKER for schizophrenia.

See also EYE MOVEMENT ABNORMALITIES IN SCHIZOPHRENIA.

endocrine alterations in schizophrenia The human body is viewed in Western medicine as being composed of several major "systems." In the 20th century, these systems, which were conceptualized and studied as if they operated in isolation from one another, became increasingly integrated. Recent medical research has focused on how the nervous system, the immune system, and the endocrine system communicate with one another in both disease and health. The endocrine system is composed of the subcortical structure known as the hypothalamus, its connection to the pituitary gland (the "master gland" in the brain that "controls" the activity of the system of other glands throughout the body), and the various hormones produced by the glands, which have a stimulating effect on both the nervous system and the immune system as well as other aspects of growth and metabolism. The scientific discipline devoted to the study of metabolic processes is called endocrinology. A related field, neuroendocrinology, focuses specifically on the interdependence of the endocrine and nervous systems.

History of the rise of endocrinology Throughout the latter half of the 19th century, physiologists sought to understand the mechanisms of metabolism. For most of that time, physiological changes in the body were explained by theories of nervous regulation. Between 1890 and 1905—the year Ernest Starling first proposed the modern concept of "hormone"—metabolism was increasingly explained by theories of chemical regulation through secreting organs such as glands. Endocrinology emerged from physiology in a recognizable form in the years following British physiologist Edward Schaefer's address "On Internal Secretions" to the British Medical Association in Physiology in London on August 2, 1895. *Internal secretions* was a term introduced by physiologist Claude Bernard in 1855 but reframed by Schaefer in terms of clinical medicine. Metabolic diseases as a separate category of illness were caused by the overproduction or underproduction of internal secretions in the glands with ducts (liver, pancreas, and kidneys), those without ducts (thyroid, adrenals, pituitary), and the sex glands (gonads). As Schaefer proposed in his famous lecture, secreting organs, both with and without ducts, return secreted materials to the blood. The ductless glands, however, produce only internal secretions. Blood (and later the cerebral spinal fluid) thus became the medium through which to detect and measure internal secretions, or later in the 20th century, hormones and NEUROTRANSMITTERS (originally called neurohormones).

Dementia praecox as an endocrine disorder (1896) This emerging new endocrinological paradigm was immediately seized upon by the first biological psychiatrists. If an overproduction or underproduction of internal secretions could produce physical diseases such as diabetes, why not also insanity? Since it was clear that the brain was the organ underlying mental diseases, perhaps the true ETIOLOGY of the insanities originated elsewhere in the body, places where substances toxic to the brain (internal secretions, ptomaines, bacteria, and so on) were produced and then transmitted to the central nervous system via the blood. This AUTOINTOXICATION theory of mental disorders first became prominent in France in 1893 and influenced a generation of alienists, neurologists, and psychiatric researchers. And indeed the most prominent among them was Emil KRAEPELIN.

Edward Shorter, in his 1997 volume, *A History of Psychiatry: From the Era of the Asylum to the Age of Prozac,* emphasized the irony that Kraepelin, the icon of the first biological psychiatry, was instrumental in putting an end to it because he was "agnostic about cause" and had "declared [brain] anatomy to be unimportant." This is only partially correct. Although Shorter correctly reports that Kraepelin introduced DEMENTIA PRAECOX in 1896 as a "metabolic disorder," the close connection between metabolic disorders and autointoxication theory in Kraepelin's medical cognition was not explored by Shorter. Kraepelin is perhaps better characterized as having been "tentative about cause" rather than agnostic. From the fifth edition of *Psychiatrie* in 1896 until the eighth edition in 1913, autointoxication (*Selbstvergiftung*) arising from a metabolic disturbance, probably in the sex glands—and not heredity—was Kraepelin's prime candidate for the cause of dementia praecox.

The search for "internal secretions" in dementia praecox (schizophrenia) The early experimental literature on the search for traces of internal secretions in the BLOOD OF THE INSANE reflects the confusion in the emerging field of endocrinology regarding the nature of hormones and their similarities to enzymes, general metabolites, drugs, toxins, antitoxins, and vitamins. These studies are too numerous, perplexing, and contradictory to summarize here. Perhaps the most extensive early review of this literature was conducted by the Russian psychiatric researcher Aleksandr Ivanovich Iushchenko (1869–1936) in a series of lectures delivered in 1911 and then translated into German and published in 1914. He hypothesized that dementia praecox was caused by glandular dysfunctions, especially disease processes in the parathyroid. In 1920 Bayard Taylor HOLMES, a major proponent of the autointoxication theory of dementia praecox, published a massive bibliography of works relating to the "toxaemia of dementia praecox" that remains the best source of information on early 20th century endocrine studies in dementia praecox (SCHIZOPHRENIA).

From hormones to neurohormones Endocrinological research provided a direct and important analogical bridge that led to the discovery of neurotransmitters in the brain. Following the 1921 discovery by Otto Loewi (1873–1961) of a substance in the brain later identified as acetylcholine, neurotransmitters were referred to as neurohormones or neurohumors. Indeed, the term *neurotransmitter* did not come into use until the 1960s. Neurotransmitter theories of the pathophysiology of schizophrenia (not the etiology—an important distinction to remember) involving the measurement of serotonin, DOPAMINE, glutamate, and so on, in the blood or cerebral spinal fluid (CSF) evolved directly from the metabolic paradigm in studies of the blood of the insane.

The "modern" era of endocrinology Modern endocrinological research into the biological substrates of dementia praecox/schizophrenia began in the 1920s, increased in number from the 1960s to the 1980s, and has declined markedly in the past 20 years. The early literature was reviewed in the works of one of its major proponents, Nolan D. C. Lewis (1889–1959), who believed the thyroid, adrenals, and gonads were implicated in dementia praecox. In the 21st century, publications of basic research on the endocrinology of schizophrenia have slowed to a trickle. Most of the research into the endocrine disorder hypothesis of schizophrenia has yielded little of value. There is no consistent or conclusive evidence for the role of the endocrine system in the cause (etiology) or pathophysiology (disease process) of schizophrenia.

The introduction of ANTIPSYCHOTIC DRUGS in 1952 has made endocrine research in schizophrenia more difficult. Endocrine abnormalities found in schizophrenia research may be due to the effects of antipsychotic medications. Recently, however, a few studies have once again examined the role of the sex glands and sex hormones in schizophrenia—a return to the initial 1896 hypothesis of the cause of dementia praecox put forth by Emil KRAEPELIN. The best evidence for an endocrine link to schizophrenia involves the anterior pituitary gland. The anterior pituitary contains gland cells that respond to releasing or inhibiting factors from the hypothalamus, which eventually may be found to be the source of the myriad confusing findings of endocrine dysfunction in schizophrenia.

See also DOPAMINE HYPOTHESIS; IMMUNE SYSTEM ALTERATIONS IN SCHIZOPHRENIA; METABOLIC DISORDER HYPOTHESIS.

Holmes, B. T. "A Guide to the Documents in Evidence of the Toxaemia of Dementia Praecox," *Dementia Praecox Studies* 3 (1920): 23–107.

Justschenko, A. I. *Das Wesen der Geisteskrankheiten und deren biologische-chemische Untersuchungen.* Dresden and Leipzig, Verlag von Theodor Steinkopf, 1914.

Kraepelin, E. *Psychiatrie. Ein Lehrbuch für Studierende und Aerzte.Fuenfte, vollstaendig umgearbeitete Auflage.* Leipzig: Verlag von Johann Ambrosius Barth, 1896.

Lewis, N. D. C. *Constitutional Factors in Dementia Praecox, with Particular Attention to Circulatory System and Some of the Endocrine Glands.* New York: Nervous and Mental Disease Publishing Co., 1923.

———. *Research in Dementia Praecox.* New York: National Committee For Mental Health, 1936.

Lieberman, J. A., and A. R. Koreen. "Neurochemistry and Neuroendocrinology of Schizophrenia: A Selective Review," *Schizophrenia Bulletin* 19 (1993): 371–429.

Schaefer, E. "Address in Physiology: On Internal Secretions," *Lancet* 2 (1895): 321–324.

Shorter, E. *A History of Psychiatry, From the Era of the Asylum to the Age of Prozac.* New York: John Wiley and Sons, 1997.

Stevens, J. R. "Schizophrenia: Reproductive Hormones and the Brain," *American Journal of Psychiatry* 159 (2002): 713–719.

Welbourn, R. B. "Endocrine Diseases." In *Companion Encyclopedia of the History of Medicine, Volume I,* edited by Bynum, W. F. and R. Porter. London and New York: Routledge, 1993.

endogenous psychosis See PSYCHOSIS.

endophenotype In genetics research, an endophenotype is perhaps best thought of as a BIOLOGICAL MARKER of a particular MENTAL DISORDER. It is a biological abnormality that is a much more direct result of the hypothesized genetic defect than the actual symptoms and behaviors of the disorder itself. For example, such an abnormality could be sought as a marker that indicates a person is genetically vulnerable to developing the disorder. It would then be said that the endophenotype demonstrates greater penetrance (i.e., it occurs with greater frequency) than the mental illness itself. The endophenotype may be found in the close relatives of the person with the disorder (known as the INDEX CASE or the PROBAND), but the symptoms of the mental illness itself may be fully evident only in the person in question.

See also CANDIDATE GENES; CONCORDANCE RATE; GENETICS STUDIES; INCOMPLETE PENETRANCE.

England Studies of the prevalence rates for schizophrenia in England have found substantial differences in different parts of the country, thus producing a mixed picture. Some researchers have suggested that if the diagnostic criteria differences between England and the United States were resolved, England would have a higher prevalence rate than the United States. A 1965 study of a working-class area by South London's Maudsley Institute found a prevalence rate of 3.4 per 1,000. One clear fact is that in England, schizophrenia occurs much more often in the lower socioeconomic groups. Scotland has a higher rate of schizophrenia than England.

Studies done on immigrants to the United Kingdom who suffer from their first episode of schizophrenia show that Asian immigrants tend to have a considerably lower relapse and readmission rate than white British-born citizens, whereas Afro-Caribbean immigrants have higher rates. The differences are thought to be due to the degree to which the immigrant group retains its traditional cultural values and group cohesion after moving to a new country. In Asians these qualities were maintained, whereas in Afro-Caribbeans in Britain these qualities were not maintained.

Birchwood, M., et al. "The Influence of Ethnicity and Family Structure on Relapse in First-Episode Schizophrenia. A Comparison of Asian, Afro-Caribbean and White Patients," *British Journal of Psychiatry* 161 (1992): 783–790.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

environmental causes of schizophrenia The environmental causes of schizophrenia are unknown. Over the years, epidemiological studies have pointed to numerous possibilities: infections (such

as viruses), the weather, the seasons, pregnancy complications, emotional traumas such as early parental loss, unhealthy expressed emotion styles in families, toxins, and a whole host of others. After a century of research, no one is certain of an environmental cause for schizophrenia. What is sure is that there is a genetic component to the origins and development of psychotic disorders such as schizophrenia, and that genetics do interact with (unknown) environmental factors.

See also RISK FACTORS; SEASONALITY OF BIRTH.

enzyme In biochemistry, an enzyme is a protein, secreted by cells, that acts as a catalyst to induce chemical changes in other substances, itself remaining largely unchanged by the process. For this reason enzymes are also called "biocatalysts," "biocatalyzers," and "organic catalysts." Most modern enzymes, as they are discovered, are named by adding the suffix "-ase" to the name of the substance on which the enzyme acts or activates, and/or the type of reaction it causes.

enzyme disorder hypothesis One of the BIOCHEMICAL THEORIES OF SCHIZOPHRENIA is that the disease is caused by abnormal enzyme activity. In fact, between 1957 and 1979 one of the most active areas in schizophrenia research was the search for metabolic (i.e., biochemical, neurochemical, neuroendocrinologic) changes in certain substances (neuroenzymes, neurohormones, neuropeptides and their metabolites) in the neurophysiology of people diagnosed with schizophrenia.

Several diverse areas of research have yielded biological markers of uncertain significance. First, there was suggestive evidence for elevations in the activity of the enzyme creatine kinase (CK) during acute psychotic phases of schizophrenia and affective disorders. This was first reported by H. Y. Meltzer in 1968, and later work by him indicated that serum CK activity was genetically regulated.

Second, many studies since 1941 (by Birkhauser) have indicated decreased levels of the enzyme monoamine oxidase, or "MAO," in the blood platelets of psychiatric patients, particularly schizophrenics. Much of the interest in this work was stimulated by a series of studies conducted by researchers Murphy and Wyatt and published in 1972. It was thought that this decrease in MAO activity may be a genetic marker of vulnerability to a range of mental disorders, not just schizophrenia.

Third, some reports indicated a decrease in the activity of the enzyme dopamine-beta-hydroxylase ("DBH") in the blood and the cerebrospinal fluid ("CSF") of schizophrenics. The first published finding of this DBH abnormality was by scientists Wise and Stein in 1973.

Fourth, many other enzymes (such as choline acetyltransferase and glutamic acid decarboxylase), other NEUROTRANSMITTERS than DOPAMINE (such as GABA, norepinepherine and serotonin), and peptides (such as the endorphins) have also been investigated as possible causal factors in the development of SCHIZOPHRENIA.

The research in this area is often incomprehensible to those not educated in the language of biochemistry, but a 1987 review by Meltzer published in *Schizophrenia Bulletin* provided one of the more accessible sources of information in this important area of schizophrenia research.

See also METABOLIC DISORDER HYPOTHESIS; TRANSMETHYLATION HYPOTHESIS.

Berger, P. A. "Biochemistry and the Schizophrenias: Old Concepts and New Hypotheses," *Journal of Nervous and Mental Disease* 169 (1981): 90–99.

Birkhauser, V. H. "Cholinesterase und monoaminoxydase in zentralen nervensystem," *Schweitzer. Med. Woch.* 71 (1941): 750–752.

Meltzer, H. Y. "Creatin Kinase and Aldolase in Serum: Abnormality Common to Acute Psychoses," *Science* 159 (1968): 1370.

———. "Biological Studies in Schizophrenia," *Schizophrenia Bulletin* 13 (1987): 77–114.

Wise, C. D., and L. Stein. "Dopamine-beta-hydroxylase Deficits in the Brains of Schizophrenic Patients," *Science* 181 (1973): 344–347.

epidemiology Epidemiology is an area of study that combines the methods of many different disciplines (demographic, sociological, psychological,

and medical) to study diseases. Of particular interest is the incidence and prevalence of a disease in a population, the demographic factors involved (e.g., race, sex, area inhabited), the natural history of the disease (e.g., age of onset, subtypes), and how the disease affects the environment. Most medical phenomena have been studied in this way, including the epidemiology of mental disorders.

Incidence and prevalence rates for a disease are the two most commonly encountered epidemiological statistics in research reports. Incidence refers to how frequently a particular disease occurs in a given population, whereas prevalence refers to the total number of cases of a particular disorder in a population in a given time period. Both incidence and prevalence rates can vary from study to study, depending upon the demographic characteristics of the area. Studies of the prevalence of SCHIZOPHRENIA have reported lifetime prevalence rates averaging 1 percent in the general population. For bipolar disorder (manic-depressive psychosis), prevalence rates have ranged from .4 percent to 1.2 percent of the adult population of the United States. Some research (summarized by L. F. Saugstad in 1989) indicates a marked increase of manic-depressive psychosis over the previous 30 years in several countries (mainly Scandinavia).

Perhaps the most readable source of information on the epidemiology of schizophrenia is psychiatrist E. Fuller Torrey's book, *Schizophrenia and Civilization* (1980). Chapter by chapter he reviews the epidemiological evidence collected on schizophrenia. Torrey reaches the following conclusions:

1. Schizophrenia appears to be a disease of civilization, since it appears to be found in more urban and technologically advanced areas of the world than in so-called "Third World" countries.
2. In the United States, prevalence rates for schizophrenia have ranged from 1.1 to 4.7 persons per 1,000.
3. Chinese-Americans and Mexican-Americans appear to have low schizophrenia rates. Schizophrenia is more common among the lower socioeconomic groups, among blacks, and among urban dwellers.
4. Scandinavian prevalence rates for schizophrenia are two to three times that of the United States. Rates also appear to be higher in the Soviet Union and Eastern European countries, but may be very low in Southern European countries, especially in Italy.
5. The two areas of the world with perhaps the highest prevalence rates for schizophrenia (and for manic-depressive psychosis) are Croatia, in Yugoslavia and—in particular—Western Ireland. In fact, the likelihood that a person will be hospitalized for schizophrenia in certain counties in Ireland is higher than 1 in 25 (4 percent), the highest of any area in the world. The counties most affected are Mayo, Sligo, Roscommon, Galway, Clare, Kerry, Cork, and Waterford. Irish immigrants to the United States and Canada have also traditionally had high rates of psychiatric hospitalization.
6. The prevalence rate for schizophrenia in Japan is about 2.3 per 1,000.
7. Schizophrenics may have a typical "season of birth," since, according to Torrey, studies indicate that—for unknown reasons—schizophrenics are disproportionately born in the late winter and early spring months in the Northern Hemisphere.
8. There is evidence that there are cultural differences in the response to antipsychotic medication. Europeans have been found to require lower doses of certain drugs than American patients.

Since viruses follow seasonal patterns and have been studied with epidemiological approaches, it has been suggested that some of this data point to the role of viruses in the case of schizophrenia. However, a 1985 comprehensive review of the epidemiological evidence on schizophrenia by William W. Eaton of the Center for Epidemiological Studies at the NATIONAL INSTITUTE OF MENTAL HEALTH concluded that genetics is the most important factor worldwide in the development of this disorder. Current interpretations of the vast literature on the epidemiology of schizophrenia by Assen Jablensky (1997 and 2003) confirm Torrey's summary and support Eaton's conclusion about the importance of genetics.

See also CROSS-CULTURAL STUDIES; GENETICS STUDIES; RISK FACTORS; VIRAL THEORIES OF SCHIZOPHRENIA.

Eaton, W. W. "Epidemiology of Schizophrenia," *Epidemiological Review* 7 (1985): 105–126.
Jablensky, A. "The Epidemiological Horizon." In *Schizophrenia,* edited by S. R. Hirsch and D. R. Weinberger. London: Blackwell Science, 2003.
———. "The 100-Year Epidemiology of Schizophrenia," *Schizophrenia Research* 28 (1997): 111–125.
Rawnsley, K. *Epidemiology of Affective Psychoses.* London: Cambridge University Press, 1982.
Saugstad, L. F. "Social Class, Marriage, and Fertility in Schizophrenia," *Schizophrenia Bulletin* 15 (1989): 11–43.
Torrey, E. F. "Geographical Distribution of Insanity in America: Evidence for an Urban Factor," *Schizophrenia Bulletin* 16 (1990): 591–604.
———. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

epilepsy and schizophrenia There has been a long controversy as to whether epilepsy and schizophrenia are related in any way. For example, the CONVULSIVE THERAPIES were invented by von MEDUNA in the 1930s and were based on a scientifically unsupported theory that epilepsy and schizophrenia are biologically incompatible; it was thought that inducing a seizure in schizophrenics might "cure" them. Many studies both pro and con have explored this relationship. One finding that seems to be reliable is that the symptoms of one type of seizure disorder, temporal lobe epilepsy, very often resemble schizophrenia in presentation. In fact, evidence presented by K. Davison in 1983 suggests that as much as 17 percent of people suffering from temporal lobe epilepsy display some symptoms of schizophrenia. In particular, temporal lobe epileptics have been known to have symptoms that resemble PARANOID SCHIZOPHRENIA, including grandiose, mystical, and religious DELUSIONS and HALLUCINATIONS.

Davison, K. "Schizophrenia-like Psychoses Associated with Organic Cerebral Disorders: A Review," *Psychiatric Developments* 1 (1983): 1–34.

epistaxis From the Greek, meaning a "nosebleed." Profuse bleeding from the nose was one of the variations of BLEEDING as a treatment for mental illness in the 18th and early 19th centuries. ESQUIROL in 1838 mentions its successful use in the treatment of a young man.

equinoxes Certain times of the year were thought to cause madness or exacerbate its symptoms more than at other times. For example, the mentally ill were called "lunatics" because of the mistaken belief that the phases of the moon, particularly the full moon, had a role in causing madness. The vernal and autumnal equinoxes, were singled out by many authorities in centuries past as critical periods for the development of "madness." ESQUIROL notes in 1838 that "a house for the insane is most disturbed, and requires more careful supervision, at the period of the equinoxes." Philippe PINEL, however, differed, writing in 1801 that the critical period of "maniacal paroxysms" "generally being immediately after the summer solstice, are continued with more or less violence during the heat of summer, and commonly terminate towards the decline of autumn."

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity.* Translated by E. K. Hunt. 1838. Reprint, Philadelphia: Lea and Blanchard, 1845.
Pinel, P. *A Treatise on Insanity.* 1801. Reprint, Sheffield: W. Todd, 1806.

erotic jealousy syndrome See OTHELLO SYNDROME.

erotomania "Love is a madness" (*furor amoris*) the Roman orator and statesman Cicero once wrote, and indeed there are very few human experiences that can generate more DELUSIONS than our erotic passions can. Forms of "love-madness" have been called *erotomania* at least since the 17th century. The word first appears in English in 1640 in a book by Jacques Ferrand, which was originally published in French in 1623, entitled *Erotomania or a Cure of Love or Erotique Melancholy.* For the next several centuries different authors defined erotomania in different ways, often confusing what we now know as nymphomania for this essentially delusional phenomenon.

Erotomania is often referred to as CLÉRAMBAULT'S SYNDROME after French psychiatrist Gaétan Gatian de Clérambault (1872–1934). In an article published in December 1920, Clérambault described erotomania as a type of "passional psychosis" (*les delires passionels*), his term for a category of delusional states in which a paranoid delusion is accompanied with passionate feeling. Clérambault, as head of the psychiatric emergency service of the Paris Prefectures of Police, was interested in how such delusional states led persons to commit crimes. Clérambault identified very specific characteristics of this delusional syndrome: "A conviction of being in amorous communication with a person of much higher rank, who has been the first to fall in love and the first to make advances." Clérambault thought that women in particular were susceptible to this delusion, and he published supporting case histories of women who had developed delusional beliefs that particularly desirable men (who, in reality, may never have met the women or had any contact with them) had fallen in love with them. This picture of erotomania was termed *pure erotomania* by Clérambault to distinguish it from the descriptions of other psychiatric authorities, who tended to define it as a form of PARANOIA.

As a type of delusional syndrome, erotomania generally does not appear alone and is usually an aspect of a serious psychotic disorder, such as SCHIZOPHRENIA or BIPOLAR DISORDER. A tragic modern example of this is would be presidential assassin John Hinckley Jr.'s erotomanic fascination with the actress Jodie Foster, which led him to attempt to assassinate President Ronald Reagan in 1981, in order to forever link their names together in history.

In French psychiatry (which has always resisted outside diagnostic systems), erotomania holds a special place as a separate delusional disorder. In *DSM-IV-TR* (2000) it is a subtype of DELUSIONAL DISORDER. In *ICD-10* (1992) it is similarly considered a subtype of PERSISTENT DELUSIONAL DISORDERS. Erotomanic delusions have been known to be present in persons suffering from schizophrenia, bipolar disorder, and major DEPRESSION, but these other disorders are the primary diagnosis, and the erotomanic delusions are secondary.

Enoch, M. D., and W. H. Trethowan. "De Clérambault's Syndrome." In *Uncommon Psychiatric Syndromes.* 2nd ed., edited by Enoch and Trethowan. Bristol, England: John Wright & Sons, 1979.

Segal, J. H. "Erotomania Revisited! From Kraepelin to *DSM-III-R*," *American Journal of Psychiatry* 146 (1989): 1,261–1,266.

erotomania, paranoid type See PARANOIA EROTICA.

erotomania proper The name given in 1882 by J. C. Bucknill and D. H. Tuke to what was later called pure erotomania. Following a distinction made in 1838 by ESQUIROL, Bucknill and Tuke distinguished the delusional syndrome of erotomania from those syndromes in which the sexual passions were actually acted out, such as nymphomania. They write:

> Erotomania, in its extended signification, not infrequently follows upon religious melancholy. . . . It is not uncommon in the old, and . . . in persons who have been patterns of chastity during life. . . . It is more frequent among women than in men, and . . . among the unmarried and widows than the married. . . . It may attack any age; but the sentimental form—erotomania proper—more especially affects the young, and those of an ardent, susceptible temperament. . . . Erotomania is often complicated with hysteria, and sometimes with hypochondriasis.

Bucknill, J. C., and D. H. Tuke. *A Manual of Psychological Medicine.* 2nd ed. London: J. & A. Churchill, 1882.

erotomanic type One of the variants of DELUSIONAL DISORDER as defined in *DSM-IV-TR* (2000). It corresponds to EROTOMANIA as defined by de Clérambault.

ERP The acronym for "event-related potentials." See also EEG STUDIES OF SCHIZOPHRENIA.

Esquirol, Jean-Étienne-Dominique (1772–1840) A student of Philippe PINEL's at the SALPÊTRIÈRE in

Paris and the author of the 1838 book *Des Maladies Mentales,* a classic textbook in the field of PSYCHIATRY, or *médecine mentale* as it was then called. A recent study of the 19th-century French psychiatric profession by Goldstein concludes that until well past the middle of the century, approximately 95 percent of all French *aliénistes* had studied in Paris with either Pinel or Esquirol. Esquirol received his doctorate in 1805 with the completion of his thesis, entitled "Passions Considered as Causes, Symptoms, and Therapeutic Means of Mental Diseases." He won the position of an attending physician at the Salpêtrière in 1811, and in that year instituted the very first official training courses on mental diseases for medical students and other physicians. A select group of young physicians who had trained under Esquirol and had become his disciples formed the "Esquirol Circle," an informal intellectual society that met for Sunday luncheons, which were presided over by Esquirol himself. Many of these "Circle" members became famous in their own right as their careers developed during the 19th century, notably, J.-P. FALRET, A. J. F. BRIERRE DE BOISMONT, J.-J. Moreau de Tours, and Jules BAILLARGER.

The search for BIOLOGICAL MARKERS of mental disorders has always existed in one form or another, and in Esquirol's day PHYSIOGNOMY was considered an important diagnostic tool. According to an entry for March 22, 1818, in the diary of Sir Alexander Morison, which described his visit to the Salpêtrière, Esquirol showed Morison his large personal collection of plaster casts of the faces of insane persons. The search for physiological markers of insanity also led Esquirol to become involved in the autopsies of deceased patients, referred to at that time as "openings (*ouvertures*) of corpses." Following the lead of his mentor Philippe PINEL, who also conducted *recherches cadavériques* between 1802 and 1804, Esquirol believed that visceral lessions were more likely to cause insanity than brain abnormalities, particularly in melancholics in which, he purported, the transverse colon was displaced.

Esquirol traveled widely in his life and inspected many institutions for the insane throughout Europe. His review of the inhumane conditions in French institutions moved him enough to write a strong report of his experiences to the French minister of the interior in 1818. In 1823 he was named inspector general of the faculty of medicine at the Salpêtrière; he left in 1825 to become the superintendent of the Maison de Charenton, one of France's oldest mental hospitals. The Maison de Charenton was the place where the Marquis de Sade was held for many years until his death. Esquirol spent 15 years working on his famous textbook, which was instantly recognized as a classic and translated into Italian, English, and German soon after publication. Esquirol is particularly remembered for providing the first clear description of HALLUCINATIONS and, especially, how they differ from illusions.

Esquirol, J. E. D. *Des Maladies Mentales.* 2 vols. Paris: J. B. Baillière, 1838.

Goldstein, J. *Console and Classify: The French Psychiatric Profession in the Nineteenth Century.* Cambridge: Cambridge University Press, 1987.

Mora, G. "On the Bicentenary of the Birth of Esquirol (1772–1840), the First Complete Psychiatrist," *American Journal of Psychiatry* 129 (1972): 562–566.

etherization After the anesthetic properties of ether were discovered in 1846, it was highly recommended for use in American asylums, from about 1849 to 1860, for acute excitements and for agitated depression. In France it was especially given to those patients suffering from mental DEGENERATION, most likely those suffering from the general paralysis of the insane and dementia praecox. However, this form of somatic treatment for mental illness fell into decline in the remaining decades of the 19th century.

The discovery of ether's effects also eclipsed the use of hypnosis as anesthesia during surgery. British "civil-surgeon" James Esdaille had perfected the use of hypnosis anesthesia to perform thousands of minor operations and about 300 major ones (including 19 amputations) between 1846 and 1848, in the experimental "Mesmeric Hospital" that he had been granted permission to establish in Calcutta, India, by the governor of Bengal. Although the medical discipline of anesthesiology evolved from the early surgical use of ether, the use of hypnosis anesthesia during surgery did not come into any significant use again until the 20th century.

Bramwell, J. M. *Hypnotism: Its History, Practice and Theory.* London: Alexander Morning, 1906.
Diethelm, O. "Somatic Treatment in Psychiatry," *American Journal of Psychiatry* 95 (1938): 1,165–1,179.

ethnicity and schizophrenia See BLACKS, INCIDENCE OF SCHIZOPHRENIA IN; CROSS-CULTURAL STUDIES; EPIDEMIOLOGY; RISK FACTORS.

etiologic heterogeneity This is essentially a term for expressing the idea that a single disease may have many different causes (etiologies). This idea, which is prominent in GENETICS STUDIES, is derived from the growing body of evidence that several MENTAL DISORDERS—especially SCHIZOPHRENIA and BIPOLAR DISORDER—are in reality a *spectrum* of disorders, not just a single, homogeneous disease entity. The subtypes of schizophrenia and bipolar disorder, while somehow related, may develop from different causes. Etiologic heterogeneity may result from NONALLELIC GENETIC HETEROGENEITY, PHENOCOPIES, or both.

See also GENETIC TRANSMISSION.

Tsuang, M. T., and Farone, S. V. "The Case for Heterogenity in the Etiology of Schizophrenia," *Schizophrenia Research* 17 (1995): 161–175.

etiology The cause or causes of a disease.

evacuants Now called "laxatives," these were substances that induced defecation in order to "purge" (and therefore "purify") the body. Evacuants and purgatives, especially emetics that caused vomiting, were a popular form of treatment for the mentally ill. The use of these substances continued in one form or another until the late 19th and early 20th centuries. Wilhelm GRIESINGER, the noted German psychiatric authority, writes of the significance of evacuants for the treatment of mental illness in the 1861 second edition of his famous textbook:

> Those medicines which act upon the digestive canal are the oldest, and still those that are most frequently used. Besides their evident indication in constipation—which is common in these diseases–, and very often better obviated by dietetic means and mild clysters than by medicines—they are also given with advantage in all recent cases associated with cerebral congestion, and are the chief remedy in acute inflammatory states of the brain.

Evacuants are no longer used as a treatment for mental illness, although laxatives may be prescribed for a limited time to counteract the constipation that may be one of the side effects of some types of ANTIPSYCHOTIC DRUGS.

Griesinger, W. *Mental Pathology and Therapeutics.* 1861. Reprint, New York: William Wood & Company, 1882.

exacerbations Those periods when the symptoms of a disease flare up and become worse. They then may go into remission. Many of the psychotic disorders are characterized by exacerbations and remissions. Such is also the case with most other mental and physical diseases (such as multiple sclerosis). These ACUTE episodes may accompany a more chronic course of an illness, such as the POSITIVE SYMPTOMS (delusions and hallucinations) of schizophrenia, which may wax and wane over the lifetime course of a disease.

See also COURSE OF SCHIZOPHRENIA.

existential analysis See DASEINANALYSE.

exogenous psychosis See PSYCHOSIS.

exorcism Throughout history, many diseases—and mental illnesses in particular—were thought to be the result of "possession" by malevolent spirits or "demons." Therefore, the remedy for this, exorcism, entailed the forceful removal of these entities by magical means. This spirit possession theory of disease and exorcism has been recorded in "primitive" societies worldwide and is mentioned in historical works dating back as far as ancient Egypt.

In the New Testament, particularly the Gospel according to Mark (A.D. 64), one of the defining attributes of Jesus is his magical ability to cast out "devils" from "demoniacs" and thereby cure them. As a treatment, formal exorcisms by practitioners of all sorts, clerical or otherwise, were carried out with regularity in Europe until the 17th century.

See also CACODEMONOMANIA; POSSESSION SYNDROME.

Kemp, S., and K. Williams. "Demonic Possession and Mental Disorder in Medieval and Early Modern Europe," *Psychological Medicine* 17 (1987): 21–29.

Noll, R. *Vampires, Werewolves and Demons: Twentieth Century Reports in the Psychiatric Literature.* New York: Brunner/Malec, 1991.

Smith, M. *Jesus the Magician.* San Francisco: Harper & Row, 1978.

expressed emotion It has long been suspected that the behavior of the family has an influence on the development of mental illness in afflicted family members. Proponents of most FAMILY INTERACTION THEORIES propose that abnormal communication patterns actually cause mental illness, and many theories have been put forth to describe the role of the family in the cause of schizophrenia. However, the research in this area has been difficult and so far inconclusive, and many of the older research tends to disregard entirely the role of biological factors in the causation of SCHIZOPHRENIA. Instead, many researchers have turned their attention to the effect of the family on the course of an illness. These studies try to identify family behavior patterns that influence—either positively or negatively—the mental illness of a particular family member. The strength of this approach is that it is not incompatible with the impressive body of research that points to significant biological factors in the causation of mental illness (particularly schizophrenia).

One of the most significant findings is that the "expressed emotion" or "EE" within a particular family environment is a suggestive predictor of relapse in patients after their discharge from hospital care. EE was measured in families indirectly by analyzing interviews with family members (without the patient being present). The first published report on EE appeared in 1962 and was the result of the work in England of Brown and colleagues; replications of this work that consistently support the role of EE in relapse continued into the 1980s. The consistent finding is that patients returning to families with low levels of EE have consistently lower relapse rates and had less of a need for antipsychotic medication. The conclusion is that in people with schizophrenia (at least in its earliest years of manifestation), there is a lower tolerance for intense environmental stimuli, particularly critical or intensely emotional comments or interactions involving family members. Thus, a family environment that is relatively supportive and emotionally undemanding may help a person with schizophrenia to reduce dependence on medication and help prevent relapse. Given this finding, other research has been conducted that has had trained families of schizophrenics with high levels of EE (high emotional overinvolvement of family members and high numbers of critical comments) monitor their interactions and actually lower their levels of EE. Controlled studies have shown that relapse rates can be significantly reduced for patients whose families can learn to lower their usually high levels of EE.

Some research has examined other variables than EE as the source of important influences on the course of a family member's mental illness. For example, an important study by the UCLA Family Project (reported by Goldstein in 1985) found that instead of EE, which is measured indirectly, other factors, such as a directly measured index of a family's "affective style" or "AS" and a family's "communication deviance" or "CD," had more of an effect either independently or together in the development of schizophrenia.

More research clearly needs to be done in this area. But what is important about these studies is the knowledge that, to some extent, schizophrenia can be managed by reducing or changing emotional interactions within the family.

Brown, G. W., J. T. L. Birley, and J. K. Wing. "Influence of Family Life on the Course of Schizophrenic Disorders: A Replication," *British Journal of Psychiatry* 121 (1972): 241–258.

Goldstein, M. J. "Family Factors That Antedate the Onset of Schizophrenia and Related Disorders: The Results

of a Fifteen Year Prospective Longitudinal Study," *Acta Psychiatrica Scandinavica* 71, Suppl. 319 (1985): 7–18.
Hooley, J. M., and J. Hiller. "Expressed Emotion and Pathogenesis of Relapse in Schizophrenia." In *Origins and Development of Schizophrenia: Advances in Experimental Psychopathology,* edited by M. F. Lenzenweger and R. H. Dworkin, 447–468. Washington, D.C.: American Psychological Association, 1998.

expressivity In genetics, expressivity is the extent to which a given phenotype, or observable trait, is manifest in an individual. It is the extent to which a trait (an observable behavior or a physical characteristic), known to be caused by the influence of a particular gene or genes that predisposes an individual to that trait, can be observed in the individual.

extrapyramidal symptoms/syndromes In the human body, the extrapyramidal system encompasses those parts of the central nervous system that are responsible for the coordination and integration of body movements. Perhaps the most serious drawback to the use of ANTIPSYCHOTIC DRUGS in the treatment of the psychotic disorders is their very serious adverse effects on the extrapyramidal system. The symptoms that these side effects produce can include tremors, muscular rigidity, drooling, eyes rolling upward toward the forehead, odd or jerky movements, blurred vision, dry mouth, odd motions of the tongue and hands, and a shuffling gait. There are four extrapyramidal syndromes: acute dystonic reactions, AKATHISIA, PARKINSONISM, and TARDIVE DYSKINESIA. Of these, the first three syndromes can be alleviated with drugs such as BENADRYL or COGENTIN, or through the reduction or cessation of antipsychotic medication. However, the fourth of these syndromes, tardive dyskinesia, is a chronic condition that develops from the prolonged use of antipsychotic medication (usually many years, although sensitivity levels differ from person to person).

eye movement abnormalities in schizophrenia One of the clearest candidates for being a BIOLOGICAL MARKER OF SCHIZOPHRENIA is certain eye movement dysfunctions. These abnormalities were first detected in schizophrenics in 1908 by researchers Diefendorf and Dodge, and have been studied for their possible link to schizophrenia ever since. The majority of these studies have involved "smooth pursuit eye movements" (SPEM), that is, those eye movements made when following a moving object. With recent advances in technology, scientists have also found that eye movement dysfunctions are detectable even while the eyes are focused on a stationary target.

Overall, smooth pursuit eye movements have been found to be abnormal in about 50 percent to 85 percent of schizophrenics in most studies, with the same dysfunctions found in about 8 percent of the general population. Furthermore, 40 percent to 50 percent of first-degree relatives of schizophrenics also have smooth pursuit eye movement abnormalities. The rate of abnormalities in persons with bipolar disorder (30 percent to 50 percent) is thought to be inflated due to LITHIUM treatment, and the number of first-degree relatives of manic-depressives that have these abnormalities is just 10 percent to 13 percent—only slightly above the rate for the general population. Thus, smooth pursuit eye movement abnormalities seem to be a genetically transmitted dysfunction and are thus becoming more and more accepted as a solid biological marker for schizophrenia. There is great hope that SPEM dysfunction is, indeed, such a marker, since it could then be used as a predictor for identifying which high-risk individuals are at true genetic risk for one day developing schizophrenia.

Diefendorf, A. R., and R. Dodge. "An Experimental Study of the Ocular Reactions of the Insane from Photographic Records," *Brain* 31 (1908): 451–489.
Erlenmeyer-Kimling, L. "Biological Markers for the Liability to Schizophrenia." In *Biological Perspectives of Schizophrenia,* edited by H. Helmchen and F. Hein. New York: Wiley, 1987.
Levy, D. L., P. S. Holzman, S. Matthysse, and N. R. Mendell. "Eye Tracking Dysfunction and Schizophrenia: A Critical Perspective," *Schizophrenia Bulletin* 19 (1994): 461–536.

eyes, subduing patients with See FIXING.

factor analytic models of schizophrenic symptoms See DIMENSIONS OF SCHIZOPHRENIA.

"Factors of Insanities, The" In 1894 John Hughlings Jackson (1835–1911), a British neurologist who is still considered one of the most important in his field, published a paper on "The Factors of Insanities" in which he proposed some very important ideas that are still used today. In particular, Jackson defined the difference between POSITIVE SYMPTOMS and NEGATIVE SYMPTOMS and their relationship to the nervous system. In the 1980s, these concepts became especially important in SCHIZOPHRENIA research with the work of research psychiatrist Nancy Andreason (1938–). Jackson divided the presenting symptoms found in the psychotic disorders according to whether they are the result of the "dissolution" of certain centers in the brain (the negative symptoms), or whether they are caused by the remaining "healthy nervous arrangements" left intact but nonetheless affected in their functioning by the destruction of neural tissue in other parts of the brain (the positive symptoms). The positive symptoms, then, should disrupt the normally complex integrative functions of the higher cortical functions (for example, thoughts and perceptions) and make them caricatures—less differentiated, less complex, and more automatic or involuntary variations (such as delusions and hallucinations). Jackson wrote:

> We must not speak crudely of disease causing the symptoms of insanity. Popularly the expression may pass, but properly speaking disease of the highest centres no more causes positive mental states, however abnormal they may seem, than opening flood gates causes water to flow or cutting the vagi causes the heart to beat more frequently. Disease only causes the negative element of the mental condition: the positive mental element, say a delusion, obviously an elaborate delusion however absurd it may be signifies activities of the healthy nervous arrangements, signifies evolution going on in what remains of the highest cerebral centres.

Jackson's observation that the "disease" or "dissolution" of brain tissue is related to negative symptoms influenced Crow's "type II schizophrenia," in which negative symptoms, such as flat affect, poverty of speech, blocking, are correlated with structural abnormalities in the brain.

See also BRAIN ABNORMALITIES IN SCHIZOPHRENIA.

Jackson, J. H. "The Factors of Insanities." In *Selected Writings*. Vol. 2. 1894. Reprint, New York: Basic Books, 1958.

Falret, Jean-Pierre (1794–1870) A noted French *aliéniste* who was a member of the "Esquirol Circle," the group of influential physicians to the insane females at the SALPÊTRIÈRE in Paris (males were kept at another hospital, the BICÊTRE), who met regularly for case seminars with their mentor, J. E. D. ESQUIROL. Falret joined the medical staff at this hospital in 1815. After assuming charge of the section for lunatics at the Salpêtrière in 1841, Falret began a program of treatment based on the belief that religion should play a role in psychiatric treatment, a belief that sharply contrasted with his mentors Pinel and Esquirol. He induced a cleric—a certain Abbé Christophe—to come to the hospital and lead group religious activities that included

hours of praying, singing, and biblical recitations. He believed that religious practice helped to bring about the cure of mental illness and to avoid relapses. In addition, as he told a journalist in the 1840s, religion played another role in the lives of his female patients at the Salpêtrière because, "Not being able to give them a lover to comfort the solitude of their hearts, I seek to give them God."

Falret is best remembered for his 1854 description of *la folie circulaire,* or the CIRCULAR INSANITY, as it became known in English and which is now known as BIPOLAR DISORDER. However, his linkage of phases of MELANCHOLIA and MANIA together into a separate disorder from either of these mental disorders alone had been preceded only two weeks earlier by fellow "Esquirol Circle" member Jules BAILLARGER's published description of *la folie à double forme*. Thus, it is Baillarger who was given credit for what was later named by KRAEPELIN as MANIC-DEPRESSIVE insanity. Falret, however, claimed he had published a description of this disorder in 1851 but did not use the term *la folie circulaire* in that earlier paper. Falret stressed the role of heredity in the transmission of this disorder, and he argued that the disorder was more commonly found in women.

Falret's other contributions include: in 1853, authoritative diagnostic indicators for the GENERAL PARALYSIS OF THE INSANE; and in 1822 *the* first published study of suicide that used statistical data. He believed that suicide was the result of a combination of predisposing and environmental causal factors.

Falret, J.-P. *De l'hypochondrie et du suicide.* Paris: 1822.

———. "Marche de la folie," *Gazette des Hôpitaux,* January 14, 1851.

———. "Mémoire sur la folie circulaire, forme de maladie mentale caractérisée par la reproduction successive et régulière de l'état manaiaque, de l'état mélancolique, et d'un intervalle lucide plus ou moins prolongé," *Bulletin de l'Académie Impériale de Médecine* 19 (February 14, 1854): 382–400.

———. *Recherches sur la folie paralytique et les diverses paralysies générales.* Paris: 1853.

Goldstein, J. *Console and Classify: The French Psychiatric Profession in the Nineteenth Century.* Cambridge: Cambridge University Press, 1987.

Falret, Jules-Philippe-Joseph (1824–1902) A French *aliéniste* and the son of Jean-Pierre FALRET. He continued his father's work in the understanding of the "circular insanity" and of the general paralysis of the insane. However, he is perhaps best remembered for his identification (along with Ernest Charles Lasègue) in 1877 of a form of "communicated" or "shared" delusional disorder, which is still known as FOLIE À DEUX.

Lasègue, E., and J.-Ph.-J. Falret. "La folie à deux (ou folie communiquée)," *Annales médico-psychologique* 18 (1877): 321.

family care The placement of mentally ill people in households under the care of unrelated families. In Europe this tradition has persisted since at least the 1300s in Gheel, Belgium, where a shrine to the patron saint of the mentally ill, Saint Dymphna, attracted far too many of the afflicted seeking miracle cures for the local hospital to handle. Thus, a tradition of boarding the mentally ill in private households began and is continued to this day on a reduced scale under the sponsorship of the Belgian government. Foster home care of the mentally ill became more prevalent in Europe only in the 19th century. British psychiatrist Henry MAUDSLEY, who dominated the field in his country in the latter third of the 1800s, strongly advocated the return of the most chronic patients to the care of their own families. In the United States, the very first such formal foster home program was apparently instituted in Massachusetts in 1885.

family interaction theories Popular from the 1950s to the 1970s, this group of theories asserts that severe mental illness (and in particular schizophrenia) is caused by abnormal family communication patterns. The assumption is that the underlying pathological communication patterns of the family create the mental illness in a selected person who is the "scapegoat" or the bearer of the "sick role" for the other members of the family, which acts together in an organized whole usually called a "system." Treating the mentally ill person ("the identified patient") is often depicted by pro-

ponents of family interaction as a group "family therapy" during which pathological communication patterns can be pointed out and changed, thus, theoretically, healing or curing the "identified patient." When applied to SCHIZOPHRENIA, most of these theories usually completely ignore biological evidence for the cause of the psychosis.

The family interaction theories were derived from the interest of PSYCHOANALYSIS in family dynamics as the cause of schizophrenia. For example, psychoanalyst Frieda FROMM-REICHMANN first used the term *schizophrenogenic mother* in 1948 to single out the mother as the primary cause of schizophrenia in her children. This concept was later "verified" in a study of 25 mothers of schizophrenics by Trude Tietze in 1949. Also in the 1940s, Leo Kanner wrote about the role of the "refrigerator mother" as the cause of AUTISM in infancy and childhood.

By the 1950s, more sophisticated family interaction theories were proposed that shifted from the focus on the single mother-child relationship to the study of the family as an interactive system that works together as a whole. As early as 1949 Theodore Lidz and his colleagues at Yale University began to publish work on the study of communication patterns in families with schizophrenic members. The family triad of father, mother, and schizophrenic child was of particular interest, and two typical patterns of families were discerned, schizmatic, and skewed. In the "skewed family," an unempathetic and intrusive mother is the guilty party, and she paired with an ineffectual male who is passive and perhaps mentally ill or alcoholic himself. The lack of a strong male role model and the over-intrusiveness of the mother tends to produce schizophrenic sons in these families, according to Lidz. In families characterized by a "marital schism," the entire family (rather than just the mother) seems to be at war with one another, with the parents continually threatening separation and undercutting one another. Lidz believed this sort of pattern was more characteristic of the lives of female schizophrenic patients that he and his colleagues studied.

In 1956 Gregory BATESON and his colleagues at Stanford University (the "Palo Alto Group") proposed the theory of the double bind (see DOUBLE-BIND THEORY). The theory is that schizophrenia develops in people from families that engage in "double-bind" communications, i.e., communications in which the content of the verbally expressed message does not match, or is "incongruent," with the underlying message expressed in the tone of voice, gesture, facial expression, or context of the message. For example, "I love you" may be said while the parent may have a facial expression of total apathy, or perhaps during a situation in which the parent is being particularly cruel to the child. The double-bind theory was the basis of further elaborations of "family systems theory" by Jay Haley, one of Bateson's original colleagues, and a major influence in the development of "family therapy" as a treatment modality. The essence of the rationale for using family therapy as the treatment for schizophrenia was expressed by Haley in a 1962 article when he notes, "It became apparent that it was not entirely reasonable to have a child driven mad by his family, then hospitalize him and get him on his feet and send him right back into his family to be driven mad again."

Other family interaction theorists have invented other terms for the types of family communications that seem to cause a schizophrenic break in one of the children. For example, in research spanning more than a decade Wynne and various colleagues have identified deviant styles of parental communication that may lead to the development of thought disorder in genetically susceptible children. Communication deviance (CD) is thought to comprise such characteristics as the lack of firm commitment to ideas, unusual language patterns, and problems in bringing closure to ideas or in interactions with others. However, it cannot be as yet determined whether the CD of the parents is the expression of a latent genetic trait, such as deficits in attention that have not fully developed into schizophrenia (but which their child *is* experiencing as schizophrenia), or whether it is the parents' response to daily communication with a psychotic child. Several prospective studies of children at high risk for schizophrenia are currently underway to determine whether family factors such as CD are present prior to the development of schizophrenia.

In the 1988 edition of *Surviving Schizophrenia,* E. Fuller Torrey asserts that, "Family interaction

theories, like psychoanalytic theories, have by now been discarded and for many of the same reasons." He argues that research has been of poor quality or has not held up to replication by others, and that it fails to distinguish between family communication patterns that cause schizophrenia versus those that are caused by it. However, research in this area continues, since at present only a portion of the "cause" of schizophrenia can be attributed to genetics, suggesting that the environment—specifically, family interaction patterns—may still play a significant role in the development, or at least the severity of the course, of schizophrenia.

See also EXPRESSED EMOTION.

Bateson, G., et al. "Towards a Theory of Schizophrenia," *Behavioral Science* 1 (1956): 251–264.

Lidz, R., and T. Lidz. "The Family Environment of Schizophrenic Patients," *American Journal of Psychiatry* 106 (1949): 332–345.

Lidz, T. *The Origin and Treatment of Schizophrenic Disorders.* New York: Basic Books, 1973.

Tietze, T. "A Study of Mothers of Schizophrenic Patients," *Psychiatry* 12 (1949): 55–65.

Wynne, L. C., et al. "Schizophrenics and Their Families: Research on Parental Communication." In *Developments in Psychiatric Research,* edited by J. M. Tanner. London: Hodder & Stoughton, 1977.

family studies (genetics) See CONSANGUINITY METHOD.

family therapy See FAMILY INTERACTION THEORIES.

farming (as treatment) The physical exercise of work has long been employed in the treatment of some mentally ill persons, and well into this century many institutions continued the practice of using patients to help farm or take care of the institutional grounds. However, due to the decline of a farming-based society, most institutions now have pragmatic "occupational therapy" training programs that are designed to help patients gain and maintain skills they will need upon discharge back to an urban community. ESQUIROL in particular recommended farming as the best form of therapeutic physical exercise for the mentally ill, particularly depressed people. In 1838 he writes:

> Corporeal exercises, riding on horseback, the game of tennis, fencing, swimming and traveling, especially in melancholy, should be employed, in aid of other means of treatment. The culture of the earth, with a certain class of the insane, may be advantageously substituted for all other exercises. We know the result to which a Scottish farmer arrived, by the use of labor. He rendered himself celebrated by the cure of certain insane persons, whom he obliged to labor in his fields.

Esquirol, J. E. D. *Mental Maladies. A Treatise on Insanity,* trans. E. K. Hunt. Philadelphia: Lea and Blanchard, 1845; first published, 1838.

Faxensyndrom Also known as the clown syndrome, it is a form of reactive MENTAL DISORDER, found in prisoners, that simulates a true psychosis. "Childish" or "silly" behavior predominates in this syndrome as a dissociated reaction to the confines of prison. It was first identified by Eugen BLEULER, and it is related to the more commonly described GANSER'S SYNDROME, also known as "prison psychosis."

Bleuler, E. "Das Faxensyndrom," *Psychiatr.-Neurol. Wochenschrift* 12 (1910–11): S. 375.

Feighner research criteria In the 1970s, researchers in the field of SCHIZOPHRENIA began to develop specific criteria for defining schizophrenia that would be universally acceptable and used in all future studies. For many decades, scientists had been conducting research studies on "schizophrenics" without any commonly accepted definition of what a "schizophrenic" was. Furthermore, many studies did not list their criteria for defining schizophrenia, and many studies reported using "schizophrenics" as a single generic group without regard to important differences in the subtypes of schizophrenia. Hence, most of the research prior to 1980 is not cited in scientific journals today, because the

patients that were used then might not match the generally accepted definition of the schizophrenic subjects used in research today. The assumption is that the knowledge gained in those earlier studies may not be generalizable to the results of today.

The Feighner research criteria were developed at the Washington University School of Medicine in St. Louis and first proposed in a 1972 publication. They were referred to as the Feighner criteria because of the name of the senior author of the publication. The Feighner criteria consists of suggested diagnostic criteria for 14 mental disorders (including schizophrenia), criteria that would ensure that all future research used subjects with the same characteristics. The Feighner criteria was used extensively in schizophrenia research throughout the 1970s. Other research criteria that were also proposed in the early 1970s were the New Haven Schizophrenia Index and the WORLD HEALTH ORGANIZATION International Pilot Study of Schizophrenia Criteria, revised by Carpenter, Strauss and Bartko and called the "CSB system" or the "WHO Flexible System." However, in 1975 the RESEARCH DIAGNOSTIC CRITERIA (or RDC) was developed by Robert Spitzer (1932–) of the New York State Psychiatric Research Institute and Eli Robins (1921–95) of the Washington University School of Medicine in St. Louis, and it is the RDC that has been the most widely accepted research criteria in the study of schizophrenia.

Endicott, J., et al. "Diagnostic Criteria for Schizophrenia: Reliabilities and Agreement between Systems," *Archives of General Psychiatry* 39 (1982): 864–889.

Feighner, J. P., et al. "Diagnostic Criteria for Use in Psychiatric Research," *Archives of General Psychiatry* 20 (1972): 57–63.

feigned insanity Ever since laws began to accept that some severely mentally ill people could commit criminal acts for which they were not responsible due to their loss of reason, there have been otherwise-normal criminals and selected others who have "feigned" or "simulated" insanity to escape imprisonment or other punishment for criminal acts. In his 1801 classic, *A Treatise on Insanity,* Philippe PINEL devotes an entire section to "Feigned Mania: The Method of Ascertaining It." In this section he provides two illustrative case histories, one being a case of "feigned mania" in a political prisoner (whom Pinel humanely does not reveal to the authorities and thus spares the dissident a return to prison) and another exemplifying genuine mental illness. Pinel makes the observation, still all too true today (as anyone who has worked in a state psychiatric facility will admit), that "A guilty prisoner sometimes counterfeits insanity in order to escape the vengeance of the law, preferring confinement in a lunatic hospital to the punishment due to his crime." However, Pinel is honest about the difficulty of identifying simulated insanity.

> It may be thought astonishing, that in an object of so much importance as that of ascertaining the actual existence of mental derangement, there is yet no definite rule to guide us in so delicate an examination. In fact, there appears no other method than what is adopted in other departments of natural history: that of ascertaining whether the facts which are observed belong to any one of the established varieties of mental derangement, or to any of its complications with other disorders.

American physician Isaac RAY, whose 1838 book, *A Treatise On the Medical Jurisprudence of Insanity,* was perhaps the greatest contribution made by American psychiatry in the 19th century, devotes several chapters to such topics as "Simulated Insanity," "Concealed Insanity," and "Simulated Somnambulism." He criticizes the practice of using the courtroom testimony of physicians who have no experience working with the mentally ill in distinguishing cases of simulated insanity from genuine ones:

> Those who have been longest acquainted with the manners of the insane, and whose practical acquaintance with the disease furnishes the most satisfactory guaranty of the correctness of their opinions, assure us that insanity is not feigned easily, and consequently that no attempt at imposition can long escape the efforts of one properly qualified to expose it.

Ray states that all cases of simulated insanity betray a common characteristic: "The grand fault committed by impostors is, that in their anxiety to produce an imitation that shall deceive, they overdo the character they assume, and present nothing but a clumsy caricature." He then describes specific symptoms of "mania" that are often clumsily mimicked, and he gives physicians guidelines on how to trick the suspected simulator, urging them to "contrive some plan for outwitting the pretender, and entrapping him in his own toils."

Many techniques have been employed through the centuries to detect feigned insanity. Ray relates a tale reported by Benjamin RUSH of Philadelphia in which Rush was called in by the courts to determine whether a man who had just been condemned to execution was "feigning madness" or not. Incredibly, Rush based his decision on the man's PULSE, which he found "twenty beats more frequent than in the natural state," and therefore, "he decided, chiefly on the strength of this fact, that the prisoner was really mad." With the rise of experimental research on psychology and psychophysiology at the end of the 19th century, objective techniques were eventually sought for use in forensic psychiatric situations. Swiss psychiatrist C. G. JUNG was a pioneer in the creation of a diagnostic device with the famous "word association" test, which had already been used in psychiatric research by others. Jung reports the application of his word association tests to forensic issues, including determining cases of "simulated insanity" in a series of papers he published between 1903 and 1908.

Today our knowledge of the psychotic disorders (particularly schizophrenia and bipolar disorder) is so widely distributed that, in most legal situations, it would be highly unlikely for someone to simulate them successfully for any great length of time. However, in nonforensic situations in which it is rarely expected that the presenting patient is lying about his or her symptoms, an impostor can gain admittance to psychiatric facilities by perhaps just claiming to "hear voices." Such was the ruse reported in a famous 1973 article by psychologist David Rosenhan and his associates at Stanford University, who sent normal impostors to a psychiatric facility and who instructed them to report only such auditory hallucinations. Most of them were admitted to the facility with a diagnosis of schizophrenia. Rosenhan's criticisms of psychiatric diagnostic practices have, in turn, been criticized by many others (see Spitzer's 1976 article) who defend the actions of the admitting psychiatrists in the Rosenhan study as rational decisions based on the context in which the claims of psychotic symptoms were made.

Jung, C. G. "On Simulated Insanity." In *The Collected Works of C. G. Jung, Volume 1: Psychiatric Studies,* edited by H. Read, M. Fordham and G. Adler. 1903. Reprint, Princeton, N.J.: Princeton University Press, 1970.

Pinel, P. *A Treatise on Insanity.* Translated by D. D. Davis. 1801. Reprint, Sheffield, England: W. Todd, 1806. .

Ray, I. *A Treatise On the Medical Jurisprudence of Insanity.* Boston: Charles C. Little and James Brown, 1838.

Rosenhan, D. L. "On Being Sane in Insane Places," *Science* 179 (1973): 250–258.

Spitzer, R. L. "More on Pseudoscience in Science and the Case for Psychiatric Diagnosis," *Archives of General Psychiatry* 33 (1976): 459–470.

Ferriar, John (1761–1815) Scottish physician who served at the Manchester Lunatic Asylum in England. He is remembered for his careful empirical observations and case histories of mental illness, provided in his 1792 book, *Medical Histories and Reflections.* He criticized BLEEDING and PURGING as treatments for mental illness and was one of the first to recommend isolation rather than mechanical restraints for violent patients. He is credited for introducing the term "hysterical conversion" into the psychiatric vocabulary.

Ferriar, J. *Medical Histories and Reflections.* London: 1792.

fertility The ability to reproduce children. Fertility rates for people diagnosed with the psychotic disorders have been determined on various populations in many countries over many decades. The low marriage rates for schizophrenic patients (particularly males) also contribute to low rates of marital fertility (the rate of children per marriage). When census data are

used, marital fertility rates for SCHIZOPHRENIA and for manic-depressive psychosis (BIPOLAR DISORDER) are lower than the norm for the population as a whole. On the whole, no studies have found evidence of any physiological dysfunction that might impair fertility in those people diagnosed with schizophrenia. Therefore the lower rates of fertility are probably due to the severe disruption in the ability to form and maintain social relationships with others.

Saugstad, L. F. "Social Class, Marriage, and Fertility in Schizophrenia," *Schizophrenia Bulletin* 15 (1989): 9–43.

fetal neural development and schizophrenia Brain abnormalities may develop early in the lives of people later diagnosed with SCHIZOPHRENIA and may already be in existence before the full onset of the disease occurs. In many areas of the brain that demonstrate structural abnormalities, particularly those involving the subcortical structures of the LIMBIC SYSTEM (e.g., the hippocampus and parahippocampal areas, amygdala, dorsolateral frontal cortex, and the globus pallidus), the damage is thought to arise during the development of the nervous system in the fetus during gestation. During fetal neural development, certain nerve cells (neurons) actually travel to specific spots (a process called neuronal migration) and form very specific connections with one another to create distinct structures in the brain (a process called the specification of cerebral cortical areas). In fact, some researchers have argued that there is a strong possibility that the development of schizophrenia later in life is related to a defect in genes controlling the migration and interconnection of these young neurons during fetal neural development.

A conference on fetal neural development and schizophrenia was held in Washington, D.C., from May 31 to June 1, 1988, and included many of the major researchers in schizophrenia and experts in brain imaging and neuropathology. A summary of the conference proceedings published in *Schizophrenia Bulletin* in 1989 listed the following findings as possible evidence that disturbances in the development of the nervous system of the fetus may be the source of the brain anomalies found in schizophrenia:

1. Recent neuropathological studies have found structural deviance that has been interpreted as evidence of fetal neural development, most likely in the second trimester.
2. Helsinki residents whose *second trimester* of gestation overlapped a particularly severe viral epidemic evidenced an increased rate of hospital diagnoses of schizophrenia. First or third trimester exposure was not associated with an elevation of rates of schizophrenia.
3. Two clinical studies have found that disturbances of gestation during the second trimester are linked to childhood and adult psychoses.
4. The extensive literature on the prenatal and perinatal experiences of schizophrenic patients contains evidence that schizophrenic patients have suffered considerably more prenatal and perinatal complications than controls. Indeed, some perinatal complications may actually be the result of a prenatal insult.
5. Minor physical anomalies are benign congenital abnormalities associated with the disruptions of fetal development. These external signs have been used as indices of otherwise cryptic fetal neural maldevelopment. Several investigators have reported that schizophrenic patients have a significantly elevated incidence of these anomalies.
6. Several investigators have found that the brains of schizophrenic patients are significantly reduced in volume. Such findings could reflect a failure in fetal neural development.

It is hoped that by studying the role of fetal neural development in schizophrenia the interaction of both genetic (neuronal migration and specification of areas) and environmental (viruses, birth complications) factors can be better understood.

At the dawn of the 21st century, the reigning scientific paradigm in schizophrenia research is the neurodevelopmental model. This theory was first articulated in 1986 by Daniel Weinberger of the NATIONAL INSTITUTE OF MENTAL HEALTH. Weinberger argued that the causes of schizophrenia begin in the womb, long before birth, and are not found in adolescence or adulthood, as many had previously thought.

The normal development of the human nervous system through early life, from embryo to fetus to infancy, childhood, adolescence, and adulthood, is still not well understood, however. Current textbooks in human embryology are filled mainly with references to embryological research on mice, chicks, zebrafish, and fruit flies—not human beings. Not only human embryology, but also developmental biology and developmental genetics are still very much in their infancy as scientific disciplines. There is so much that we do not know about normal processes that it is difficult to pinpoint the abnormalities in human fetal neural development that may be evidence of the disease process of schizophrenia. Hence, a severe limitation of Weinberger's neurodevelopmental model is that it still must refer to evidence from animal studies of fetal neural development to look for analogues to presumed causes of schizophrenia in human fetuses. Actual neuropathological evidence of schizophrenia from human fetal tissue does not yet exist.

See also NEURODEVELOPMENTAL MODEL OF SCHIZOPRENIA; PERINATAL FACTORS HYPOTHESIS.

Gilbert, S. F. *Developmental Biology.* 4th ed. Sunderland, Mass.: Sinauer Associates, 1994.

Langman, J. *Medical Embryology.* 4th ed. Baltimore: Williams & Wilking, 1989.

Larsen, W. J. *Human Embryology.* 2nd ed. New York: Churchill Livingstone, 1997.

Lyon, M., et al. "Fetal Neural Development and Schizophrenia," *Schizophrenia Bulletin* 15 (1989): 149–161.

Rakic, P. "Specification of Cerebral Cortical Areas," *Science* 241 (1988): 170–176.

Weinberger, D. R. "The Pathogenesis of Schizophrenia: A Neurodevelopmental Theory." In *The Neurology of Schizophrenia,* edited by H. A. Nasrallah and D. R. Weinberger. Amsterdam: Elsevier, 1986, pp. 397–406.

Feuchtersleben, Ernst von (1806–1849) Feuchtersleben was an influential Austrian physician whose primary contribution was the invention of many clinical terms still used today. For example, in 1845 Feuchtersleben coined the word *PSYCHOSIS* to refer to mental illness that was not due to identifiable diseases in the tissue of the nervous system. He proposed this term as a counterpart to *NEUROSIS,* already long in use to refer to a mental disorder that is due to the pathology of nervous tissue (unlike today's colloquial usage, which does not carry that emphasis on physiological causes of the disorder). Feuchtersleben also coined or popularized many other terms still in use today, most importantly *psychopathology, psychopathy,* and *psychiatrics.*

Feuchtersleben, E. v. *Lehrbuch der ärztlichen Seelenkunde.* Vienna: 1845.

fever therapy Throughout the centuries there have been many anecdotal reports of improvements in the mentally ill following physical illnesses that were accompanied by fever. For example, in the mid-1700s Malcolm Flemyng (?–1764), an English physician, made the observation that "intermittent fevers strengthen the nerves." In a chapter on "The Causes of the Disease" in his 1911 text *Dementia Praecox, Of the Group Of Schizophrenias,* Eugen BLEULER also notes, "yet we often see that mentally ill patients improve extensively after having had fever."

In 1887 Austrian neurologist and psychiatrist Julius Wagner von Jaureg (1857–1940) first proposed the idea that the introduction of fevers might be therapeutic for patients with certain mental illnesses, specifically those with the disorder known as the GENERAL PARALYSIS OF THE INSANE, which was later found conclusively to be the result of syphilis. His first experiments, in which he inoculated these "paretics" with malarial organisms, were conducted in 1917. He achieved significantly beneficial results with this malarial fever treatment, and in 1927 he won a Nobel Prize for this work.

"Malaria treatment" was first used in the United States on the patients at St. Elizabeth's Hospital in Washington, D.C., in 1922, at the initiative of its superintendent, William Alanson White, who ordered from Puerto Rico a supply of 12 mosquitoes contaminated with benign tertian malaria. Eleven of the mosquitoes died in transit, but the sole surviving insect was placed in a small cage and then strapped to the arm of a schizophrenic. After being bitten through the wire mesh of the cage, blood continued to be drawn from this

schizophrenic so as to infect 12 other syphilitics and induce the curative fevers in them. The first published report of this syphilotherapy appeared in 1924. Also in 1924, the then-29-year-old Walter FREEMAN, of later "PSYCHOSURGERY" fame, was made director of the research laboratories (bacteriology, psychology, pathology, and roentgenology) at St. Elizabeth's and subsequently continued this research. Prior to "malaria therapy," fevers were induced in patients with substances such as sterile milk and other proteins, with the intention of alleviating symptoms or producing a cure. The artificial production of fevers as a treatment for several mental illnesses was used in American institutions such as the New Jersey State Hospital at Trenton throughout the 1930s.

Lewis, N. D. C., et al. "Malaria Treatment of Paretic Neuro-syphilis," *American Journal of Psychiatry* 4 (1924): 175–188.

Finland See SCANDINAVIA.

fire and moxa treatment See CAUTERY TREATMENT.

first break The first clear onset of the schizophrenic illness in a person's life. It is an old term in the SCHIZOPHRENIA literature that is derived from the notion of a "first (nervous) breakdown." The term "first-break schizophrenics" is still used to designate those people who come to the attention of mental health professionals for the very first time with the clear psychotic symptoms of schizophrenia. "First-episode schizophrenics" is a current term for this.

first-degree relatives In the search for the genetic basis of MENTAL DISORDERS, it is assumed that the closer the relationship between an afflicted person and his blood relatives, the more likely these blood relatives will also manifest signs of the disorder. The parents, siblings (brothers and sisters), and children of an afflicted person are known as "first-degree relatives," whereas grandparents, cousins, aunts and uncles, and nieces and nephews are known as "second-degree relatives." In studies of the transmission of SCHIZOPHRENIA using the CONSANGUINITY METHOD, it has generally been concluded, since the first studies were completed in 1916, that the first-degree relatives of an afflicted person (the "index case") are nine times more likely than people in the general population to develop this disorder.

See also GENETICS STUDIES.

first-rank symptoms Due to the extremely complex nature of SCHIZOPHRENIA, many different systems using different criteria have been proposed for its diagnosis. Some systems are based on theory, whereas others are based primarily on phenomenology, i.e., the presence (or absence) of certain carefully described symptoms that are commonly observed in schizophrenic patients in clinical practice. This pragmatic approach to psychiatric diagnosis was characteristic of the "phenomenological school" of German psychiatry, which included such representatives as Jaspers, Mayer-Gross, Kleist, Leonhard, and, especially, Kurt Schneider. A phenomenological approach developed by Schneider in the 1939 book *Psychischer Befund und Psychiatrische Diagnose* (published in subsequent editions as *Klinische Psychopathologie*) purported to identify only those symptoms that he thought would discriminate schizophrenia from other forms of mental illness. The identified symptoms would be considered "pathognomonic" of schizophrenia.

Schneider identified 11 characteristic symptoms of schizophrenia, which he called "first-rank symptoms," the presence of any one of which would be sufficient for diagnosing a person with schizophrenia. The first three of Schneider's first-rank symptoms are forms of auditory hallucinations: (1) the patient hears voices speaking his or her thought out loud, (2) the patient experiences himself or herself as the subject about which the voices are discussing or arguing, and (3) the patient hears voices commenting on his or her actions as they are performed. The fourth symptom is a delusional percept, a two-stage process in which a patient's normal perception is followed by a highly personalized delusional interpretation of the perception.

The fifth through eleventh symptoms on Schneider's list are best characterized as serious defects in the experience of the normal boundaries that separate the self from the environment: (5) in somatic passivity, the patient experiences him- or herself as the passive and reluctant recipient of body sensations that are imposed from the outside (6) in thought withdrawal, the patient believes his thoughts are being taken out of his mind by some external force (7) in thought broadcast, the private thoughts in the mind of the patient are experienced as being magically transferred into the minds of others and (8) in thought insertion, the patients experience certain thoughts as being inserted into their head by others. First-rank symptoms, 9 through 11 consist of affect, impulses, and motor activity that are experienced as imposed and controlled from outside the patient's body.

Schneider's first-rank symptoms were adopted in Europe and in many other parts of the world as a primary method of diagnosing schizophrenia. The first-rank symptoms became familiar to American psychiatrists only in the 1970s, and although many of the individual symptoms are mentioned in *DSM-IV-TR* (2000), they have not achieved the prominence attributed to them in other parts of the world. Many research studies have been conducted that show that the first-rank symptoms are not pathognomonic of schizophrenia, that the mere presence of any one of the 11 is not sufficient for giving someone a diagnosis of schizophrenia. For example, AUDITORY HALLUCINATIONS can occur in other mental disorders, such as bipolar disorder or in depression with psychotic features. Furthermore, Schneider's first-rank symptoms seem to represent only the POSITIVE SYMPTOMS of schizophrenia (DELUSIONS and HALLUCINATIONS) and do not take into account the presence of NEGATIVE SYMPTOMS (FLAT AFFECT, poverty of speech, etc.) in some forms of schizophrenia.

See also AUDITORY HALLUCINATIONS; SUBJECTIVE EXPERIENCE IN SCHIZOPHRENIA.

Carpenter, W. T., J. S. Strauss, and S. Muleh. "Are There Pathognomonic Symptoms of Schizophrenia?," *Archives of General Psychiatry* 28 (1973): 847B–852.

Schneider, K. *Clinical Psychopathology.* Translated by M. W. Hamilton. New York: Grune & Stratton, 1959.

five-point restraints The label given to a technique of restraining violent patients in a psychiatric setting. It refers to the practice of tying a violent patient to a bed, usually with thick cotton cords. Each ankle is tied to a leg of the bed as the patient either lies or is restrained physically on the bed, and the wrists are tied to portions of the bed frame on either side of the patient's body. This technique is called FOUR-POINT RESTRAINTS. For particularly violent patients, a bed sheet or another restraint cord is wrapped across the chest and under the arms and tied under the bed to keep the patient restrained flat on his or her back.

See also MECHANICAL RESTRAINT.

fixing A technique recommended by some 18th- and early 19th-century physicians who worked with "lunatics" or "madmen" to subdue unmanageable patients by "fixing," "setting," or "catching the patients by the eye." Although it is unclear whether this practice was derived from the hypnotic induction techniques of practitioners of the "animal magnetism" of Franz Anton Mesmer (1734–1815), which was popular at the time, this willful gazing or staring into the eyes of patients in order to quiet them was recommended by English physician William Pargeter (1760–1810) in his 1792 book, *Observations on Maniacal Disorders.* However, this practice was ridiculed by John HASLAM in his 1798 manual, *Observations on Insanity.* Nonetheless, American physician Benjamin RUSH of Philadelphia's Pennsylvania Hospital recommended this practice as an effective "Remedie for Mania" in his 1812 textbook, *Medical Inquiries and Observations Upon the Diseases of the Mind.* After isolating the violent patient from his family and placing him in a private chamber in either "a public or private madhouse," Rush then gives physicians the following advice:

> This preliminary measure being taken, the first object of the physician, when he enters the cell, or chamber, of his deranged patient, should be to catch his EYE, and look him out of countenance. The dread of the eye was early imposed upon every beast of the field. The tyger, the mad bull, and the enraged dog, all fly from it: now a man deprived of

his reason partakes so much of the nature of those animals, that he is for the most part easily terrified, or composed, by the eye of a man who possesses his reason. I know this dominion of the eye over mad people is denied by Mr. Haslam, from his supposing that it consists simply in imparting to the eye a stern or ferocious look. This may sometimes be necessary; but a much greater effect is produced, by looking the patient out of countenance with a mild and steady eye, and varying its aspect from the highest degree of sternness, down to the mildest degree of benignity; for there are keys in the eye, if I may be allowed the expression, which should be suited to the state of the patient's mind, with the same exactness that musical tones should be suited to the depression of spirits in hypochondriasis. Mr. Haslam again asks, "Where is the man that would trust himself alone with a madman, with no other means of subduing him than by his eye?" This may be, and yet the efficacy of the eye as a calming remedy may not be called in question. It is but one of several other remedies that are proper to tranquilize him, and, when used alone, may not be sufficient to that purpose. Who will deny the efficacy of bleeding for the cure of madness? and yet who would rely upon it exclusively, without the aid of other remedies? In favour of the power of the eye, in conjunction with other means, in composing mad people, I can speak from the experience of many years. It has been witnessed by several hundred students of medicine in our hospital, and once by several of the managers of the hospital, in the case of a man recently brought into their room, and whose conduct for a considerable time resisted its efficacy.

The most famous case of a "cure" using the technique of "fixing" by a physician was the successful treatment of King George III of England for an attack of "MANIA" in 1788 by MAD-DOCTOR Francis Willis, who demonstrated his use of "the EYE" to a parliamentary committee inquiring into the physician's activities.

Rush, B. *Medical Inquiries and Observations upon the Diseases of the Mind.* Philadelphia: Kimber & Richardson, 1812.

Scull, A. "The Domestication of Madness," *Medical History* 27 (1983): 233–248.

flat affect One of the NEGATIVE SYMPTOMS of SCHIZOPHRENIA. In flat affect there is virtually no expression of affect, and in behavior this may mean that the person speaks in a monotone and that the face is relatively immobile and without expression. Although some contemporary critics of the use of ANTIPSYCHOTIC DRUGS point to such behavior as evidence that these substances reduce people suffering with schizophrenia to "zombies," in fact, such behavioral qualities have been described for more than a century, long before the widespread use of antipsychotic drugs in the 1950s.

flexibilitas cerea See CATATONIC WAXY FLEXIBILITY.

flight of ideas This term refers to the rapid, continuous flow of a person's speech in which there are quick jumps form topic to topic. These rapid shifts are usually based on common associations, plays on words, or are in response to events happening in the immediate environment. "Ideas" literally "fly" rapidly from the mouth of the person speaking, and this is a very characteristic symptom of someone experiencing a MANIC EPISODE. This can be a sign of BIPOLAR DISORDER, as well as a sign of ORGANIC MENTAL DISORDERS, SCHIZOPHRENIA, or acute reactive psychoses. Flight of ideas may also appear in nonpsychotic conditions, such as an acute reaction to stress.

See also LANGUAGE ABNORMALITIES IN SCHIZOPHRENIA.

flogging In the Middle Ages, a common practice in Europe (especially in German-speaking areas) was the ritual beating or "flogging" of wandering, mentally ill people before escorting them back to the towns from which they originated. At other times, public flogging (sometimes at a whipping post) was the prescribed treatment for the inappropriate behavior of the mentally ill. In his *Dialogue of Cumfort* of 1533, Sir Thomas More of England relates the story of an instance when he ordered the public flogging of "a lunatic" for disruptive behavior in church during the Mass. Apparently the mentally ill person in question would lift the skirts of praying

women just as the Host was elevated by the priest during the ceremony. More ordered his seizure and he was flogged until the lesson "was beaten home. For he could then very well rehearse his faults himself, and speak and treat very well, and promise to do afterward as well" (cited in Tuke).

Formally prescribed beatings were common even in institutions for the insane until the early 1800s. Although the practice had disappeared in English and French institutions by the 1820s, it was still a part of the treatment regime in German asylums. Reviewing primarily rare German-language texts from the 18th and early 19th centuries, Emil KRAEPELIN documents this form of "treatment" in his 1917 historical sketch, *Hundert Jahre Psychiatre (One Hundred Years of Psychiatry):*

> Rivaling chains in popularity was the lash. Müller (in 1700) related that in the Juliusspital attendants were generously provided with many restraining and punitive devices—chains, manacles, shackles, and efficient, leather-encased bullwhips. They made ample use of these instruments whenever a patient complained, littered his quarters, or became recalcitrant or abusive. "Thrashing was almost part of the daily routine," he concluded. Lichtenberg explained that thrashings were often better for lunatics than anything else, and that they helped them to adjust to the harsh realities of daily life. Even Reil, the enthusiastic champion of mental care for the insane, noted that the straight jacket, confinement, hunger, and a few lashes with the bullwhip would readily bring patients into line. Frank was also of the opinion that a "light blow" was "effective in dealing with malicious or unreasonable patients." Autenreith found that women who persisted in going around naked quickly dressed in response to a few applications of the lash. . . .

See also ABUSE OF PSYCHIATRIC PATIENTS.

Kraepelin, E. *One Hundred Years of Psychiatry.* Translated by W. Baskin. 1917. Reprint, New York: Philosophical Library, 1962.

Marx, O. "Descriptions of Psychiatric Care in Some Hospitals during the First Half of the 19th Century," *Bulletin of the History of Medicine* (1967): 208–214.

Tuke, D. H. *Chapters in the History of the Insane in the British Isles.* London: Kegan, Paul, Trench, 1882.

fluphenazine See ANTIPSYCHOTIC DRUGS.

focal infection as cause of psychotic disorders A disputed autointoxication theory of the cause of mental illness that has not been seriously considered since the 1930s. The short-lived "focal infection" theory of American psychiatrist Henry A. COTTON (1876–1933), which he first formulated and investigated in 1916, held that the "functional psychoses" were due to chronic infections in specific areas of the body that nonetheless had an effect on the entire physiological system. It was proposed by Cotton that the weakest infections would result only in "psychoneuroses" in people, but the stronger the infection the more severe the disorder it produced, with DEMENTIA PRAECOX (SCHIZOPHRENIA) apparently the result of the most severe systemic focal infections. These infected areas may not appear to be infected nor give the patient any unusual distress, but they were verified as being infected through laboratory tests. The primary areas of focal infection were thought to be the teeth and tonsils. From these areas infections then spread (by constantly swallowing the bacteria originating in the mouth) to the stomach and lower intestinal tract (including the duodenum, small intestine, gall bladder, appendix, and colon) and the genitourinary tract. In mentally ill women, Cotton claimed in 1922, the cervix was infected in about 80 percent of the cases—even in virgins.

From 1916 to 1918 Cotton investigated the suspected foci of infection on the patients of the New Jersey State Hospital at Trenton, where he was the superintendent. By July 1918 Cotton decided to take his bizarre theory one step further and actually devised a surgical procedure of treatment based on the theory that this would cure PSYCHOSIS. In an October 1922 article that summarizes his work, Cotton explained his rationale with the following claim: "For the general practitioner can, not only arrest many cases after a psychosis has developed, but, better still, by eliminating the foci of infection can

easily prevent the occurrence of a psychosis." Thus, between 1918 and 1922, Cotton and medical and surgical colleagues from other disciplines performed "detoxication" surgery on some 1,400 patients, removing teeth, tonsils, colons, parts of the stomach and intestines, and glandular tissue form the cervix. In 38 women, full hysterectomies were performed, and some patients—both male and female—also lost their thyroid glands. Cotton claimed that, because of this "detoxication" surgery, the recovery rate from psychosis from 1918 to 1922 jumped to 80 percent of all cases, up from an average of 37 percent for the 10-year period prior to 1918.

Even in Cotton's time, this theory and his surgical techniques for "arresting" psychosis were considered bizarre by many of his contemporaries. In a publication of the remarks of other prominent psychiatrists following Cotton's research summary article in the *American Journal of Psychiatry* in 1922, one critic made the following remarks to Cotton:

> Now, to my mind a colostomy or a colectomy is a somewhat serious operation. Mr. Cotton speaks of them in a way that would almost lead one to think the operation as simple and as devoid of danger as the extraction of a tooth . . . we find ourselves told by the friends of patients, people who have heard of these activities and this theory, not through medical publications, seldom through their family physicians, but through lay journals and the daily press, that something is being done at Trenton by Dr. Cotton and his associates which the rest of us are not doing, and they are demanding that we shall adopt these theories and follow the methods pursued at Trenton.
>
> We should study this matter so carefully and so thoroughly, not being carried away by the enthusiasm of Dr. Cotton. . . . Shall we have our daughter's uterine cervix enucleated, or the tonsils cut out, or the colon removed in whole or part, or my son's teeth extracted with a hope of recovery from dementia praecox or some other bad mental state(?) . . .

The support of the popular media, however, was not enough to keep Cotton in good scientific standing. A carefully designed study to test Cotton's theory was conducted in 120 patients at the New York State Psychiatric Institute on Ward's Island in New York City by the medical director (George Kirby) and a bacteriologist (Nicholas Kopeloff). They found that the removal of focal infections in 58 of the cases did not result in a higher improvement rate than that of the other 62. Surgical work was done on infected teeth, tonsils, sinuses, and genitals, but not on the intestinal tract. Furthermore, the study strongly criticized as "unsatisfactory" from a scientific point of view Cotton's methods for establishing focal infection. Thus, the study conclusively rejected Cotton's claim that focal infection is the cause of functional psychoses.

Until his death in 1933, hundreds of patients died from such operations performed by Cotton and his staff at Trenton.

Cotton, H. A. "The Etiology and Treatment of the So-called Functional Psychoses. Summary of Results Based on the Experience of Four Years," *American Journal of Psychiatry* 2 (1922): 157–210.

Kopeloff, N., and G. H. Kirby. "Focal Infection and Mental Disease," *American Journal of Psychiatry,* 3 (1923): 149–199.

Scull, A. *Madhouse: A Tragic Tale of Megalomania and Modern Medicine.* New Haven, Conn.: Yale University Press, 2005.

folie à deux Literally a "psychosis of two." Folie à deux is a MENTAL DISORDER afflicting at least two closely related persons in which identical delusions and sometimes psychotic behavior are shared and, indeed, strongly supported by each of the partners. Although this disorder is most commonly found in relationships between two people, case histories have been published that show that it can afflict as many as 12 persons in a family (*folie à famille*). In *DSM-IV-TR* (2000), the diagnosis of shared psychotic disorder was given to those people who were initially not psychotic, but in whom a delusion or delusions develop as the result of a close relationship with another person who already had the delusion prior to the relationship. The many case histories that have been recorded indicate that the "primary case" individual may have a higher IQ or some other elevated social status when compared to the person or persons in whom the psychosis is induced.

Because this disorder occurs in the context of close and longlasting relationships, folie à deux seems to follow a chronic course that can be eliminated only partially by treatment.

French alienists Ernest-Charles Lasègue (1816–83) and Jules-Philippe-Joseph FALRET (1824–1902) first described and named this disorder in a famous paper published in 1877 (translated into English and published in 1964) in which they provide seven case history examples of folie à deux. Prior to this time and as early as 1838, similar disorders had been called "infectiousness of insanity" (Ideler) or "psychic infection" (Hoffbauer), but the conditions under which they occurred were not described. Lasègue and Falret describe these conditions that lead to the "contagion on insanity" in the following way:

> In "folie à deux," one individual is the active element; being more intelligent than the other he creates the delusion and gradually imposes it upon the second or passive one; little by little the latter resists the pressure of his associate, continuously reacting to correct, modify, and coordinate the delusional material. The delusion soon becomes their common cause to be repeated to all in almost identical fashion.

Other names given to folie à deux after the time of Lasègue and Falret have been as follows: "contagious insanity" (Seguin); "reciprocal insanity" (Parsons); "psychosis of association" (Gralnick); "induced insanity" (Lehman, 1883); "insanity by contagion" (Carrier); "double insanity" (Tuke); "collective insanity" (Ireland); "conjugal insanity" (Rhein); "influenced psychosis" (Gordon); "mystic paranoia" (Pike). *DSM-III* (1980) referred to this syndrome as shared paranoid disorder. *DSM-IV-TR* (2000) refers to it as "shared psychotic disorder," and (*ICD-10* (1992) refers to it as "induced delusional disorder."

At least four different subtypes of folie à deux have been suggested over the years:

1. *Folie imposée,* in which the psychotic delusions of the psychotic "primary case" are induced in a mentally healthy person and disappear in the healthy person after the individuals are separated.
2. *Folie simultanée,* in which two related persons who are morbidly predisposed in some way simultaneously develop a paranoid and depressive psychosis.
3. *Folie communiquée,* in which the delusional ideas are induced in a second person, after that person had initially resisted them for a long period of time, and are maintained in the second person even when the related persons are separated.
4. *Folie induite,* in which a relationship between two psychotic persons results in the weaker person's adoption of new delusions that initially belonged only to the stronger one—a commonly observed phenomenon in many psychiatric hospitals even today.

When a group of people (such as a family) succumbs to the delusional beliefs of a stronger personality within the group, this has been termed *folie à plusieurs* or *folie partagée* ("shared madness"). The famous "Manson family" case of the late 1960s would be a good example of this phenomenon.

Dewhurst, K., and J. Todd. "The Psychosis of Association—Folie à Deux," *Journal of Nervous and Mental Disease* 124 (1956): 451.

Enoch, M. D., and W. H. Trethowan. *Uncommon Psychiatric Disorders.* 2nd ed. Bristol, U.K.: John Wright & Sons, 1979.

Lasègue, C., and J. Falret. "La folie à deux (ou folie communiquée)," *Annales Medico-psychologique* 18 (1877): 321. English translation by R. Michaud in *American Journal of Psychiatry* 121, Suppl. (1964).

folie à double forme This is the very first name given by BAILLARGER in 1854 to the MENTAL DISORDER we know as manic-depressive PSYCHOSIS.

See also BIPOLAR DISORDER.

folie à famille See FOLIE À DEUX.

folie circulaire The name given to manic-depressive psychosis by FALRET in 1854—but two weeks after BAILLARGER's publication of a description of this syndrome. Although the two

famous French ALIENISTS argued over who was first in describing this disorder, Falret's term was more widely used in the English psychiatric literature of the late 1800s, and as a result, people whom we would now call "manic-depressives" were referred to as "circulars" until the early 1900s.

See also BIPOLAR DISORDER.

food allergies as a cause of psychosis With the rise in interest in the effects of nutrition on the mind and the emotions in the 1960s, many have suggested that even such serious mental disorders as SCHIZOPHRENIA and BIPOLAR DISORDER may be due to imbalances in nutrition. In particular, a commonly discussed theory is that these psychotic disorders may be due to the effects of allergic reactions to certain substances in various foods. Since the list of possible allergens in food is gigantic, it has been difficult to support this hypothesis in controlled research studies, although many researchers who hold to the principles of "orthomolecular psychiatry" have continued the search. Most adequately controlled studies have not been able to find evidence of antibodies in the bodies of schizophrenics that would support the notion that the physical system was fighting a substance that it was allergic to. However, it is probable that nutrition does, in some way, contribute either to the development of some psychotic disorders or at least affects the course of the disease.

See also MEGAVITAMIN THERAPY; TRANSMETHYLATION HYPOTHESIS.

Kinnell, H. G., et al. "Food Antibodies in Schizophrenia," *Psychological Medicine* 12 (1982): 85–89.

formal thought disorder A central characteristic of many psychotic disorders, and SCHIZOPHRENIA in particular, in which the form of thought processes is disturbed. This is distinguished from disturbances in the content of thought (such as BIZARRE IDEATION). Formal thought disorder may include such commonly observed phenomena in the psychotic disorders as LOOSENING OF ASSOCIATION, INCOHERENCE, BLOCKING, CLANGING, ECHOLALIA, NEOLOGISMS, PERSEVERATION, and POVERTY OF CONTENT OF SPEECH.

formication This is the term for a tactile HALLUCINATION (a hallucination of touch) in which a person believes insects or other living creatures are crawling around under the person's skin. Although it is rare among the psychotic disorders, it can be more commonly found in people who may exhibit signs of an ORGANIC PSYCHOSIS induced by substance abuse, particularly cocaine intoxication, or may be a part of delirium tremens in alcoholism. In Europe, formication may be one of the defining symptoms of a delusional syndrome known as the MONOSYMPTOMATIC HYPOCHONDRIACAL PSYCHOSIS.

Four A's, the A useful mnemonic term invented by later generations of scholars to refer to the four FUNDAMENTAL SYMPTOMS OF SCHIZOPHRENIA proposed by Eugen BLEULER in 1911. The "Four A's" are AUTISM, AFFECTIVE DISTURBANCES, ASSOCIATION DISTURBANCES, and AMBIVALENCE.

four-point restraints See FIVE-POINT RESTRAINTS.

Franklin, Benjamin (1706–1790) Early American statesman and scientist. He founded the Pennsylvania Hospital in Philadelphia in 1752, the first hospital in the United States and the place where Benjamin RUSH served (starting in 1785) and made his observations of the mentally ill (who had been allowed admission since the hospital first opened its doors). The original buildings are still used today, at their location on Pine Street in Philadelphia. Franklin and Rush were political as well as scientific contemporaries, and Franklin's signature can be seen just below Rush's on the Declaration of Independence. Franklin's experiments in electricity led to the development of treatments by physicians that consisted of passing weak electrical currents into patients to cure a variety of ills—including mental illness. Franklin was chosen by King Louis XVI of France to chair the famous royal commission to investigate "animal magnetism" in March 1784. The eight other members included the distinguished scientist Lavoisier and Guillotin, the inventor of the famous device of execution used extensively during the Reign of Terror following

the French Revolution. The committee essentially debunked Franz Anton Mesmer's claims about the special "fluids" that were supposedly transferred from the operator to the patient and that supposedly caused the sometimes wondrous manifestations. In its report, the committee did not deny that healing and curing was effected by the use of animal magnetism, but asserted that the mechanism at work was simply "imagination."

See also ELECTROSHOCK THERAPY.

Laurence, J.-R., and C. Perry. *Hypnosis, Will and Memory: A Psycho-Legal History.* New York: Guilford, 1988.

McConnkey, K. M., and C. Perry. "Benjamin Franklin and Mesmerism," *International Journal of Clinical and Experimental Hypnosis* 33 (1985): 122–130.

Freeman, Walter (1895–1972) The "father of lobotomy." Freeman was born into a prominent Philadelphia medical family and studied neurology in Philadelphia and in Europe. Upon the recommendation of former mentors, in 1924, at the age of 29, Freeman was hired by William Alanson White to direct the research laboratories of St. Elizabeth's Hospital in Washington, D.C. His influential contact in Europe with Wagner-Jauregg, who invented the "malaria treatment" for syphilis, led to Freeman's continuation of this FEVER THERAPY work at St. Elizabeth's in the 1920s. He remained at St. Elizabeth's until 1933, when he required recuperation for a "nervous breakdown" caused by overwork and the ingestion of the barbiturate Nembutal, which he had taken every night for many years. At a neurological conference in London in August 1935, Freeman met António EGAS MONIZ, a Portuguese neurosurgeon who had been conducting PSYCHOSURGERY experiments with animals. Egas Moniz excited Freeman with his theories about behavior change through psychosurgery; after returning to Portugal, Egas Moniz performed the first psychosurgery on a human subject (a chronic, severely depressed female patient from a local mental hospital) on November 15, 1935. Egas Moniz published his classic book on the subject in the spring of 1936 and sent a copy to Freeman.

Freeman and his colleague James Watts studied Egas Moniz's book; after procuring the "Moniz leucotome"—the surgical instrument designed by Egas Moniz for psychosurgery—they practiced these techniques on the brains of cadavers. Finally, on September 14, 1936, Freeman and Watts performed the first American leucotomy (psychosurgery on the white fibers that connect the frontal lobe to the rest of the brain) on a 63-year-old woman who had been admitted to George Washington University Hospital in Washington, D.C., with "agitated depression." In November 1936, Freeman used the term *lobotomy* for the first time to describe these operations instead of Egas Moniz's term, *leucotomy.* Lobotomy simply referred to the severing of the nerve fibers of a lobe of the brain. However, Freeman streamlined psychosurgery with the invention of the technique of transorbital lobotomies, in which a gold-plated icepick was inserted directly into the frontal lobes of the brain through the corner of each eye socket (the orbit of the eye) rather than drilling through the skull, as was Egas Moniz's technique. This allowed for the "assembly-line" approach to psychosurgery that enabled the procedure to be performed quickly and with a minimum of preparation on large numbers of patients. In January 1946, Freeman performed the first transorbital lobotomies, assembly-line-style "icepick surgery," on 10 patients in his consulting office. Since the "leucotome" was too fragile for such a procedure, on this historic occasion Freeman used an ordinary icepick found in his kitchen drawer at home.

Based on their lobotomies of 80 patients, Freeman and Watts published their famous textbook, *Psychosurgery,* in 1942, and became world-renowned. Although later discontinued as a dangerous and inhumane technique, it is estimated that, due to the influence of Freeman and Watts, as many as 30,000 lobotomies were performed in the United States in the 1940s and the 1950s. Freeman had high hopes for psychosurgery as a treatment for the psychotic disorders, in particular, schizophrenia. In the preface to the 1950 second edition of *Psychosurgery,* Freeman and Watts argue, "Even more important from the strictly psychiatric point of view is the recognition that some chronically disturbed schizophrenic patients may become completely restored to effective citizenship." On a personal mission to make state hospitals obso-

lete with psychosurgery, Freeman made dozens of road trips to a dozen or more states in the early 1950s and performed rapid transorbital lobotomies on thousands of mental patients in V.A. and state hospitals. Freeman informally dubbed his missionary travels "Operation Icepick." Many patients still exist in psychiatric hospitals today who were subjected to surgery, their condition either unchanged or worse.

When the U.S. Food and Drug Administration approved the use of CHLORPROMAZINE in March 1954, PSYCHOSURGERY and the chemical CONVULSIVE THERAPIES gradually fell into disuse. Treatment with antipsychotic drugs began to be viewed as the most humane treatment for the psychotic disorders, and there was a public and scientific backlash directed at Freeman and his psychosurgery work. Freeman moved from Washington to California in 1954 and never again performed lobotomies on such a grand scale. He performed his last lobotomy on a previously lobotomized woman at Herrick Memorial Hospital in Berkley, California, in February 1967, when he was 72. Freeman died of cancer in May 1972.

See also COLUMBIA-GREYSTONE PROJECT.

Egas Moniz, A. *Tentatives Opératoires dans le Traitement de Certaines Psychoses.* Paris: Masson, 1936.

Freeman, W., and J. Watts. *Psychosurgery.* 1942. Reprint, Springfield, Ill.: Charles C. Thomas, 1950.

Shutts, D. *Lobotomy: Resort to the Knife.* New York: Van Nostrand Reinhold, 1982.

Fregoli's syndrome One of the delusional MISIDENTIFICATION SYNDROMES of the psychotic disorders (along with the CAPGRAS SYNDROME and the INTERMETAMORPHOSIS SYNDROME. In this delusion, a familiar person, who is seen as a persecutor, exists in the bodies of various others in the immediate environment, who are unknown to the delusional person. The afflicted person recognizes that physical differences exist between the body of the persecutor and the bodies of the people in which the persecutor is thought to exist. This distinguishes Fregoli's syndrome from Capgras syndrome, in which the physical body of the "impostor" is transformed to match the delusion as well. This syndrome was first reported by French psychiatrists Courbon and Fail in 1927, in the case of a woman who felt that a famous actor of that time, Fregoli, was making himself known to her by occupying the bodies of various persons in her environment. The actor Fregoli was known for his effectiveness at changing facial expression on stage and was in this regard similar to the famous American silent screen actor Lon Chaney—"The Man of a Thousand Faces." Cases of Fregoli's syndrome are extremely rare and may involve an organic component.

Courbon, P., and G. Fail. "Syndrome d'illusion de Fregoli et schizophrénie," *Bull. Soc. Clin. Med. Ment.* 15 (1927): 121.

Christodoulou, G. N. "Delusional Hyper-identification of the Fregoli-type: Organic Pathogenic Contributors," *Acta Psychiatrica Scandanavica* 54 (1977): 305.

Freud, Sigmund (1856–1939) An Austrian-Jewish neurologist and the creator of PSYCHOANALYSIS, the famous "talking cure," which had a profound influence on the treatment of mental illness in the 20th century. Today's various psychotherapies all owe a major debt to Freud and psychoanalysis for demonstrating that certain MENTAL DISORDERS can be treated or even cured through the use of psychotherapeutic techniques that were not physical (such as drugs or baths). Although the bulk of Freud's clinical experience was not with patients suffering from severe psychotic disorders (unlike that of his one-time disciple, C. G. JUNG), Freud proposed and revised several theories about psychosis during the course of his lifetime.

Due largely to the influence of the German psychiatric literature in the latter half of the 19th century, by Freud's time the terms *neurosis* and *psychosis* had become mutually exclusive categories, and Freud's earliest writings reflect this distinction. As early as 1894, in a letter to his mentor Wilhelm Fliess ("Draft H," dated January 24), Freud speaks of the psychoses as being composed of "hallucinatory confusion," "paranoia," and "hysterical psychosis." From the earliest, Freud considered the psychoses as disruptions in the way in which a person relates to the outside world. Since Freud determined that many of the psychological and psychosomatic symptoms found in his neurotic

consulting-room patients were due to an inner "defensive" conflict between the drive to express sexuality and the efforts to "repress" these feelings and ideas, in his earliest work he mentions "defense psychoses" that are likewise the result of a defensive conflict against sexuality. In other words, people with psychotic disorders defended against their sexual drives by "projecting" the source of their problems on the outside world (e.g., "hallucinations" are internal images or thoughts experienced as "external"; paranoid delusions are the projection of internal strife on the outside world). In fact, their problems are internal in origin. Psychotic people thus withdraw from the external social world because it is mistakenly perceived as a threat.

Between 1911 and 1914, Freud developed his first detailed model of the mind ("the psychical apparatus"). His interpretation of the case history of the paranoid psychosis of Schreber, and his famous 1914 essay "On Narcissism," both led to an interpretation of psychosis as a withdrawal of libido (the energy of the sexual instinct) from its normal attachment to objects and people of the external world (object-love) and a return to an infantile attachment on the self ("infantile auto-eroticism"). This withdrawal of energy to an infantile state was a process of "regression" to a state of "primary narcissism." In practical terms, this means that Freud thought that psychotics "regressed" to an egocentric mental state akin to that experienced by preverbal infants, as evidenced by the loss of connection to the "real world" ("abandonment of object-love") that is observed in people with psychotic disorders. After this withdrawal of libido, there is an ineffective attempt to reestablish a connection with the "object world" of external reality, but this is instead done with the projection of delusions and hallucinations, which take the place of reality. Psychotic symptoms were thus seen by Freud as a defense, a way of shutting out the demands of the external world.

In the early 1920s, Freud developed his second theory of the psychical apparatus—the famous structural theory of the interplay of the ego, id, and superego in psychic life. While convalescing from the first of many major surgical operations for cancer during the last 16 years of his life, Freud wrote a short paper in 1923 on "Neurosis and Psychosis," which described how these two clinical classes of disorders could be caused by specific disturbed relationships among the three parts of the human mind. In this paper, Freud distinguishes among "transference neuroses" (the type of distorted relationship that arises in a patient in psychoanalysis in which the patient transfers to the analyst infantile thoughts and feelings that were originally "projected" onto the parents), "narcissistic neuroses" and the "psychoses" based on the following formulas: "Transference neuroses correspond to a conflict between the ego and the id; narcissistic neuroses, to a conflict between the ego and the superego; and psychoses, to one between the ego and the external world." Furthermore, in psychosis, the ego was thought to be in the service of the id, and the main defense mechanism it employed was denial or disavowal.

Even after Freud was forced by the Nazis into exile in England from his native Vienna in June 1938, he continued to write about the psychoanalytic theory of psychosis. In his very last major piece of writing, the unfinished book, *An Outline of Psycho-Analysis* (1940), Freud explained that "the precipitating cause of the outbreak of a psychosis is either that reality has become intolerably painful or that the instincts have become extraordinarily intensified." Yet, as is commonly observed in people afflicted with the psychotic disorders, no one is ever completely out of touch with reality when in a psychotic state, and there are "healthy" parts of the mind that are always intact. Freud graphically describes this phenomenon in the following passage from the same paragraph of the *Outline:*

> The problem of psychoses would be simple and perspicuous if the ego's detachment from reality could be carried through completely. But that seems to happen only rarely or perhaps never. Even in a state so far removed from the reality of the external world as one of hallucinatory confusion, one learns from patients after their recovery that at the time in some corner of their mind (as they put it) there was a normal person hidden, who, like a detached spectator, watched the hubbub of illness go past him.

Although true psychotics were generally considered "unanalyzable," Freud's psychoanalysis was used by some of his later followers to treat dementia praecox (schizophrenia). Notable analysts include Abraham, Federn, Sullivan, FROMM-REICHMANN, Searles, and John Rosen, who developed a hybrid treatment ("direct analysis") that he used with institutionalized patients. Although claims of success abound in this literature, with our present knowledge of the course of SCHIZOPHRENIA and the strong biological basis for the disease process, there is much skepticism of claims of lasting therapeutic success using this modality of treatment. Indeed, by 1980 the use of psychoanalysis for the treatment of the psychotic disorders had virtually disappeared in practice.

Freud, S. "The Loss of Reality in Neurosis and Psychosis," *Standard Edition,* 19 (1924): 183–190.

———. "Neurosis and Psychosis," *Standard Edition,* 19 (1924): pp. 149–154.

———. "On Narcissism: An Introduction," *Standard Edition,* 14 (1914): 67–104.

———. "An Outline of Psycho-Analysis," *Standard Edition,* Vol. 23. 1940. pp. 139–208.

———. "Psychoanalytic Notes on an Autobiographical Account of a Case Paranoia (Dementia Paranoides)," *Standard Edition,* 12 (1911): pp. 3–82.

———. *Standard Edition of the Complete Works of Sigmund Freud.* Edited by James Strachey and Anna Freud. 24 vols. London: The Hogarth Press and the Institute of Psychoanalysis, 1953–1974.

Fromm-Reichmann, Frieda (1890–1957) A German psychoanalyst and a student of Harry Stack Sullivan at the Chestnut Lodge sanitarium in Rockville, Maryland. Sullivan was another psychoanalyst known for his psychotherapeutic efforts with schizophrenics, and he worked with Fromm-Reichmann after her exile from Nazi Germany in 1934. Fromm-Reichmann developed her own style of treatment, which she called "psychoanalytically-oriented psychotherapy," which indicated that she was departing from the classical Freudian psychoanalytic procedure in her treatment of schizophrenia. Many of her essays on her treatment of SCHIZOPHRENIA (written from 1939 onward) are attempts to describe the inner experiences of the patient and the therapist working with such traditionally "difficult" patients. She described the "loneliness" of the schizophrenic patient and contradicted traditional psychoanalytic notions that the person suffering from schizophrenia gladly seeks out his or her withdrawal from interpersonal relationships. Fromm-Reichmann instead argued that the schizophrenic is eager to reestablish relationships with others but is prevented by a profound sense of mistrust that originates from the earliest relationships with the mother. Fromm-Reichmann was the first to use the term *SCHIZOPHRENOGENIC MOTHER* to identify the mother's role in causing the disorder, but it was only popularized through its later use by psychoanalyst Trude Tietze, in 1949.

It is believed that Fromm-Reichmann unintentionally caused pain in thousands of patients and their families in the 1950s and 1960s by using her considerable authority in psychoanalytic circles to legitimize the idea that the mother of someone with schizophrenia was to blame for the illness. Like FREUD and almost every other psychoanalyst, she sincerely believed that the cause of schizophrenia was to be found in a disturbed early childhood relationship with one's mother. Psychoanalysts like Fromm-Reichmann vigorously denied that schizophrenia could have a physical cause, and they denied the role of HEREDITY or genetics even though the scientific evidence had been accumulating for that fact since at least 1916. Psychoanalysts held experimental, quantitative, medical, and biological research in contempt, believing blindly in a dubious pseudoscience (psychoanalysis) created by a neurologist (Freud) who ignored the work of KRAEPELIN and others on the physical causes of mental disorders. For many mothers in the 1950s and 1960s, this unscientific "medical finding" by a highly psychoanalytic psychiatric establishment proved to be a disaster, as Edward Dolnick illustrates in his book on this black chapter in medical history, *Madness on the Couch.*

Dolnick, Edward. *Madness on the Couch: Blaming the Victim in the Heyday of Psychoanalysis.* New York: Simon & Schuster, 1998.

Fromm-Reichmann, F. *Psychoanalysis and Psychotherapy: Selected Papers.* Edited by D. M. Bullard. Chicago: University of Chicago Press, 1959.

functional psychoses This is a term popular since about 1915 to denote the group of psychotic disorders that do not have a known organic cause (ETIOLOGY). Four primary groups of psychotic disorders have been considered "functional." DEMENTIA PRAECOX and manic-depressive psychosis have long been described as the two main functional psychoses, although the acute recoverable psychoses and chronic paranoid psychoses have also been traditionally regarded as functional psychoses. The term *functional* is also used to point out the importance of psychological or environmental factors in the development of these psychoses. Functional psychoses are distinguished from the "organic psychoses," which are psychotic disorders caused by known organic disease processes in the brain (e.g., the dementias).

Perhaps the earliest use of the term *functional psychosis* is found in a psychiatric textbook by German psychiatrist Emanuel Ernst Mendel (1839–1907) in 1907:

> . . . there is a great difference of opinion amongst authors as to how to divide those mental diseases in which no anatomical findings have hitherto been met and which do not belong under any of the forms named. They are designated as functional psychoses, by which it is not said that anatomical changes do not exist, but only that we have so far been unable to verify them.

The term has not been used as frequently in the past decade or so, since the prevailing viewpoint is that both schizophrenia and BIPOLAR DISORDER are essentially organic (e.g., genetic, biochemical) in origin. Thus, the dichotomy between "functional" and "organic" psychotic disorders is beginning to disappear.

Mendel, E. *Textbook of Psychiatry.* Translated by W. C. Krauss. Philadelphia: F. A. Davis, 1907.

fundamental states of manic-depressive insanity When elaborating his description of manic-depressive insanity (a term he originated), Emil KRAEPELIN noted that "manic-depressives" suffered only from a "periodical insanity" and thus were not psychotic all the time. This was a major difference that separated manic-depressive insanity from DEMENTIA PRAECOX, the other "functional psychosis" identified and named by him. However, Kraepelin noticed that manic-depressives seemed to fall into four main categories of personality types, or temperament, when they were in the "free intervals between the attacks" or if the full development of the disease had not yet occurred. These four manic-depressive "fundamental states" are as follows: (1) the "depressive temperament," which is characterized by a "permanent gloomy emotional stress in all the experiences of life", (2) "manic temperament," the opposite of the depressive temperament, which Kraepelin also refers to as "constitutional excitement", (3) the "irritable temperament," which is a mixture of the manic and depressed fundamental states in which these people exhibit a chronic hypersensitivity and irritability, and (4) the "cyclothymic temperament," which is characterized by the "frequent, more or less regular fluctuations of the psychic state to the manic or to the depressive side."

By identifying these fundamental temperaments, Kraepelin was supporting the contemporary idea that mental disorders may be grouped into categories that are actually spectrum disorders, i.e., that similarities can be found in the symptoms between certain psychotic disorders and less serious personality disorders, which may suggest that they are points on a spectrum of psychopathology. Bipolar disorder, for example, may share the same underlying disease process as BORDERLINE PERSONALITY DISORDER, and schizophrenia may likewise be a variant of SCHIZOTYPAL PERSONALITY DISORDER and SCHIZOPHRENIFORM DISORDER.

See also MANIC-DEPRESSIVE ILLNESS.

Kraepelin, E. *Manic-Depressive Insanity and Paranoia.* Translated by R. M. Barclay and edited by G. M. Robertson. Edinburgh: E. & S. Livingstone, 1921.

fundamental symptoms of schizophrenia When Eugen BLEULER coined the term *SCHIZOPHRENIA* and described this group of disorders in his famous 1911 textbook, he described them as being com-

prised of a group of "fundamental symptoms" that were "permanent," "specific," and "characteristic" of schizophrenia and not of any other mental disorder. Therefore, the fundamental symptoms are said to be pathognomonic of schizophrenia, according to Bleuler. These are in contrast to the ACCESSORY SYMPTOMS of schizophrenia (e.g., hallucinations and delusions), which may be found in other mental disorders as well. A shorthand label for these fundamental symptoms is THE FOUR A'S, namely, AUTISM, AMBIVALENCE, AFFECTIVE DISTURBANCES, and ASSOCIATION DISTURBANCES.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenias,* trans. J. Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

fury (or furor) An excited state of uncontrollable violence and anger that has, since ancient times, been associated with the mental disorder of MANIA. Under Roman law, the Latin word *furor* referred to the mental disorder in which people (the *furiosi*) became manic and violent but were not legally responsible for their actions. The second major category of insanity in ancient Rome comprised those people who were mentally handicapped in a cognitive sense, such as the mentally retarded or, it is assumed, those others who experienced psychotic disorders that led to intellectual degeneration (the *mente capti*). They, too, were not responsible for their criminal acts. For almost 2,000 years "furor" or "fury" has been mentioned by authorities on mental illness as either a separate syndrome of its own or as a synonym for mania. In his 1801 textbook *A Treatise on Insanity,* Philippe PINEL confesses that patients of this type are extremely difficult to treat. He writes:

> I have found maniacal fury without delirium, which in France is called folie raisonnante, whether continued, periodical, or subject to irregular returns and independent of the influence of the seasons, the variety of the disorder most unyielding to the action of remedies. A madman of this description condemned himself to the most absolute confinement for eight years. During the whole of that time he was extremely agitated. He cried, threatened, and, whenever his arms were at liberty, broke to pieces whatever came in his way, without manifesting any error of the imagination, or any lesion of the faculties of perception, judgment and reasoning. Other madmen, subject to periodical accessions of extreme violence, are frequently sensible of the impending paroxysm, give warning of the necessity of their immediate confinement, announce the decline and termination of their effervescent fury, and retain during their lucid intervals the recollection of their extravagances.

As for the treatment of fury, Pinel recommends the following: "Opium, camphire (camphor) in large doses, sudden emersion in cold water, blisters, the moxa, and copious bleedings." However, almost four decades later (in 1838), Pinel's famous pupil, the French alienist J. E. D. ESQUIROL, devotes an entire chapter to "Fury" in his book *Mental Maladies,* primarily to put forth the idea that fury is a symptom, not a separate disorder, and that it may be found in many mental illnesses besides mania. "Fury . . . does not require special treatment," Esquirol writes, further arguing:

> It is because fury has been taken for insanity itself . . . that so many grave errors have been committed in the treatment of the furiously insane. They were bled to excess, with the intention of abating their vital force, and it was not perceived that the loss of blood augmented the evil, and that it composed the sick only by depriving them of the power of reaction, necessary for the solution of the disorder.
>
> This symptom has been the cause of the most general, as well as fatal errors in the treatment of the insane. Seeing among them only the furious, all the insane have been treated like dangerous and mischievous animals, ready to destroy and exterminate every thing; against whom it was necessary to protect society. Hence dungeons, cells, grates, chains and blows; means which, by exasperating the delirium, were a principal obstacle to its cure. Ever since these unfortunate people have been treated with kindness, the number of the furious has diminished to such a degree that, in hospitals well kept, and properly arranged, among many

hundred insane people, not one can be found in a state of fury.

For the second half of the 19th century, "fury" as a separate form of insanity fell into disuse as a concept. However, it has long been noted (and is true today) that in certain manic states people can become irritable, hostile and, at times, violent. This can be true during certain manic phases of BIPOLAR DISORDER, a fact recognized by German psychiatrist Emil KRAEPELIN in the eighth edition of his famous *Textbook* on psychiatry (which appeared in four volumes between 1909 and 1915), in which he mentions the violent variety called the "raving mania" or "acute delirious mania."

See also MANIA.

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity.* Translated by E. K. Hunt. 1838. Reprint, Philadelphia: Lea & Blanchard, 1845.

Kraepelin, E. *Manic-Depressive Insanity and Paranoia.* Translated by R. M. Barclay and edited by G. M. Robinson. Edinburgh: E. & S. Livingstone, 1921.

Pinel, P. *A Treatise on Insanity.* Translated by D. D. Davis. 1801. Reprint, Sheffield, England: W. Todd, 1806.

Ganser's syndrome A rare psychotic syndrome (a cluster of symptoms) that likely occurs as a response to overwhelming stress. It has often been referred to as "PRISON PSYCHOSIS," since, from the time it was first described by German psychiatrist Sigbert J. M. Ganser (1853–1931) in 1897, it has often (but not always) been found in people in confinement, primarily prisoners. Most of the case histories of the past several decades, however, have concerned people who are not confined and who are not prisoners.

The distinguishing hallmark of Ganser's Syndrome is the symptom of "approximate answers," i.e., blatantly incorrect, absurd, and sometimes silly responses to direct questions that required a simple factual answer. In his 1897 lecture titled "A Peculiar Hysterical State," Ganser emphasized the "inability" of his patients (all prisoners) to "answer correctly the simplest questions which were asked of them, even though by many of their answers they have grasped, in a large part, the sense of the question, and in their answers they betray at once a baffling ignorance and a surprising lack of knowledge which they most assuredly once possessed or still possess." Ganser would ask his patients simple questions, and they would give the following responses to him: "Have you eyes? I have no eyes. How many fingers do you have? Eleven. How many legs does a horse have? Three." Ganser remarked on how these people would deliberately pass over the correct answer and select an obviously false one. He concluded, however, that they were not malingering, but that this was a genuine symptom of a mental disorder.

The symptom of approximate answers is sometimes referred to by the German word *Vorbeireden,* meaning "to talk past the point." However, Ganser never used this term himself. Further case studies of Ganser's syndrome have found that there is usually a clouding of consciousness, as well as reports of hallucinations, delusions and later periods of amnesia for the intervals when the symptoms of Ganser's syndrome were present. Although Ganser thought it was a form of hysteria, it is most often considered either a true psychotic disorder or simple malingering, an instance of FEIGNED INSANITY. However, due to reports of clouded consciousness, amnestic episodes, and its possible origin as a reaction to extreme stress, it is classified among the nonspecific dissociative disorders under that category in *DSM-IV* (1994).

See also *FAXENSYNDROM.*

Auerbach, D. B. "The Ganser Syndrome." In *Extraordinary Disorders of Human Behavior,* edited by C. H. Friedman & R. A. Faguet. New York: Plenum, 1982.

Ganser, S. J. "Über einen eigenartigen hysterischen dämmerzustand," *Arch. Psychiatr. Nervenkr.* 30 (1898): 633. An English translation by C. F. Shorer appears in the *British Journal of Criminology* 5 (1965): 120.

gating See ATTENTION, DISORDERS IN; SENSORIMOTOR GATING.

Genain quadruplets The Genain quadruplets are a rare set of monozygotic ("identical") sisters who all developed SCHIZOPHRENIA in the mid-1950s when they were in their twenties. They have been studied by David Rosenthal and his colleagues at the NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH) in Bethesda, Maryland, at periodic intervals ever since. At the time of their initial hospitalization at NIMH in the 1950s, they were extensively studied in the hope that they

could provide clues to the genetic transmission of schizophrenia. Being monozygotic quadruplets, they were genetically identical. However, the four sisters all differed in the severity of their disorder, and this has remained true throughout their lives. They were last under extensive study at NIMH in 1981, but an update on their progress was published in *Schizophrenia Bulletin* in 1988 by NIMH scientists Allan Mirsky and Olive Quinn; it revealed that the then-57-year-old sisters "are faring about as well now as they ever have in their adult lives."

The name Genain is a pseudonym chosen by Rosenthal and is derived from the Greek for "dreadful gene." Likewise, the names for the sisters, given in birth order, were Nora, Iris, Myra, and Hester and were chosen from the acronym NIMH. Rosenthal summarized the initial psychological and physiological studies conducted in the 1950s in his book, *The Genain Quadruplets* (1963). Rosenthal felt that the Genain quadruplets were evidence of the genetic determination of schizophrenic subtypes, since they all developed nonparanoid types of schizophrenia, thus fitting the pattern of monozygotic twins. The 1981 follow-up study at NIMH utilized all the neurological and biochemical techniques of investigation that had been developed since the 1950s. He and his researchers found that there were similar biological and biochemical abnormalities in the quadruplets when compared to normals, but that their CT SCANS were all normal, showing no evidence of ventricular enlargement and little atrophy of brain tissue.

See also BRAIN ABNORMALITIES IN SCHIZOPHRENIA; BRAIN IMAGING TECHNIQUES; TWINS METHOD AND STUDIES.

Mirsky, A. F., and O. W. Quinn. "The Genain Quadruplets," *Schizophrenia Bulletin* 14 (1988): 595–612.

Rosenthal, D. *The Genain Quadruplets.* New York: Basic Books, 1963.

gender differences in schizophrenia It has long been observed that there are many differences between men and women who are afflicted with SCHIZOPHRENIA. This observation is almost a century old. In Emil KRAEPELIN's original description of DEMENTIA PRAECOX in the 1896 fifth edition of his famous textbook, *Psychiatrie,* he makes the observation that: "Men appear to be three times more likely than women to suffer from the forms of illness described here." In the 1980s, as researchers collected evidence on the heterogeneity of schizophrenia, gender differences became an increasingly important area of research. Some of the major findings can be summarized here:

(1) Men have an earlier age of onset for schizophrenia than women.
(2) Men with schizophrenia have a poorer premorbid history than women with schizophrenia.
(3) Males have more NEGATIVE SYMPTOMS than females.
(4) Neurocognitive functioning is different across many parameters between males and females with schizophrenia.
(5) Males have a poorer course of schizophrenia than females.
(6) Males have a poorer response to antipsychotic drugs than females.
(7) Males have more structural and functional brain abnormalities than women. Thus, by almost any measure, women with schizophrenia as a whole tend to do better than men with the disorder.

A special issue of *Schizophrenia Bulletin* published in 1990 was devoted to the theme of "Gender and Schizophrenia."

As of this writing there is still no plausible scientific explanation for the gender differences we know to exist in schizophrenia.

Bryant, N. L., et al. "Gender Differences in Temporal Lobe Structures of Patients with Schizophrenia: A Volumetric MRI Study," *American Journal of Psychiatry* 156 (1999): 603–609.

Goldstein, J. M., and M. T. Tsuang. "Gender and Schizophrenia: An Introduction and Synthesis of Findings," *Schizophrenia Bulletin* 16:2 (1990): 179–184.

gender-identity confusion A commonly reported experience, usually during the onset of SCHIZOPHRENIA or during periods of exacerbations, in which a person becomes confused about which

gender he or she is. They tend to feel themselves transforming into the opposite sex. If it occurs in a man, he may feel he is becoming a woman, and in extreme cases may report the feeling of being "pregnant." This symptom is not to be confused with the "switching" into an alternate personality of the opposite sex that sometimes occurs in multiple personality disorder, as this phenomenon is situation-specific and is not related to the pervasive sense of one's entire being undergoing the sexual transformation that is found in psychotic states.

gene The word *gene* is derived from an ancient Greek word meaning "birth." It is often defined as the functional unit of heredity, or sometimes as an inherited "Mendelian factor" transmitted from parent to offspring. Each gene occupies a specific place on a CHROMOSOME, and this place is called the locus (plural: loci). Each gene is able to reproduce itself exactly at each cell division and is capable of directing the formation of an enzyme or other protein. Genes normally occur in pairs in all cells as a consequence of the fact that all chromosomes are paired (except the sex chromosomes X and Y of the male). If any one of a series of two or more different genes must occupy the same locus on a chromosome, it is referred to as an allele.

general paralysis of the insane This was the name given to a mental and physical disorder suffered by large numbers of people admitted to asylums in the 19th century; early in this century the disorder was conclusively found to be the effects of the tertiary stage of syphilis (neurosyphilis). People suffering from general paralysis of the insane (often referred to as "paretics" due to the paresis, or muscular weakening, that characterized the disorder) would first experience difficulties in speaking, then movement problems, epileptic-like convulsions, then a more paralytic stage, which would develop to the point where these people would need constant help in feeding, dressing, hygiene, and simply moving their bodies in any desired manner. Psychological symptoms would almost invariably begin with DEPRESSION, then DELUSIONS (sometimes grandiose ones), then a degeneration of memory and other cognitive functions that rendered the sufferer psychologically—as well as physically—paralyzed.

It has been suggested by medical historian George Rosen that the condition may have been observed in the mentally ill as early as 1672 by English physician Thomas Willis (1621–75), and a mental disorder with similar symptoms was also described by John HASLAM in 1798. The label "general paralysis of the insane" was given to the disorder in 1826 by French ALIENIST Louis Calmeil (1798–1895). However, the progression of stages in the disorder were accurately described first by another French alienist, Antoine-Leurente Bayle (1799–1858), in 1822. As a result, this disorder was commonly known in France throughout the 19th century as *"la maladie de Bayle."* In reviewing the psychiatric literature of his day, German psychiatrist Wilhelm GRIESINGER (1817–68) found that estimates from asylums in many European countries put the number of admissions of patients with this disorder at anywhere from 6 percent to 25 percent of total admissions by 1861, with France reporting the highest rates.

With the growing interest in the study of the brain and the nervous system in the latter half of the 1800s some researchers began to suspect that syphilis might be related to the cause of general paralysis of the insane. In 1905 two German researchers identified the spiral-shaped bacterium that caused syphilis, *SPIROCHAETA PALLIDA* (later renamed) *TREPONEMA PALLIDUM*). In 1906 German bacteriologist August von Wassermann and his colleagues devised the diagnostic blood test for syphilis that still bears his name, and in 1913 the issue was finally laid to rest when the syphilitic organism was found in the brains of paretics by Noguchi and Moore.

See also DEGENERATION.

Bayle, A. L. *Traité des maladies du cerveau et de ses membranes.* Paris: 1826.

Noguchi, H., and J. W. Moore. "A Demonstration of Treponema Pallidum in the Brain in Cases of General Paralysis," *Journal of Experimental Medicine* 17 (1913): 232–238.

Rosen, G. *Madness in Society: Chapters in the Historical Sociology of Mental Illness.* Chicago: University of Chicago Press, 1968.

genetic counseling for schizophrenia With the advances made in linking certain medical disorders to specific genes (e.g., Huntington's chorea with chromosome 4, in 1983), more and more prospective parents have sought genetic counseling to discover the risks involved when there is a family history of a particular disease. This presents difficulties for those who seek genetic counseling for schizophrenia, since the patterns of transmission are still unknown. The only solid information that can presently be offered are risk factors calculated by certain computer programs that are based on a polygenetic or multifactorial model for the transmission of SCHIZOPHRENIA. These computer programs can calculate the risks for each combination of affected or unaffected family members, ranging from a risk of 1 percent (the base rate found in the general population) to over 50 percent (when both biological parents and other relatives have the illness). Given this lack of knowledge, should a genetic counselor ever advise schizophrenics or their mates not to have children? In this situation, a well-known textbook on genetic counseling by Fuhrmann and Vogel argues that the risks are high enough even with present knowledge always to discourage having children. Others, however, may argue only that this advice should "usually" be given in this situation. For example, in a 1976 article a major figure in schizophrenia research, L. Erlenmeyer-Kimling, observes that, "Parenthood and schizophrenia tend to mix poorly." She adds the following explanation:

> In addition to the genetic risks to the children of schizophrenic parents, there is considerable likelihood that any children of such parents will be exposed to a disrupted home environment, and frequently to a grossly unsuitable one. The birth of a child often exacerbates the patient's illness, and the responsibilities of bringing up the children tend to trigger further difficulties.

An experimental program for genetic counseling for schizophrenia was set up in London's Maudsley Hospital Genetic Clinic in 1983–84, with the results reported by Adrianne Reveley in 1985. Most of the cases inquired about the risk of potential offspring developing schizophrenia in situations where (a) one of the prospective parents was schizophrenic or (b) when a relative of one of the two prospective parents had schizophrenia. Contrary to the strong opinions of some scholars in the field, in practice, genetic counselors cannot scientifically make these decisions for people, and the staff at the Maudsley Clinic did not do so. Their philosophy should be remembered by those who either seek or give genetic counseling for schizophrenia: "It is not the role of a genetic counsellor to advise individuals, but rather to present the evidence of risk, and provide enough information for those seeking counsel to make their own decisions."

A similar situation presently exists for the genetic counseling of bipolar disorder. A review of this issue by Cadoret in 1976 (still valid today) concludes that such counseling might be so tentative at present as to be virtually useless.

See also GENETIC TRANSMISSION.

Cadoret, R. J. "The Genetics of Affective Disorder and Genetic Counseling," *Social Biology* 23 (1976): 116–122.

Erlenmeyer-Kimling, L. "Schizophrenia: A Bag of Dilemmas," *Social Biology* 23 (1976): 123–134.

Gottesman, I. I., and S. O. Moldin. *Schizophrenia and Genetic Risks: A Guide to Genetic Counseling.* Arlington, Va.: NAMI, 1992.

Reveley, A. "Genetic Counselling for Schizophrenia," *British Journal of Psychiatry* 147 (1985): 107–112.

genetic heterogeneity This is one of the possible modes of the GENETIC TRANSMISSION of SCHIZOPHRENIA. It is also sometimes referred to as ETIOLOGIC HETEROGENEITY. The idea is that schizophrenia (or other psychotic disorders such as BIPOLAR DISORDER) may be caused by any one of a number of single genes, located, perhaps, even on different chromosomes, each one of which is entirely capable of predisposing to the disease without the additional effect of other genes.

genetic markers of vulnerability In the search for BIOLOGICAL MARKERS OF SCHIZOPHRENIA and bipolar disorder, the assumption is that certain mea-

surable physiological processes accompany specific diseases and, it is hoped, may be related to the cause of the disease. Furthermore, it is hoped that these characteristic biological markers are indeed true genetic markers for the disorder, that is, that the biological characteristic and the disease are genetically linked and follow related patterns of genetic transmission. Identifying such a biological characteristic (such as "smooth pursuit eye movement abnormalities" in SCHIZOPHRENIA) may then be considered a sign or a marker of the genetic vulnerability of the person with the marker for the disease to which it is linked.

According to a report on *Behavioral Genetics* by the NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH), a genetic marker must meet the following criteria:

1. The characteristic must be associated with an increased likelihood of the illness (although all people with the illness need not show the characteristic nor vice versa). It is then a marker for the illness, though not necessarily a genetic one.
2. It must be heritable and not be a secondary effect of the illness. That is, it must be genetic and not a result of having had the illness.
3. It must be observable (or evocable) in the well state in addition to the ill state. Since the marker is a predisposition to the illness, not a marker of the illness itself, we should expect it in at least some well relatives and the recovered ill.
4. Transmission of both the characteristic and the illness must be related within pedigrees. This demonstration shows the characteristic is a necessary or contributing genetic factor in an illness.

Therefore, the search for genetic markers is a quest for the underlying biological predisposition or vulnerability to a particular disease that is detectable in the afflicted person during periods of remission as well as when actively symptomatic. This shifts the attention of research away from studying just those periods when the disease is most visible.

There are several strategies for searching for genetic markers of vulnerability. In well-state studies, patients, either in remission or actively psychotic, along with their relatives who do not have psychotic disorders can be matched according to a marker they all share, and which distinguishes them from "normals" who do not have the marker nor the disorder. For example, EYE-MOVEMENT ABNORMALITIES may be such a marker for schizophrenia, since it has been found in many schizophrenics and their nonschizophrenic relatives and is thought to have a genetic basis. Or, such genetically vulnerable people and normals may be distinguished from one another if they have different reactions to a specific drug that is experimentally administered for a short period, a technique known as a PHARMACOLOGIC CHALLENGE.

Once a suspected biological marker of vulnerability is identified, it can be analyzed according to how highly correlated the transmission of the marker and the disorder is in families. One of the most powerful statistical procedures for this is SEGREGATION ANALYSIS. In segregation analysis, the observed frequency of illness in a SIBSHIP (the group of all siblings of the afflicted person, and their parents) or in a pedigree (the multigenerational extended family group) is compared with a hypothetical pattern of inheritance that is based on a particular model of a mode of genetic transmission (for example, possible patterns based on the theory that only one gene is the cause of the disorder or the theory that more than one gene is, in combination, responsible for the disease).

If a biological marker is identified that seems to be transmitted throughout a family in a highly similar manner to the way the disease is inherited, then the next strategy would be to link the marker to a single CHROMOSOME or to a location on a specific chromosome. The marker is then called a LINKED MARKER. This search for disease-related genes is done through a statistical procedure known as LINKAGE ANALYSIS. Linkage analysis is considered more sensitive than segregation analysis for detecting a single "locus" or place that is responsible for predisposition to the illness (monogenetic transmission), and it is less suited to a model of genetic transmission that hypnothesizes that many genetic places or loci, and perhaps the environment, may be responsible together for predisposition to the illness (polygenetic transmission). Therefore, the linkage of a particular disorder to a specific chromosome (such as the linkage

of schizophrenia to abnormalities on chromosome 6) only lets us know where on the chromosome the genetic predisposition may originate and does not necessarily tell us anything about the actual cause of the disorder, which may involve many factors, both genetic and environmental.

With remarkable improvements in PCR (polymerase chain reaction) techniques and computerized DNA sequencing technology during the l990s, vast screenings of large areas of the human genome are now possible. Current approaches to finding the genes that make people susceptible to schizophrenia still include linkage analysis, association studies, searches for chromosome abnormalities, the DNA analysis of other physical or mental disorders or syndromes that may resemble schizophrenia in some of their characteristics, studies of ANTICIPATION, and (genetic) efforts to facilitate genetic analysis by reducing the phenotypic complexity of the disease (primarily FACTOR ANALYTIC STUDIES OF THE SYMPTOMS OF SCHIZOPHRENIA). Large-scale ongoing studies of hundreds of families that have schizophrenic members are conducted by the NIMH Genetics Initiative for Schizophrenia, which uses all these new genomic technologies. NIMH and other laboratories in the United States and Europe have found many weak CHROMOSOME LINKAGES TO SCHIZOPHRENIA. However, it must be emphasized that these linkages are not strong ones and that there are no certain genetic markers for schizophrenia.

See also CANDIDATE GENES; CHROMOSOME ABNORMALITIES; GENETIC TRANSMISSION.

Karayiorgou, M., and J. A. Gorgos. "Dissecting the Genetic Complexity of Schizophrenia," *Molecular Psychiatry* 2 (1997): 211–223.

National Institute of Mental Health. *Behavioral Genetics, Science Monographs No. 2,* DHEW Publication No. (ADM) 80–876. Washington, D.C.: U.S. Gov't. Printing Office, 1980.

genetics studies The idea that "madness" or "insanity" is inherited in some way from generation to generation has been hypothesized for thousands of years. Although family patterns of disease were observed, the causes people attributed them to were not scientific. The "sins of the father" (or perhaps some other family member), which may have brought a Divine curse upon the family, were considered to be manifested in the mental illness of certain family members. Or people simply attributed the mental illness in an afflicted family to "bad blood."

Many of the earliest psychiatric manuals from the early 1800s all comment on the fact that some mental disorders are associated with certain families and not others. By mid-century, so many informal studies had been compiled by alienists at various asylums that Wilhelm GRIESINGER could write in 1860:

> Statistical investigations strengthen very remarkably the opinion generally held by physicians and the laity, that in the greater number of cases of insanity a hereditary predisposition lies at the bottom of the malady; and I believe that we might, without hesitation, affirm that there is really no circumstance more powerful than this (page 106).

Heredity and variation in the 19th century The science of genetics is an early 20th-century creation. Throughout the late 18th and the entire 19th centuries, discussions instead revolved around the issues of heredity and variation. HEREDITY is the transmission of "characters" (physical and behavioral traits) from past generations to new ones. Variability referred to the changes in inherited characters or traits from one generation to the next. Variability also referred to the differences among individuals of the same generation. Animal breeders and horticulturalists (plant breeders) had evolved techniques over the centuries to blend "bloodlines" to create new ones that possessed characters or traits that were desirable in their livestock, crops, or flowers. These techniques of "hybridization"—the art of the creation of hybrids—were documented since the late 1700s in a sizeable literature that influenced Charles Darwin (1809–82). It also influenced the generation of biologists after Darwin's death who eventually developed new ideas and statistical methods that evolved into the science of genetics. Because animal and plant breeders deliberately created hybrids to combine desirable char-

acters or traits in new generations that had been stable in old generations, they viewed unstable characters or traits (variation) as undesirable. Their assumption was that heredity and variation were two violently opposing forces, and that variation could be mastered through the carefully controlled art of breeding hybrid animals or plants over many generations.

It was inevitable that the theories and techniques of animal and plant breeders would be applied to human beings. Of particular interest was the persistence of undesirable characters or traits in human beings, or the creation of new ones in new generations (variability)—such as immorality, addictions, or mental illnesses—and how to prevent them from being passed on to future generations.

Throughout history it had been recognized that some mental disorders are associated with certain families and not others. The inheritance of insanity became a particular concern in the 1800s, when there was a sharp rise in the numbers of person developing psychotic disorders in Europe and America. For example, the question "whether heredity?" was one of the routine inquiries that MAD-DOCTORS made at the BETHLEM ROYAL HOSPITAL ("Bedlam") and is reflected in patient records as early as the 1820s. In his *Traite des degenerescences physiques, intellectuelles et morales de l'espece humaine* (Treatise on the Physical, Intellectual and Moral Degeneration of the Human Species) of 1857, the French ALIENIST Benedict-Augustin MOREL proposed the theory that physical and mental diseases, immorality, substance abuse, and living in unsanitary urban centers, led to the hereditary transmission of a physical, mental, and moral weakness of one's children. Each generation would thus pass this along, making each less and less fit to survive. This process of DEGENERATION would end family lines when the last generations were populated with persons who were too physically ill, mentally retarded, or insane to survive and reproduce. This notion of "hereditary taint" or "bad blood" was akin to the notion of "original sin in the germ plasm"—that is, one was born burdened by the sins of the fathers (previous generations). Dementia praecox—a term first used by Morel—was seen as evidence of a "bloodline" nearing the end of its degeneration process because it was a form of dementia arising in young people that is usually only seen in old age. Forms of insanity such as DEMENTIA PRAECOX (SCHIZOPHRENIA) were thought to have an earlier AGE OF ONSET and a more severe course in each new generation. Today this phenomenon is known as genetic ANTICIPATION. It has been observed to occur in some neurodegenerative diseases and is being studied for its possible connection to schizophrenia. DEGENERATION THEORY became a dominant medical theory and a major source of paranoia among the public by the end of the 19th century but subsided in importance by the end of the First World War.

Backed by the authority of Francis Galton (1822–1911) in England, in the first half of the 20th century programs of EUGENICS (a term Galton coined) led to the promotion of selective breeding among humans to produce stronger bloodlines of healthy human beings; forced sterilization of the insane, the immoral, and the criminal; and, in Nazi Germany, the murder of individuals (such as persons with dementia praecox/schizophrenia) who were deemed too biologically "unfit" to live and reproduce. The geneticist Eolf Axl Carlson traced the tragic history of eugenics in his 2001 volume, *The Unfit: A History of a Bad Idea.*

Dementia praecox and degeneration In his first detailed clinical description of dementia praecox in 1896, Emil KRAEPELIN estimated that in approximately 70 percent of the cases he had observed, "hereditary predisposition" was present and "the so-called signs of degeneration were frequently observed" (*Psychiatrie,* 6th edition, p. 97). However, this hereditary predisposition did not lead directly to dementia praecox but instead to a metabolic self-poisoning of the body, or AUTOINTOXICATION (*Selbstvergiftung*), probably arising from the sex glands, which eventually affected the brain and produced psychotic symptoms (hallucinations and delusions) and dementia. This belief was shared by another prominent German psychiatrist, Wilhelm Weygandt (1870–1939), who speculated in 1907 that, "I should like to put forward a tentative explanation of dementia precox of my own. . . . I would suggest that so far as the organic side is concerned the most plausible concept is one of autotoxic damage affecting genetically predisposed brains."

Genetics in the 20th century Although heredity and variation were known facts, no one knew

their underlying biological mechanisms. Heredity and variation were major components of Darwinian evolutionary theory (although the Darwinians put a positive spin on variation as a desirable strength in populations, enhancing the ability of populations to survive and reproduce). However, Charles Darwin died in 1882 without knowing anything about genes. The usual turning point cited by historians is the reputed "rediscovery" of an 1866 article in which a way to study hereditary units was proposed. In the year 1900, at least three different biologists published papers in which they cited a forgotten and/or ignored research report by the monk Gregor Mendel (1822–84). Mendel had analyzed eight years of garden experiments that traced the hereditary transmission of characteristics (traits) in hybrids he created from different lineages of peas. Proposing formulas for the prediction of the appearance of characteristics in future species, and reporting that his actual findings matched his predictions (much too well, others said later, indicating unconscious bias on the part of Mendel—or worse, deliberate falsification), Mendel was turned into a hero and an icon for the transformation for the study of heredity into a science. Although he has used the term in a private letter in 1905, British biologist William Bateson proposed that this new science be called "genetics" in a lecture in 1906. In 1909 the Danish biologist Wilhelm Johannsen (1857–1927) proposed that a hypothetical basic biological unit of heredity be called the "gene." In the same book, *Elemente der Exacten Erblichkeiten* (Elements of Exact Heredity), Johannsen introduced the terms PHENOTYPE and GENOTYPE. A lecture tour of the United States in 1911 helped promote these ideas there, influencing the prominent geneticist T. H. Morgan (1866–1945) of Columbia University. Johannsen insisted that this orienting concept of the gene be free of any speculation about its material nature, and this open-ended view of the gene led to a multitude of debates about the nature of the gene throughout the 20th century: Was the gene a corpuscule or a chemical? Was it found in the nucleus of cells or in the cytoplasm of cells? Were the chromosomes themselves genes or were the genes segments of the chromosomes? Was the gene stable and unchanging, or instable and mutating? Was it a protein (a theory popular in the 1930s and 1940s) or was it composed of nucleic acids (as was suspected by 1950, and reflected in the 1953 discovery by James Watson and Francis Crick that the DNA molecule had a double helix structure of two chains of nucleic acids twisted around each other)? Did the gene have a definite structure, or should it be defined solely in terms of functions (for example, as the physiological unit that guides development and growth)? How do environmental forces affect genes—or do they? Many of these questions have been answered to the satisfaction of biologists. And yet, how, precisely, a gene should be defined is still a matter of debate among many biologists and philosophers of science. As one such philosopher of science, Philip Kitcher, put it in 1992, "A gene is anything a competent biologist chooses to call a gene."

Psychiatric genetics It was inevitable that the statistical study of the inheritance of traits or characteristics would be applied to persons with mental disorders and their families. Influenced by Galton's pioneering of statistical techniques of correlation in his studies of the transmission of genius and other traits, 19th-century proponents of degeneration theory in medicine used simple statistical procedures to trace hereditary taint in families. Galton's basic statistical tools were refined and exceeded by new statistical techniques and research methods invented by R. A. Fisher (1918) and Sewall Wright (1912). Fisher and Wright extended Mendel's single-gene model of the transmission of characters or traits to a new model in which predictions can be made about the probabilities of multiple genes combining to have effects that result in measurable traits. This introduction of quantitative genetics continues to have a profound effect on genetics research.

The first true attempt to discern the role of genetics in the development of mental disorders was a study conducted in Germany and published in 1916 (see below), and from this eventually developed a specialty known as psychiatric genetics. There were two influential centers of psychiatric genetics prior to the 1970s: the German psychiatric research group centered around Emil Kraepelin in Munich in the first third of the 20th century, and the British research group led by Eliot Slater (who had first trained in Munich) beginning in 1935 at the

Maudsley Hospital in London. Slater set up the first psychiatric research unit at that hospital in 1959, and in 1971 he published the first true textbook in the field of psychiatric genetics, *The Genetics of Mental Disorders.* Starting in the late 1960s, a third group of influential researchers into the genetics of mental disorders was led by Semour Kety and David Rosenthal at the NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH), the Institutes of Health, in Bethesda, Maryland. In addition to the ongoing schizophrenia research at NIMH, significant medical genomic research continues at deCODE genetics in Reykjavik, Iceland, led by Dr. Kari Stefansson.

Following the influence of Harvard biologist E. O. Wilson, whose theory of sociobiology (1975) proposed that complex social behaviors in all species, including humans, had a strong genetic influence, the 1980s witnessed the rise of behavioral genetics as a scientific discipline. Behavioral genetics research involves sorting out how much of schizophrenia (and other disorders) is due to the influence of genes and how much is due to environmental factors. Behavioral genetics is an influential area of research in the early 21st century, providing an important data base for an equally influential subdiscipline of psychology known as evolutionary psychology. Evolutionary psychology examines present-day behaviors (mating, parenting, cooperation, competition, and so on) as reflecting adaptations formed in the prehistoric human past. Genes are assumed to play a key role in shaping the structure and functions of the human brain, which is itself a product of Darwinian natural selection.

Genetic theories of the causes of mental disorders were highly unpopular in mainstream psychiatry from the 1920s to the 1970s, when the profession was dominated by Freudian psychoanalysts who placed the root cause of adult mental life, normal and abnormal, in early childhood experiences before the age of five. The adoption of the pseudoscience of eugenics as a state policy by the National Socialist government in Germany (1933–45), and the subsequent exposure of the Holocaust, also fueled extreme environmentalism as a backlash to hereditary theories of mental illness. By the late 1960s, the results of the family, twins, and adoption studies reviewed below eventually provided strong evidence for the biological roots of schizophrenia and manic-depressive illness and directly refuted the claims of psychoanalysts, paving the way for the return of biological psychiatry in the 1980s.

Today research methodologies for studying the role of the genetics in schizophrenia fall into two broad categories: behavioral genetics, which consists of the inferences we can indirectly draw about the influence of genes on complex human behaviors and diseases (such as schizophrenia), and is characterized by the methods found in family, twin, and adoption studies; and molecular genetics, which is devoted to discovering the actual sequences of DNA (genes) linked or associated with the expression of schizophrenia as a disease process. Although the causal links connecting molecular genetics and behavioral genetics are currently unknown, the great assumption is that this tremendous gap in understanding will vanish through future research.

Behavioral Genetics

Family studies Perhaps the historical starting point for psychiatric genetics is the 1916 study by Ernst Rüdin (1874–1952) of Munich, Germany. In *Zur Vererbung und Neuentstheung der Dementia Praecox* (*On the Inheritability and Cause of Dementia Praecox*), he studied patients with dementia praecox (schizophrenia) using the CONSANGUITY METHOD. The consanguity method involves constructing family trees of genetic relatedness, or "pedigrees," centered on one person as a starting point who is the "proband" or "index case." It is essentially a demographic method that involves interviews or correspondence with as many members of an afflicted person's family or friends of the family (such as parish priests, in Rüdin's case) as is possible in order to document the presence or absence of schizophrenia throughout the family.

Rüdin, who worked under Kraepelin in Munich, compiled data on 701 families with 4,823 children living in Bavaria who had a family member who had been diagnosed with dementia praecox. He found higher rates of schizophrenia in children for which one parent was schizophrenic (6.2 percent of children) than in children who had two healthy, unaffected parents (4.5 percent of the children).

Although this indicated a hereditary component to dementia praecox, the production of schizophrenic children by two healthy parents pointed to the complexities of the pattern of genetic transmission, as too did the relatively small number of schizophrenic children produced when there was one schizophrenic parent. From this point onward, researchers began to suspect that schizophrenia followed a pattern of NON-MENDELIAN PATTERNS OF TRANSMISSION. Further family studies of schizophrenia continued throughout the 20th century, many finding similar perplexing patterns of genetic transmission of schizophrenia in families. The most notable of these was perhaps the research of Franz J. Kallman (1897–1965), a German immigrant to the United States who worked at the New York State Psychiatric Institute. His 1938 volume, *The Genetics of Schizophrenia,* is regarded by many behavioral geneticists as the true starting point for the study of the genetics of schizophrenia.

Since 1916, more than 40 family studies of schizophrenia have been published. They consistently show that schizophrenia runs in families. All studies show that the lifetime risk of developing schizophrenia increased with the degree of genetic relatedness to the schizophrenic index case (or proband) that is the starting point of the pedigree in such studies. Those closer "in blood" to the person with schizophrenia consistently are shown to bear a higher risk of also developing the disease. The average risk for first-degree relatives of a person with schizophrenia (parents, siblings, children) is 9 percent, and for second-degree relatives (grandparents, grandchildren, and so on) is 4 percent. The average lifetime risk of the general population is approximately 1 percent. When the various amounts of risk averaged for first-degree relatives are broken down according to relationship, new patterns emerge: the median risk for each parent was 6 percent, for each sibling 9 percent, and for each child 13 percent. Since the vast majority of persons with schizophrenia are born to two biological parents who do not have the disease, the lower risk of 6 percent reflects this fact. One parent with schizophrenia (and rates for mothers and fathers are the same) conveys a 13 percent risk to each child, whereas two persons with schizophrenia who produce a child gives it a 46 percent risk of developing schizophrenia later in life.

The "family design" or consanguity method also forms the basis of HIGH-RISK STUDIES of schizophrenia. In these studies, children with mothers who suffer from schizophrenia are studied from birth into adulthood. Since such children are at genetic "high-risk" for developing schizophrenia by early adulthood, their cognitive, emotional, and behavioral development is thoroughly studied over time. Currently, there are 15 long-term follow-up studies being conducted that have been coordinated through the Risk Research Consortium since 1984, consisting of the continuous study of at least 1,200 children with a schizophrenic mother and 1,400 children born to parents without schizophrenia. As these children age, new studies will be published using this data.

The problem with traditional family studies is that they do not provide a method of figuring out how much of schizophrenia might be due to genetic inheritance, and how much might be due to "nurture" or environmental causes. Two other methods have been developed to address the issue of "genetics v. environment" or "nature v. nurture": the twins studies and adoption studies.

Twins studies: logic of the design Studies of twin pairs in which one member is affected with schizophrenia provide strong evidence for both the influence of genetics and the role of environmental factors in the development of the disease process in schizophrenia. Twins studies compare the CONCORDANCE RATE for schizophrenia in MONOZYGOTIC TWINS ("identical twins," who are assumed to share 100 percent of their genes and thus are natural "clones" of one another) with that for the disease in DIZYGOTIC TWINS (who are assumed to have 50 percent of their genes in common). If schizophrenia is a genetically transmitted disease, then the likelihood that both MZ twins would develop the disease, if one of them has it, should be much higher than the likelihood of the same thing happening in pairs of DZ twins. In fact, based on the relative percentages of shared genes (100 percent v. 50 percent), the assumed prediction is that MZ twins will both be affected with schizophrenia at twice the rate of DZ twins. Additionally, the concordance rates for DZ twins, one of which has schizophrenia, should be

higher than randomly selected twin pairs from the general population in which schizophrenia may or may not be present. Such a pattern would indicate the clear influence of genetics in schizophrenia. In all twins studies of persons with schizophrenia since the very first one in 1928, the general pattern has always been along these lines (MZ more than DZ more than nonaffected twin pairs in the general population), although the actual concordance rates have been far less than the predicted concordance rates of 100 percent for MZ twin pairs and 50 percent for DZ twin pairs—indicating once again that genetics is not the whole story behind the development of schizophrenia.

Twins studies are used to calculate an estimate known as heritability. Using a formula based on the MZ/DZ ratio, the heritability statistic (*h*) can be estimated. Heritability is defined as that proportion of phenotypic variance that is due to genetic variance in a population. The portion of variance found in a population that is not due to genotypic variance is therefore assumed to be due to unknown environmental influences or error. There is both narrow heritability (that corresponding to the assumptions of the animal breeders) and broad heritability (that corresponding to most known genetic phenomena, which involve multiple genes and complex traits). There are drawbacks to the usefulness of the heritability statistic, however. Heritability changes in populations over time and place and is therefore highly sensitive to environmental changes. Citing the heritability of a disease is often used incorrectly to imply cause, but a high heritability statistic (such as found in twins studies of schizophrenia) merely means that genes play a significant role in a given population at a given time in a given environment but that this may not have been true in the past or will be true in the future.

Twins studies: "premodern" studies using varying diagnostic definitions of "schizophrenia" The first application of the twins design to study the genetics of psychiatric disorders was conducted by Hans Luxenburger (1894–1976) in Munich. While employed at the German Psychiatric Research Institute founded by Emil Kraepelin and his associates, Luxenberger located 211 twin pairs in which one twin had been diagnosed with dementia praecox (schizophrenia) in a Bavarian asylum. Publishing his results in 1928 in the *Zeitschrift fuer die gesamte Neurologie und Psychiatrie* (Journal of Combined Neurology and Psychiatry), Luxenburger reported concordance rates of 64 percent for MZ twins and 0 percent for DZ twins—a very strong indication of the genetic basis of schizophrenia. How to explain the fact that there were pairs of identical (MZ) twins in which one twin had schizophrenia and the other didn't? Could the discordant MZ pairs be evidence for a "nongenetic schizophrenia" caused by something other than heredity? Looking specifically at the 36 percent of MZ pairs that were discordant for schizophrenia Luxenburger found that first-degree relatives had the same risk for developing schizophrenia as the concordant MZ pairs. This finding gave support to the notion that genes that predispose a person to schizophrenia are indeed spread throughout the family of biological relatives of a person with schizophrenia and that nongenetic forms of schizophrenia are probably uncommon. Otherwise, families of the discordant MZ pairs, assuming that the one MZ twin with schizophrenia has a nongenetic form of the disorder, would have little or no affected members. This was not found to be the case. Virtually every schizophrenia study using the twins method has replicated Luxenburger's finding. Even though one twin in a discordant MZ pair has not been afflicted with the disease, that twin still has the same high genetic risk for developing the disease as the other twin who has schizophrenia. What, then, threw the genetic switch that started the schizophrenia disease process in one identical twin and not in another? Environmental factors must be the missing clue to this puzzle, but they remain a mystery.

With respect to fraternal or DZ twins who are not genetically identical, the general finding in twins studies is that the children of the DZ twin with schizophrenia are at a much greater risk for developing the disease than the children of the DZ twin who is not afflicted. This, too, lends support to the theory that schizophrenia is a brain disease with a strong genetic component.

Three other early genetics studies of schizophrenia in twins added weight to the arguments against the extreme environmentalism of Freudian psychoanalysis among the American and British psychiatric elite of the mid-20th century. In a

study published in the journal *California and Western Medicine* in 1932, a Los Angeles private practice psychiatrist, Aaron J. Rosanoff (1878–1943), found a concordance rate of 85 percent for schizophrenia in 48 MZ twin pairs and a rate of 38 percent in 79 DZ twin pairs. In 1946 Franz J. Kallman published a study in the *American Journal of Psychiatry* that found concordance rates of 89 percent for MZ twin pairs and 15 percent for DZ twin pairs. British psychiatric researcher Eliot SLATER (1904–83) reported concordance rates of 75 percent for MZ and 11 percent for DZ in his 1953 book, *Psychotic and Neurotic Illnesses in Twins.* Thus, consistently strong evidence suggesting a hereditary or genetic component to the cause of schizophrenia has accumulated since the early 20th century.

Twins studies: "modern" studies using equivalent diagnostic definitions of schizophrenia Until the development in 1978 of the FEIGHNER CRITERIA for diagnosing schizophrenia and other mental disorders, diagnostic definitions of schizophrenia widened and narrowed throughout the 20th century. Such a diversity of opinions about how to define and identify persons with schizophrenia makes the pre–1980 scientific literature on schizophrenia difficult to generalize to the more "modern," narrowly defined view that has been in existence since *DSM-III* of 1980 adopted the Feighner diagnostic criteria for schizophrenia. *DSM-III* narrowed the definition of schizophrenia in a manner that brought it closer to Emil Kraepelin's early views of dementia praecox and separated schizophrenia from other mental disorders (such as schizoaffective disorder, schizotypal disorder, and schizoid personality disorder), which were previously diagnosed as forms of schizophrenia since the time of Eugen BLEULER's 1911 volume, *Dementia Praecox, or the Group of Schizophrenias.* A further tightening of the diagnostic criteria was reflected in *DSM-III-R* (1987) and *ICD-10* (1992). This tightening of the diagnostic criteria for schizophrenia since 1980 has produced stronger data for the role of genetics in this disease.

The first twin study to use "modern" diagnostic criteria was conducted by S. Onstead and colleagues in Norway and published in 1991.Using the *DSM-III-R* definition of schizophrenia, they found concordance rates of 48 percent for the MZ twin pairs and 4 percent for the DZ twin pairs. The results of five recent studies in Europe and Japan published between 1996 and 1999 that used both *ICD-10* and *DSM-III-R* definitions of schizophrenia were combined and analyzed by researchers Cardno and Gottesman in an article that appeared in the *American Journal of Medical Genetics* in 2000. When using the *DSM-III-R* definition of schizophrenia, concordance rates were 50 percent for MZ twin pairs and 4.1 percent for DZ twin pairs, indicating a liability-heritability estimate of 88 percent. Using *ICD-10* criteria, the concordance rates were 42.4 (MZ), 3.9 (DZ), and a heritability estimate of 83 percent. Cardno and Gottesman stress that two important conclusions can be drawn from these data: first, that schizophrenia is a strongly genetic disorder and nongenetic forms of schizophrenia (phenocopies), if they exist, are relatively uncommon. Second, people who are at genetic risk for developing schizophrenia but do not have it possess genotypes that are not expressed. (That is, despite having the genes that may cause schizophrenia, these genes do not "switch on" and begin the disease process.)

Still, although there is evidence that schizophrenia is a "strongly" genetic disorder, the recent (post 1996) MZ concordance rates for schizophrenia of 42 to 50 percent still do not match the MZ concordance rate of 100 percent for Huntington's disease, a monogenetic neurological disease. Perhaps the characterization of schizophrenia as "strongly" genetic is best retermed "suggestively" genetic.

Adoption studies Despite the strongly suggestive evidence from twins studies that genetics plays a role in the development of schizophrenia, many critics flipped the data upside down and emphasized the opposite conclusion: that nongenetic factors are equally important. In particular, critics focused on the fact that the twins in these studies were raised in the same homes. The idea that there may have been something about the "shared environment" of these twins—sharing the same mother, father, experiences, and so on—that could be the true cause of schizophrenia. To investigate this issue, Leonard Heston (1930–), a psychiatry resident at the University of Oregon Medical School, conducted a study of children of mothers suffering from schizophrenia who had been given up for adoption. Adopted children were raised by

persons with whom they shared no genes. Also, the "shared environment" of schizophrenic parents and children in previously studies was eliminated. Heston found that children of schizophrenic mothers who had been given up for adoption had an 11 percent risk for developing the disease (5 of 47 children of schizophrenia mothers), which corresponds closely to the 9 or 10 percent risk of a child of a schizophrenic parent. In other words, the genetic risk was the same, regardless of what environment the child was raised in. Heston published his results in 1966 in the *British Journal of Psychiatry.*

Two major adoption studies conducted in Denmark by three schizophrenia researchers at the National Institute of Mental Health in Bethesda, Maryland—Seymour Kety (1915–2000), David Rosenthal (1919–96), and Paul Wender (1934–)—in collaboration with Danish psychiatrist Fini Schulsinger (1923–)—confirmed Heston's conclusions. Using Danish adoption registers, the researchers examined the records of approximately 5,500 children adopted between 1924 and 1947, and 10,000 of their 11,000 biological parents. Of these, they found 44 biological mothers (two-thirds of the parents) or fathers (one-third of the parents) who had been diagnosed with schizophrenia and whose children had been adopted away. The 44 adopted-away children of a schizophrenic parent were matched against 67 control children who had been adopted away and whose biological parents had no psychiatric history. A 7 percent risk for developing schizophrenia (3 of 44 children of schizophrenics) was found, with no risk found among the control adoptees whose biological parents had no psychiatric history. This famous study using the adoptees' study method was published in the *Journal of Psychiatric Research* in 1968.

A second study based on the same data used a different method combining the methods of adoption studies with that of family studies. In examining the medical histories of the extended family members of the 47 of the approximately 5,500 adopted children who had developed schizophrenia, and matching them against 47 children who had not developed schizophrenia, they found that first-degree biological relatives of schizophrenic adoptees had a 5 percent risk for developing schizophrenia, and a 0 percent risk for first-degree relatives of adoptees who had no mental illness. When the researchers broadened their definition of schizophrenia to include "schizophrenia spectrum disorders" (nonpsychotic disorders thought to be related to schizophrenia but that are not as severe, such as schizoid personality disorder), they found much higher rates of risk among the biological parents of adopted-away children with schizophrenia 20.3 percent, than among biological parents of nonaffected adopted-away children, 5.8 percent. These famous Danish studies further confirmed the role of heredity in the development of not only schizophrenia but also "schizophrenia spectrum" disorders. The results of this first adoptees family design was published in the journal *Behavior Genetics* in 1976.

The most recent adoption study of schizophrenia was carried out by P. Tienari and colleagues in Finland and published in *Acta Psychiatrica Scandinavica* in 1991. They found lifetime prevalence risk for developing schizophrenia that was consistent with earlier adoption studies, a 9.4 percent risk for adopted-away children of schizophrenic parents, and an analogous risk of only 1.2 percent in adopted-away children of nonaffected parents. However, an interesting finding of the Finnish adoption study pointed to an association between the genetic predisposition to schizophrenia and psychological abnormalities in the adopting parents. Whether this evidence for a specific "shared environment" effect is supported in future studies remains to be seen.

Critics of some of the adoption studies, such as E. Fuller Torrey and R. H. Yolken, argue that "shared environment" effects cannot be ruled out. In an article they published in *Brain Research Reviews* in 2000, Torrey and Yolken note that the adopted-away children in these studies shared a uterine environment with their mothers. Factors such as oxygenation, possible exposure to drugs, chemical agents, or infectious agents (such as viruses) may be part of the common shared environment of mother and child that has had a more important influence on the development of schizophrenia than genes. Also, many of the adopted-away children in adoption studies lived with their biological mother for weeks or months before being adopted, thereby sharing a postnatal environment.

Subtype differences One of the enduring dilemmas in schizophrenia research is whether or not scientists are studying one disease or several related diseases. The noted schizophrenia researcher Irving Gottesman and others take the position that the various classical subtypes of schizophrenia (paranoid schizophrenia, hebephrenia or the disorganized subtype, catatonic schizophrenia, and so on) are perhaps best viewed as expressions of a single disease process on a continuum from less to more severe forms of the disorder and are not genetically distinct disorders. In fact, genetics studies of schizophrenia do not provide support for these classic subtype differences, indicating that future diagnostic manuals that may be based on as-yet undiscovered facts about the biological nature of schizophrenia may no longer include such subtypes. The only evidence suggestive of a genetic basis for a subtype of schizophrenia involves (a) the classic hebephrenic or disorganized subtype, considered to be a much more chronic and disabling form of the disorder, and (b) T. J. Crow's Type II schizophrenia, which is characterized by early onset, poorer prognosis, and predominance of negative symptoms. However, even this genetic evidence is weak and may not be supported in future studies.

Molecular Genetics

Molecular biology The computer revolution that began in the 1970s and has changed our world forever has been the driving force behind an analogous revolution in biology. Increasingly new and more powerful computing technologies have enabled us to study life at the level of molecules, resulting in the current international effort to understand the location and functioning of the genes in the human genome. This effort will be followed by the rise of proteomics, the study of the formation and dynamics of proteins. All that genes do, after all, is code for specific proteins. The causal link between genes, proteins, and the development of complex bodily structures and behaviors (including diseases such as schizophrenia) is a task that may very well take us into the 22nd century. Still, the current revolution in molecular genetics will go hand in hand with future studies of behavioral genetics in an effort to close the yawning chasm of our gap in knowledge of how segments of certain DNA molecules and a person suffering from schizophrenia are somehow causally related. At present, the two primary methods for identifying the genes involved in schizophrenia are linkage analysis and association studies.

Linkage analysis Linkage analysis is a useful method for locating single genes that have a powerful effect. These genes are located through tracing DNA markers that are linked, or are in close proximity to them, on a particular chromosome. Until the development in 1980 by D. Botstein and colleagues of the technique of using restriction fragment length polymorphisms (RFLP) as a mapping tool, it was not possible to search reliably for specific candidate genes for schizophrenia. In the late 1980s, RFLP research was supplanted by the development of new methods for detecting variations within genomic DNA. These also led to the identification of segments of DNA on chromosomes that could be used as "DNA markers" that could be traced through the pedigrees of families afflicted with schizophrenia and other diseases. There are several different classes of DNA markers that are used in this research, such as restriction endonucleases (REs), variable number of tandem repeats (VNTRs), simple sequence repeat (SSR) polymorphisms, and single nucleotide polymorphisms (SNPs or "snips"). In linkage analysis, DNA must be taken from many members of different generations in multiple families in which schizophrenia is present (multiply affected pedigrees). Linkage analysis is a powerful technique for tracing monogenetic traits (such as the single genes leading to monogenetic diseases like Huntington's disease) but is a much less powerful technique for identifying the genes underlying complex traits—like most human behaviors or diseases such as schizophrenia.

The completion of the first draft of the Human Genome Sequence in 1999, and the availability of this map for researchers, has accelerated research in the search for the candidate genes that are implicated in the cause and/or pathophysiology of schizophrenia. Specific regions of almost every chromosome have been suspected of containing schizophrenia genes, but many of the studies have not found confirmation in replication attempts by other researchers,

The first linkage analyses in schizophrenia research both implicated segments of chromosome

5. In an article published in the British journal *Lancet* in 1988, Anne Bassett and her colleagues published a study of an Asian-Canadian family in Vancouver in which they identified a locus on chromosome 5q found in a young man with schizophrenia and his schizophrenic uncle but which did not appear in the rest of the family. That same year, in an article published in *Nature,* Robin Sherrington and colleagues reported the results of the first true linkage analysis of schizophrenia, using data from 7 British and Icelandic families. They, too, found a link between schizophrenia and chromosome 5q (specifically, 5q11-13). Replication studies by others found that the results of these two studies were due to false positives and therefore were incorrect. Other linkage studies over the past 18 years have implicated the following regions: chromosome 22q, chromosome 8p, chromosome 6p, chromosome 10p, chromosome 6q, chromosome 13q, chromosome 15q13-q14, chromosome 18, chromosome 1q, and the X chromosome. Overall, at the present time there is no reliable agreement about the involvement of any of these regions in schizophrenia, although chromosomes 6, 8, 13, and 22 hold the most promise at present for the location of schizophrenia susceptibility genes.

One recent finding of great interest has been the location of a candidate gene for schizophrenia, *neuregulin 1,* that was found on region 8p in an Icelandic study conducted by Hreinn Stefansson and colleagues. The results were published in the *American Journal of Human Genetics* in 2002. This particular gene plays a role in the expression and activation of neurotransmitter receptors in the central nervous system, especially receptors for glutamate, a neurotransmitter that has been linked to the pathophysiology of schizophrenia since 1980.

Candidate genes for schizophrenia found on chromosomes 1, 1, 20, and 22 were found in a unique study by Ming T. Tsuang, C. C. Liew, and their colleagues in which they claim to have developed an RNA-based blood test for differentially diagnosing schizophrenia from bipolar disorder and from other psychiatric disorders and normal controls. These candidate genes have been previously linked to inflammatory/immunological processes in the body and to human brain development (this latter finding perhaps lending support to the NEURODEVELOPMENTAL MODEL OF SCHIZOPHRENIA). This study, published in January 2005 in the *American Journal of Medical Genetics Part B* (*Neuropsychiatric Genetics*) may be the first step toward developing a reliable diagnostic BLOOD TEST FOR SCHIZOPHRENIA.

Association studies Due to the confusing results of linkage studies, it is thought that perhaps schizophrenia is not caused by the expression of one or more powerful genes, but instead by multiple genes of small effect, none of which alone is necessary or sufficient to cause the disorder. Linkage analysis cannot detect small-effect genes contributing in an additive way with other such genes, nor can it detect small-effect genes interacting with other genes, nor small-effect genes interacting with the environment. The methods of association studies are more sensitive to detecting genes with small effects.

Association studies compare the frequencies of genetic marker alleles in a group of persons with schizophrenia and to those found in a sample of control subjects who do not have schizophrenia. A statistically significant difference suggests (a) a tight linkage to a marker allele and a disease mutation (linkage disequillibrium), or (b) the marker allele itself contributes to the cause of schizophrenia. The assumption is that the two loci are so close together that they have not been separated by recombination over several generations. Alleles at the two loci are therefore assumed to be "associated," even in individuals with schizophrenia from different families.

Candidate genes Candidate genes that have been examined to see if there is an association to schizophrenia have primarily been those that code for proteins that are involved in the neurochemistry of the disorder—specifically, dopamine, serotonin, and glutamate receptors. The inspiration for these genetic studies derived from the DOPAMINE HYPOTHESIS of schizophrenia. It had been suggested in 1966 by Jac van Rossum that antipsychotic drugs worked by blocking dopamine at the post-synaptic receptor cite, so the next logical step was to infer that schizophrenia might be caused by a dysfunction of the dopamine neurotransmitter system in the brain. By 1972 the technology of radio-labeling allowed, for the first time, the positive identification of neurotransmitter receptors in the brain. Five dopamine

receptors have been identified since then, two D1 receptors and three D2 receptors. ANTIPSYCHOTIC DRUGS work on the D2 receptors and not the D1 receptors. The regions of the chromosomes that code for these D2 receptors are now known, and are located on chromosomes 3 and 11. Seven serotonin receptors have been identified (5HT-1 to 5HT-7) and the corresponding genes have been located. Three genes linked to dopamine and serotonin are among the top 12 candidate genes for schizophrenia thus far (see below). However, none of these genes for dopamine or serotonin receptors have been conclusively linked to the cause of schizophrenia—meaning that schizophrenia is not caused by a neurotransmitter dysfunction—but they certainly must play a role in the pathophysiology of the disorder.

As of July 2005, the strongest evidence for candidate genes for schizophrenia centers on four genes: *DISC1* (*Disturbed in schizophrenia 1*), located on chromosome 1 (1q42.2); *DTNBP1* (*Dystrobrevin binding protein 1*), located on chromosome 6 (6p22.3); *NRG1* (*Neuregulin1*), located on chromosome 8 (8p12); and *RGS4* (*Regulator of G-protein signaling 4*), located on chromosome 1 (1q23.3). Eight other candidate genes have less support but are still considered possibilities: *AKT1* (14q32.33); *COMT* (22q11.21); *DRD3* (3q13.31), the dopamine receptor D3 gene; *G30/G72* (13q33.2); HTR2A (13q14.2), the serotonin receptor 2A gene; *PRODH* (22q11.21); *SLC6A4* (17q11.2), the serotonin transporter gene; and *ZDHHC8* (22q11.21).

Treatment implications of genetics studies of schizophrenia The most likely innovation in the treatment of schizophrenia that may follow from basic genetic research is the development of designer drugs tailored to treatment-resistant patients. Medical geonmics companies are focusing their research on single nucleotide polymorphisms (SNPs or "snips"), very small differences in the same gene in a population, which may be responsible for the commonly observed fact in medicine that some persons respond to a new drug but others do not. The term for this area of research—*pharmacogenetics*—was first used in an article by F. Vogel in a German pediatrics journal in 1959 in reference to the speculation that adverse effects of medication in some persons and not in others may be due to genetic differences. As of September 2005, no such pharmacogenetic drugs for schizophrenia have been developed. Gene therapy for the treatment of disease has turned out to be an exceedingly problematic (and sometimes dangerous) experimental therapy and is unlikely to be an option for persons with schizophrenia at anytime in the near future.

Useful Web Sites

Trying to keep up with the almost daily reports of new research on the genetics of schizophrenia is difficult. The Web sites of the following associations continually post new scientific information relating to the genetics of schizophrenia and other mental disorders and genetic counseling: the International Society of Psychiatric Genetics (www.ispg.net), the Behavior Genetics Association (www.bga.org), the International Society for Twin Studies (www.ists.qimr.edu.au), and the National Society of Genetic Counselors (www.nsgc.org). For more information on the terminology and history of genetics, see the Web site of the Cold Spring Harbor Laboratory (http:vector/cshl/org).

Summary

The following conclusions can be drawn from the present state of research into the genetics of schizophrenia:

(1) Schizophrenia is a familial disease, passed from one generation to another within a family in unpredictable ways, and genes are involved in transmitting a vulnerability to the disease.
(2) Almost all 23 chromosomes have been implicated as continuing regions where possible genes linked to schizophrenia may reside, but the evidence for specific candidate genes is generally weak and contradictory. There is no evidence of "schizogenes" that directly lead to the development of schizophrenia that are analogous to the gene that causes Huntington's disease, to name one example.
(3) Behavioral genetics studies of schizophrenia indicate that nongenetic factors play a sizeable role in the cause and pathophysiology of schizophrenia, and some RISK FACTORS are well known from epidemiological studies.
(4) Schizophrenia is not caused by a chemical imbalance in the brain (i.e., dopamine system dysfunctioning) as so many family members of people with schizophrenia are told every

day, but such neurotransmitter irregularities are instead representative of the disease process (pathophysiology).
(5) Estimates of the high heritability of schizophrenia derived from twins studies must be interpreted with caution. High heritability does not imply causation.
(6) Schizophrenia is most probably related to the activity of multiple genes with small effects.
(7) The cause of schizophrenia is unknown. What is known is that genes alone do not cause schizophrenia.

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Weygandt, W. "Kritische Bemerkungen zur Psychologie de Dementia praecox," *Monatsschrift für Psychiatrie und Neurologie* 22 (1907): 289–301.

genetic transmission Despite almost 90 years of the study of the genetics of SCHIZOPHRENIA, the pattern of the transmission of the disease from family member to family member is unknown. Several possible models of the mode of genetic transmission of schizophrenia have been proposed.

There are, however, essentially two major varieties. One type of model proposes that a single major gene has defects that predispose an individual to a particular disease. This is known as a monogenetic transmission model. It is also sometimes called the "generalized single locus (GSL) model" or, by others, a "Mendelian pattern," since the defective gene in classical MENDELIAN TRANSMISSION patterns (the first genetic transmission patterns ever identified) is either a dominant gene, a recessive gene, or a sex-linked gene (a single gene located on a sex chromosome). This is the oldest model for the genetic transmission of schizophrenia and was first proposed by Rosanoff and Orr in 1911. This monogenetic model of genetic transmission is the type more likely to be detected through LINKAGE ANALYSIS statistical procedures, which are considered more powerful than SEGREGATION ANALYSIS in the detecting of a single gene that may be responsible for the predisposition to schizophrenia.

More than 3,000 physical diseases (albeit somewhat rare ones) have been found to be monogenetic and are transmitted according to Mendelian patterns. Much research continues to be conducted in the hope that mental illnesses may also be transmitted in this "single gene" fashion.

The second type is polygenetic models of transmission, sometimes called "non-Mendelian models of transmission." The assumption here is that the genetic predisposition to a particular disease is the result of an additive effect. That is, the predisposition exists only through the combined effects of several genes. There are many physical characteristics that are polygenetically determined in all of us, such as height and intelligence. Furthermore, many physical illnesses such as diabetes are polygenetically determined. MENTAL DISORDERS, especially schizophrenia and BIPOLAR DISORDER, are likewise thought to be more likely to follow a polygenetic pattern of transmission. Computer models of transmission that also account for environmental factors in the development of the disease are called MULTIFACTORIAL THRESHOLD MODELS OF GENETIC TRANSMISSION, first proposed by Falconer in 1965 and adapted to schizophrenia by Gottesman and Shields in 1967. This is a form of a DIATHESIS-STRESS THEORY of schizophrenia.

Another idea that combines concepts from the monogenetic and polygenetic models is the GENETIC HETEROGENEITY of a particular disorder. The hypothesis here is that the same disease (schizophrenia) may be caused by any one of a number of genes located in different places (multiple loci). Any one of these genes alone would be sufficient to cause the disorder. Thus, while conflicting results of research may place the "schizophrenia-gene" at first on chromosome 5, then chromosome X, this may just be confirming evidence for the genetic heterogeneity of schizophrenia.

There continues to be much debate among researchers as to whether schizophrenia and the psychotic disorders follow a monogenetic or a polygenetic mode of transmission, or a "mixed model" of the two. As of 2006 the mode of genetic transmission of schizophrenia is unknown.

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Rosenthal, D., and S. Kety. *The Transmission of Schizophrenia.* Oxford: Pergamon Press, 1968.

genome A combination of the words *gene* and *chromosome,* the word genome is the complete set of chromosomes derived from one parent; or it can refer to the total gene complement of a set of chromosomes found in higher life forms. On April 27, 1989, an announcement was made at Cold Spring Harbor Laboratory in New York State, a major genetics research center, that an international organization of geneticists was being formed to initiate an immense project to identify and define all human genes and genetic material. In 1999 an announcement was made of the completion of the first draft of the human genome. By 2005 it was estimated that there are 25,000 genes in the human genome.

genotype The genetic composition of an individual. It may also refer to a gene combination at any one locus or with respect to any specified combination of loci.

Geodon See ANTIPSYCHOTIC DRUGS.

Germany Prevalence studies for SCHIZOPHRENIA conducted in the 1930s found prevalence rates ranging from 1.9 to 2.6 per 1,000. Current evidence suggests that the prevalence rates have not changed in Germany since the 1930s.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

Ghana The West African country of Ghana (formerly the Gold Coast) has been the subject of several SCHIZOPHRENIA prevalence studies since the

1940s. The most striking finding is that in one area of northern Ghana the prevalence of schizophrenia increased sharply between 1937 and 1963. Since this coincided with the pervasive introduction of Western cultural influences, the Ghana studies are often cited by E. Fuller Torrey as possible indications that schizophrenia is a "disease of civilization."

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

Gheel Colony Gheel, Belgium, has been the home of a shrine to Saint Dymphna, the patron saint of the mentally ill, since the 11th century. Many miraculous cures are said to have taken place there. However, by the 14th century the large number of mentally ill pilgrims was becoming unmanageable, and a hospital and humane system of family care were established. Mentally ill pilgrims would be placed in local households and be under the foster care of family members. Although as recently as the late 1930s it was reported that as many as 4,000 mentally ill persons were under foster care in the community, by the 1960s this number had been significantly reduced, with about 1,700 being served in 1970. However, the Belgian Ministry of Public Health still provides psychiatric services for these people in the Gheel Colony. The hospital that works with the families of the area is called the Rijkspsychiatrisch Ziekenhuis-Centrum voor Gezinsverpleging (the "State Psychiatric Hospital Center for Family Care.").

The Gheel Colony is a remarkable example of how the severely mentally ill can be integrated into society as an alternative to institutionalization. Attempts to copy the "Gheel model" of care in Great Britain and the United States in the 19th century were known as the "cottage system" or as "boarding-out," but no successful long-term program based on the Gheel Colony has ever been devised.

American psychiatrist William Alanson While made a series of trips, beginning in 1906, to visit European hospitals for mental disease. In his memoirs, he gives a colorful description of the unique system of community care for the mentally ill at Gheel:

> One of the most interesting of my visits was to Gheel, in Belgium, where the patients for the most part live with the families that make up this settlement. The hospital itself, the so-called *asile fermé,* occupies the central position. The little town of Gheel consists for the most part of a few stores on one side of a single street, and the country for twenty miles about is occupied by peasants who live upon and cultivate the land. This condition has been maintained over many centuries. The patients who are sent there are studied in the central asylum and if found to be sufficiently reliable are sent out to the little farm cottages, where they live with the peasant's families. The doctor makes his rounds once a month on his bicycle, sees the patient, chats with him and weighs him, the weight being considered one of the outstanding evidences that the patient is being properly cared for. I visited a number of these homes and found that the patient's room was a plain affair furnished only with a bed and a chair and perhaps a table and a rug, with a crucifix at the head of the bed. The patient himself, treated as a member of the family, could usually be found downstairs or nearby, engaged in the household work or the work of the farm.

Parry-Jones, W. L. "The Model of the Gheel Lunatic Colony and Its Influence on the Nineteenth-Century Asylum System in Britain." In *Madhouses, Mad-Doctors, and Madmen: The Social History of Psychiatry in the Victorian Era,* edited by A. Scull. London: Athlone Press, 1981.

White, W. A. *William Alanson White: The Autobiography of a Purpose.* Garden City, N.Y.: Doubleday, Doran, 1938.

glossolalia This is the technical term for the phenomenon of "speaking in tongues," the bizarre babbling and emission of sounds that is often part of an ecstatic religious ritual involving an altered state of consciousness. Although the phenomenon is ancient in origin, it is commonly observed in certain fundamentalist Christian or "charismatic" Roman Catholic gatherings, especially in the United States and Canada. The speech in glossolalia may seem like the NEOLOGISMS or WORD SALAD of a psychotic disorder, but it is in fact an innocuous situation-specific behavior that does not necessarily indicate a mental disorder.

Goodman, F. *Speaking in Tongues: A Cross-Cultural Study of Glossolalia.* Chicago: University of Chicago Press, 1972.

glutamate hypothesis Glutamate is the main neurotransmitter in both the sensory and motor neural circuits of the cerebral cortex of the brain. In 1980 J. Kim and three other colleagues published a study in which it was hypothesized that a "hypoactivity" of the glutamanergic system may be linked to the pathophysiology of schizophrenia. This glutamate hypothesis of schizophrenia in its pure form has already been rejected, just as the simple "single-system" forms of the DOPAMINE HYPOTHESIS (1966) and the SEROTONIN HYPOTHESIS (1954) have been. Since 1980 numerous studies of the activity of glutamate in schizophrenia have been conducted. Glutamate receptor genes, glutamate receptor binding, and glutamate receptor expression in the cortical, striatal, and temporal lobe structures in the brain have been examined in the past decade. The exact role of glutamate in schizophrenia is presently unknown.

Kim, J., et al. "Low Cerebralspinal Fluid Glutamate in Schizophrenic Patients and a New Hypothesis on Schizophrenia," *Neuroscience Letters* 20 (1980): 379–382.

Goffman, Erving (1922–1988) Goffman was a noted Canadian sociologist who is best remembered for his book *Asylums* (1961), which contained a series of essays on his research on the interactive effects of institutions and the persons who are confined and work in them. Goffman conducted his research between 1954 and 1957 as a visiting member of the Laboratory of Socio-environmental Studies of the NATIONAL INSTITUTE OF MENTAL HEALTH in Bethesda, Maryland. For a period of one year (1955–56) he worked "undercover" in St. Elizabeth's Hospital in Washington, D.C., one of the country's largest mental hospitals with a census of over 7,000 patients. His depictions of the social world of the "hospital inmate," especially how this world is subjectively experienced by this person, offer a picture of how such institutions systematically dehumanize not only their "inmates," but the staff as well. He especially emphasized the ways in which inmates survive in the closed worlds of "total institutions" by "making-do" in a bad situation. The thesis of Goffman's book is that perhaps the most important influence on the behavior of a mental hospital patient is the institutional environment and not the illness, and that the reactions and adjustments of a patient in a mental hospital are similar to those of inmates in other types of institutions (e.g., prisons).

Goffman, E. *Asylums: Essays on the Social Situation of Mental Patients and Other Inmates.* New York: Doubleday, 1961.

Goldstein, Kurt (1878–1965) A German psychiatrist perhaps most remembered for his studies of brain-damaged patients and schizophrenics. He proposed the idea that there were two essential types of thought, "concrete" and "abstract," and that brain-damaged people and schizophrenics had lost their capacity for abstract thought and instead exhibited concrete thought patterns. Goldstein felt that brain damaged people adopted the "concrete attitude" to avoid ANXIETY and "catastrophic reactions"—an agitated state of panic and rage that is a reaction to the frustrations brought on by the limitations imposed in thought and action by brain damage. His contribution to the study of SCHIZOPHRENIA was the further recognition of the fact that, at least in some forms of the disorder, it resembles an organic brain disease.

Goldstein, K. *The Organism.* New York: American Books, 1939.

———. "The Significance of Psychological Research in Schizophrenia," *Journal of Nervous and Mental Disease* 97 (1943): 261–279.

governess psychosis In the 19th century, when much less was known about the causes of the psychotic disorders, it was thought that certain occupations might predispose one to madness. Sometimes the exposure to certain chemicals or materials was the reputed cause, such as the

chemical used by hatters or shoemakers, or the vapors inhaled from the mining of lead (causing a form of insanity known in 19th-century Scotland as "mill-reeck"). However, most of the time no such material causes could be found. Artists, poets, and other creative people are perhaps the best known example, but (at least in Europe) the profession of being a "governess" to the children of wealthy parents was also commonly regarded as possibly contributing to the development of a serious mental illness—especially DEMENTIA PRAECOX (SCHIZOPHRENIA). In the conventional folk wisdom of the time, and even in psychiatric journals, it was commonly speculated that there was a mental disorder known as a "governess-psychosis." This topic was taken so seriously in the latter half of the 19th century that Eugen BLEULER felt the need to consider the issue in his chapter on "The Causes of the Disease" in his 1911 book, *Dementia Praecox, Or the Group of Schizophrenias:*

> For decades the idea has been preserved that governesses were especially prone to develop schizophrenia. Some authors even spoke of a "governess-psychosis"; and it has been maintained that governesses suffer a particularly severe (and unpleasant) form of the disease. There may be something in this, inasmuch as young women become governesses who have ambitions of raising their social standing beyond their capacities and among whom there must be many with schizophrenic predisposition. The treatment they often receive at the hands of their employers gives occasion for determining a schizophrenia. However, it must certainly be first established whether or not governesses really do suffer in greater numbers than members of other vocations.

See also MAD HATTER, MAD AS A HATTER.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenias,* trans. J. Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

grandiose type One of the common types of delusional (paranoid) disorder. GRANDIOSE DELUSIONS are often those in which a person is convinced that he or she has some special ability or status that elevates him or her above all others. These may be delusions of unlimited riches, of the possession of special powers or abilities, or that the person has been given a divine calling of some sort. People may even believe that they are a famous person. However, in delusional disorder, these usually fixed delusions do not impair intellectual, social, and occupational functioning as similar grandiose delusions do in the paranoid subtype of schizophrenia. The early 19th-century French descriptions of the mental disorder that Esquirol named MONOMANIA are perhaps most clearly found today in this grandiose type of delusional disorder.

See also PARANOID SCHIZOPHRENIA.

grandiosity An inflated belief about one's importance, worth, knowledge, or identity. In the psychotic disorders, GRANDIOSE DELUSIONS are common, particularly in the paranoid subtype of schizophrenia and in the manic phase of BIPOLAR DISORDER. A manic individual with grandiose delusions may believe that he or she has a "special message" or "talent" that no one in the world has, or may grossly overestimate their assets and create huge debts while on a shopping spree or in business transactions. People with the paranoid subtype of schizophrenia may believe that they are a famous rock music star (Mick Jagger and Madonna seem to be the favorites in American psychiatric hospitals) or are married to one.

See also PARANOID SCHIZOPHRENIA.

Griesinger, Wilhelm (1817–1868) German psychiatrist who is regarded as the "father of biological psychiatry." The 1861 second edition of Griesinger's famous textbook, *Mental Pathology and Therapeutics,* was a turning point in the history of psychiatry as it shifted the center of major scientific contributions in the field from France, whose *aliénistes* had dominated psychiatry in the first half of the 19th century, to Germany. German psychiatrists dominated the field well into the early 20th century.

Born in Stuttgart, Griesinger was educated in Germany, Switzerland, and France. After finishing his medical studies, he took a position at the

Winnenthal asylum in Württemberg. His two years there seem to have been the only period in which he was involved in full-time clinical work with patients, as he held mainly administrative and teaching positions throughout the remainder of his life. His experience at Württemberg formed the basis of the ideas and observations of his 1845 first edition. After accepting a position as professor of medicine in Zurich in 1860, Griesinger was in charge of planning and supervising the construction of a large new hospital for the treatment of the mentally ill—the famous BURGHÖLZI HOSPITAL, which Eugen BLEULER later managed in the early 20th century. He also founded a major psychiatric journal, which continues to be published today—the *Archiv für Psychiatrie und Nervenkrankheit.*

Griesinger made a major contribution to psychiatry with his strong emphasis on the brain and nervous system as the source of all mental disorders. His classifications of mental disorders and their clinical descriptions were widely adopted in Germany and elsewhere. His scientific philosophy still reigns today in our current research efforts to unlock the secrets of the psychotic disorders:

> Insanity being a disease, and that disease being an affection of the brain, it can therefore only be studied in a proper manner from the medical point of view. The anatomy, physiology, and pathology of the nervous system, and the whole range of special pathology and therapeutics, constitute preliminary knowledge most essential to the medical psychologist.

Griesinger, W. "The Care and Treatment of the Insane in Germany," *Journal of Mental Science* 14 (1868–69): 1–34.

———. *Mental Pathology and Therapeutics.* 2nd ed., trans. C. L. Robertson and J. Rutherford. 1861. Reprint, New York: William Wood, 1882.

Marx, O. M. "Wilhelm Griesinger and the History of Psychiatry: A Reassessment," *Bulletin of the History of Medicine* 46 (1972): 522–544.

group psychotherapy Group therapy came into vogue in the latter half of the 20th century, and from an administrative and therapeutic point of view it seemed the perfect treatment for institutionalized patients. Group meetings of a wide variety have been almost universally adopted by those who perform psychiatric services in institutional or quasi–institutional settings (e.g., aftercare programs), particularly since the resources do no exist to provide every patient with consistent individualized treatment.

Insight-oriented group therapy, which is designed to explore deeply personal emotional issues, has until recently been the primary mode of group-oriented treatment for institutionalized schizophrenics. Although patients with less serious psychiatric diagnoses (that is, nonpsychotic disorders) may benefit from such emotionally intense group experiences, research shows that insight-oriented group psychotherapy may actually worsen psychotic symptoms. At best, as J. M. Kane concludes in 1989 in a major review of the research on the effectiveness of different treatments in schizophrenia,

> Many clinicians have suggested the value of group therapy during the inpatient phase of the treatment of schizophrenia. Several review articles have appeared on this topic. . . . By and large, the results from studies designed to assess the impact of group therapy when used with or without medication have not been positive, though there are some exceptions.

Instead, much of the research indicates that the focus should be shifted from the idea that the disease process in schizophrenia is somehow being alleviated through insight-oriented group (or individual) therapy, as it most probably is not, to the idea that the focus of groups should be a structured program that teaches adaptive social and vocational skills. Likewise, the research indicates that insight-oriented family therapy (see FAMILY INTERACTION THEORIES), which views the cause of the illness in family interaction patterns, should instead be replaced by structured psychoeducational programs for family members that can teach them how their behavior affects the course of the schizophrenic relative's illness and how to accentuate the positive aspects of that influence. Such

"family management strategies" can reduce the rate of relapse for schizophrenia (see EXPRESSED EMOTION).

Given the evidence that traditional insight-oriented "group therapy" is essentially useless in arresting the schizophrenic disease process, this knowledge should have profound effects on the treatment of schizophrenics in public institutions. For example, psychiatrists and psychologists would no longer be necessary for conducting "group therapy," since individuals with only a high school or college degree could be given specialized training in the methods of structured psychoeducational or supportive programming for schizophrenics. Such policies could have profound economic benefits since these people could be hired at far lower wages than clinical personnel and yet with the same therapeutic effect for the patients.

Conceptions of "group therapy" for the treatment of schizophrenics therefore have changed radically in the 1980s. When the patient is hospitalized during the acute stages of the psychosis, structured interaction with the patient, either individually or in a group situation, should be supportive and psychoeducational. However, research shows that inpatient "social skills" or "reality-adaptive-supportive therapy" or post-discharge "family management strategies" in combination with antipsychotic drugs are more effective than just the drugs alone; the research also indicates that the positive effects of these psychosocial strategies are only good for a year or so after discharge. Schizophrenia is, after all, in most of its manifestations a chronic brain disease of an unknown origin, and it appears that the organic disease process eventually counteracts the therapeutic gains of psychosocial treatment, no matter how intense or consistent the program may be. The true therapy of the future for schizophrenia will almost certainly be biologically based. And although "group therapy" is almost universally mandated by the administrators of state hospitals as part of the "usual treatment" of institutionalized patients, it may one day be regarded as quaint and as ultimately useless as the "usual treatments" of the 19th century—bleeding, bathing, and purging—seem to us today.

Penn, D. L., and K. T. Mueser. "Research Update on the Psychosocial Treatment of Schizophrenia," *American Journal of Psychiatry* 153 (1996): 607–617.

gustatory hallucination This is a hallucination of taste. People who report gustatory hallucinations often report an unpleasant taste in their mouth. This type of HALLUCINATION is less common than other types, particularly AUDITORY HALLUCINATIONS.

gyrator (or "gyrater") A mechanical device invented by Benjamin RUSH and used at the Pennsylvania Hospital in Philadelphia in the early 1800s. Based on the CIRCULATING SWING used by English physician Joseph Mason Cox (1762–1822) at the Fishponds Private Lunatic Asylum in Stapleton, England, the gyrator was a machine on which a patient would apparently sit and be rapidly spun around by its gyrations to bring the blood to the brain. In his 1812 textbook, *Medical Inquiries and Observations Upon the Diseases of the Mind,* Rush describes his "gyrater" under the heading of "Exercise" as a recommended treatment:

> EXERCISE. This should consist of swinging, see-saw, and an exercise discovered by Dr. Cox, which promises more than either of them, and that is, subjecting the patient to a rotary motion, so as to give a centrifugal direction of the blood towards the brain. He tells us he has cured eight persons of torpid madness by this mode of exercise. I have contrived a machine for this purpose in the hospital, which produces the same effects upon the body which are mentioned by Dr. Cox. These are vertigo and nausea, and a general perspiration. I have called it a Gyrater. It would be more perfect, did it permit the head to be placed at a greater distance from its center of motion. It produces great changes in the pulse.

Not satisfied with the "gyrater" he invented for use at the Pennsylvania Hospital, Rush provides the following suggestions for a more effective machine:

> A cheap contrivance, to answer all its purposes, might easily be made, by placing a patient upon

a board moved at its centre upon a pivot, with his head toward one of its extremities, and then giving it a rotary motion. The centrifugal force of the blood would exceed, in this way, that which it receives from the chair employed by Dr. Cox or from the gyrater in the Pennsylvania Hospital.

Many descriptions of Rush's "gyrater" incorrectly describe it as this latter machine suggested by Rush as an improvement on the gyrater.

Rush B. *Medical Inquiries and Observations upon the Diseases of the Mind.* Philadelphia: Kimber & Richardson, 1812.

hair pulling See TRICHTILLOMANIA.

Haiti See BOUFFÉE DÉLIRANTE.

Haldol See ANTIPSYCHOTIC DRUGS.

hallucination A hallucination is an event that is experienced as a sensory perception (e.g., the sound of a voice, the sight of someone or something) but, in fact, is not real. The relevant sensory organs, such as the ears or eyes, are not physically stimulated, yet the person reports a sensory experience. A hallucination is experienced as real, and it may be perceived as originating from outside a person's body (as with the usual sensory experiences of sight and sound), or it may be felt to come from within a person's own body. For example, a person may report "hearing voices," but the voices may be experienced as coming from within the head rather than from outside it. A delusional interpretation (if present) of a hallucination, may be consistent with a person's belief system or, if the person is psychotic, with his delusional system. Hallucinations are distinguished from delusions in that a hallucination is a disturbance of perception whereas a delusion represents a pathological distortion of normal ideation.

Hallucinations occur in the form of one or more of the five senses: sight (VISUAL HALLUCINATIONS), sound (AUDITORY HALLUCINATIONS), taste (GUSTATORY HALLUCINATIONS), touch (TACTILE HALLUCINATIONS), and smell (OLFACTORY HALLUCINATIONS). Hallucinations can be mood congruent or mood incongruent in content, with either a manic or depressed mood. For example, a depressed individual who is also experiencing auditory hallucinations may hear voices telling him that he is worthless, useless or perhaps may urge self-mutilation or suicide.

Hallucinations are only to be considered a symptom of a psychotic disorder if there is also a clearly demonstrated break with reality in the mental state of the individual. Hallucinations are often thought of as immediately signifying that a person is psychotic, but this is not the case. People who have many other types of MENTAL DISORDERS, such as effective disorder and even personality disorder, can experience transient hallucinations. Even normal individuals can experience transient hallucinations from time to time. The most commonly reported hallucinatory experience reported in people without mental disorders is hearing a voice calling one's own name. Hallucinations that occur within the context of intense religious experiences are not necessarily to be considered a sign of mental illness.

The word *hallucination* first appeared in the English language in 1572 in a work by Johann Kaspar Lavater, referring to "ghostes and spirites walking by nyght" (in other words, "apparitions"). However, its original derivation is from a Greek word meaning "to wander in mind." J. E. D. ESQUIROL was the first to recognize the importance of hallucinations as a symptom of mental disorder in his 1838 textbook, *Des Maladies Mentales.* In the chapter "Hallucinations," Esquirol constructs a definition of hallucinations that is still the basis of the one employed in the most current diagnostic manual of mental disorder—*DSM-IV* (1994). Esquirol defines a hallucination as "a thorough conviction of the perception of a sensation, when no external object, suited to excite the sensation, has impressed the senses." Esquirol was also the first

to emphasize the distinction between a hallucination and an ILLUSION, in which an actual external stimulus is misperceived or misinterpreted. A pupil of Esquirol's and a member of the "Esquirol Circle," A. J. F. BRIERRE DE BOISMONT, wrote the first comprehensive textbook on the clinical and cultural manifestations of hallucinations, and this book was translated into English and published in 1853.

Hallucinations (as well as delusions) were regarded as an important symptom of schizophrenia by many of the early authorities on schizophrenia, but they differed in regard to how necessary the presence of hallucinations in a person was to making the diagnosis of schizophrenia. For example, although many authorities have considered hallucinations, particularly auditory hallucinations, as a defining sign of schizophrenia as Kurt Schneider did with his FIRST-RANK SYMPTOMS, others have proposed that different symptoms might be better criteria for defining schizophrenia. Eugen BLEULER, for example, argued in 1911 that hallucinations and delusions are not among the four PRIMARY SYMPTOMS OF SCHIZOPHRENIA but instead are merely the ACCESSORY SYMPTOMS of the disorder. However, Bleuler realized how serious these accessory symptoms could be for the afflicted person. For as he remarks in his 1911 classic, *Dementia Praecox, Or the Group of Schizophrenias:*

> It is not often that the fundamental symptoms are so markedly exhibited as to cause the patient to be hospitalized in a mental institution. It is primarily the accessory phenomena which make his retention at home impossible, or it is they which make the psychosis manifest and give occasion to require psychiatric help.

Hallucinations, along with delusions, are considered to be the POSITIVE SYMPTOMS of schizophrenia. The most recent comprehensive review article on the theories and research findings on hallucinations was published in 1986 and was authored by G. Asaad and B. Shapiro.

With the introduction of BRAIN IMAGING techniques into the research on schizophrenia, particularly those that allow for "images" of a functioning brain (positron emission tomography and functional magnetic resonance imaging), in the 1990s many researchers succeeded in "capturing" auditory hallucinations while a person with schizophrenia was actually experiencing them. New "dysconnection," or "disconnection," theories of schizophrenia point to imbalances in the neural connection networks between the left frontal and left temporal lobes of the brain in their explanations of auditory hallucinations in schizophrenia.

Asaad, I., and B. Shapiro. "Hallucinations: Theoretical and Clinical Overview," *American Journal of Psychiatry,* 143 (1986): 1,088–1,097.

Brierre de Boismont, A. *Hallucinations, or, The Rational History of Apparitions, Visions, Dreams, Ecstasy, Magnetism and Somnambulism.* Philadelphia: Lindsay & Blakiston, 1853.

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity,* trans. E. K. Hunt. 1838. Reprint, Philadelphia: Lea & Blanchard, 1845.

Sarbin, T. R., and J. B. Juhasz. "The Historical Background of the Concept of Hallucination, *Journal of the History of the Behavioral Sciences* 3 (1967): 339–358.

Stern, E., and D. A. Silbersweig. "Neural Mechanisms Underlying Hallucinations in Schizophrenia: The Role of Abnormal Fronto-Temporal Interactions." In *Origins and Development of Schizophrenia: Advances in Experimental Psychopathology,* edited by M. F. Lenzenweger and R. H. Dworkin. Washington, D.C.: American Psychological Association, 1998.

hallucinatory verbigeration This is the term given by Emil KRAEPELIN in the eighth edition (1909–15) of his famous textbook, *Psychiatrie,* for the type of AUDITORY HALLUCINATION in which a patient hears essentially the same meaningless sentences over and over again. One of Kraepelin's patients wrote down the following nonsense sentences that he heard over and over again as an auditory hallucination: "For we ourselves can always hope that we should let ourselves pray other thoughts. For we ourselves wish to know who would let the swine's head be tormented to death with us foolishly."

Kraepelin, E. *Dementia Praecox and Paraphrenia.* Translated by R. M. Barclay and edited by G. M. Robertson. Edinburgh: E. & S. Livingstone, 1919.

haloperidol See ANTIPSYCHOTIC DRUGS.

handcuffs Until the mid-1800s, many extreme methods of MECHANICAL RESTRAINT were still in use in European asylums. Handcuffs were included among these instruments, which were more often used for punitive measures than therapeutic ones. One variant on the form of handcuffs that we think of today was a type that would hook onto iron rings on a heavy iron belt that circled the waist. Handcuffs were routinely employed at the asylum in Middlesex, England, until English physician John CONOLLY, a leading figure of the NONRESTRAINT MOVEMENT, became superintendent there in 1839.

harness, cruciform See BED SADDLE; CRUCIFORM STANCE.

Hartford Retreat An American private institution for the humane treatment of mental illness that was founded in Hartford, Connecticut, in 1824. It was based on the famous YORK RETREAT in England. For most of its first several decades, the Hartford Retreat admitted all patients who could pay and only a small portion of those who could not. However, these patients had to meet certain criteria and could not have a history of chronic mental illness. What's more, they would be discharged within six months regardless of their progress. Since "discharge rates" were often touted as "curability rates," the Hartford Retreat was praised by many, including Dorothea DIX and British author Charles Dickens, who visited it on his trip to America in 1842 and found it to be one of the few institutions in America that was worthy of merit.

However, when the retreat requested and received state funds in 1843, for the next two decades it shifted its role from one of a curative institution to a custodial one. More poor and chronic cases were admitted, and superintendents of the institution complained of the growing numbers of "filthy, noisy, or dangerous pauper lunatics" that filled its wards. In 1866 the state of Connecticut appropriated funds for a state asylum, allowing the Hartford Retreat to revert to a private institution for the wealthy. It later changed its name to the Institute for Living.

Goodheart, L. B. *Mad Yankees: The Hartford Retreat for the Insane in Nineteenth-Century Psychiatry.* Amherst: University of Massachusetts Press, 2004.

Haslam, John (1764–1844) An apothecary and researcher at the BETHLEM ROYAL HOSPITAL ("Bedlam"), Haslam produced some of the finest of the early psychiatric manuals; the 1798 *Observations On Insanity* and its expanded second edition of 1809, retitled *Observations on Madness and Melancholy.* He performed autopsies on the patients at Bedlam and described his observations in his written works. He also provided clinical descriptions of what were later known as general paralysis of the insane and the chronic, more degenerative form of schizophrenia now described by British psychiatrist T. J. Crow as Type II schizophrenia. Because Haslam and Philippe PINEL both seemed to provide the first descriptions of cases of this type of schizophrenia in 1809, Crow has given the name PINEL-HASLAM SYNDROME to Type II schizophrenia (see CROW'S HYPOTHESIS).

Haslam's descriptions of case histories seem to give a complete description of the disease process in CHRONIC SCHIZOPHRENIA, as we have come to know it, with an insidious onset in adolescence or early adulthood, classical signs and symptoms and a chronic deteriorating course. Prior to this time, many mental disorders had been described throughout the centuries, and although hallucinations and delusions had been commonly reported they had never been accompanied by descriptions of the developmental course of the disease. Therefore, Haslam and Pinel's simultaneous (but independent) publications of these case histories give us the first definite HISTORICAL EVIDENCE FOR SCHIZOPHRENIA as a distinct disease.

Haslam's descriptions in his 1798 book of what we now know as BIPOLAR DISORDER predate the French psychiatrist BAILLARGER's first thorough description in 1854 of a single disorder that combines both depressed and manic mood swings. When discussing "mania" and "melancholia" he insightfully asserts: "I would strongly oppose their being considered as opposite diseases." In a later passage in the same book, Haslam gives a

description of patients with bipolar disorder that is still accurate today:

> . . . for we see every day the most furious maniacs suddenly sink into a profound melancholy; and the most depressed and miserable objects, become violent and raving. We have patients in the Bethlehem Hospital, whose lives are divided between furious and melancholic paroxisms, and who, under both states, retain the same set of ideas.

In his writings, Haslam recommended the "gentleness of manner and kindness of treatment" of the insane popularized by Pinel with his *traitement moral* ("moral treatment"). However, some of his activities at "Bedlam" were deemed abusive by a House of Commons investigation in 1815, and he was fired from the staff of that institution without a pension after more than 20 years' service. At the time of his dismissal he was 56 years old and is credited by historians with knowing more about mental illness than any of his contemporaries in Britain. His works on the clinical and legal aspects of mental illness remain classics in the field and were influential in the early days of psychiatry.

See also BETHLEM ROYAL HOSPITAL.

Haslam, J. *Considerations on the Moral Management of Insane Persons.* London: Hunter, 1817.

———. *Medical Jurisprudence, as It Relates to Insanity, according to the Law of England.* London: 1809.

———. *Observations on Insanity, with Practical Remarks on the Disease, and an Account of the Morbid Appearances On Dissection.* London: F. & C. Rivington, 1798.

———. *Observations on Madness and Melancholy.* London: J. Callon, 1809.

Leigh, D. "John Haslam, M.D.—1764–1844, Apothecary to Bethlem," *Journal of the History of Medicine* 10 (1955): 17–44.

Hayner's wheel A device that was originally designed as a form of treatment for mental illness but was more often used as a form of MECHANICAL RESTRAINT for agitated patients. The "hollow wheel," as it was also called, was a huge, padded circular treadmill on which a patient was forced to walk for hours or days at a time. The device was not unlike those we know today, which are commonly placed in the cages of pet mice or hamsters. With prodding from the "keepers" (as the psychiatric aides or attendants were called in those days), the patient would be "encouraged" to run the treadmill until exhausted. It was used in several German asylums in the 19th century, after its construction by a German psychiatrist named Hayner, who later renounced its use. Apparently, the idea for this machine was first proposed by one of the first German psychiatrists, Johann Christian Reil (1759–1813) of the University of Halle, who recommended many varieties of what he referred to as "non-injurious torture" as effective treatments for mental illness. In the 1890s, while at the Heidelberg Clinic, Emil KRAEPELIN acquired one of Hayner's wheels for the small museum of mechanical restraint that he set up for the medical students under his tutelage.

hebephrenia One of the three distinct psychotic disorders, recognized in the last half of the 19th century, that Emil KRAEPELIN grouped together under his unifying concept of DEMENTIA PRAECOX in 1899. Hebephrenia was the name given to a psychotic disorder identified by German psychiatrist Ewald Hecker (1843–1909) in 1871, which would begin in adolescence or adulthood and result in a rapid disorganization or DEGENERATION. Hecker believed that in this disorder a person's psychological state was arrested at the developmental stage of puberty, thus resulting in severe problems in late adolescence and early adulthood, when more mature psychological integration was required. Hecker derived the name of this disorder from "Hebe," the name of the ancient Greek goddess of youth.

Hecker is given credit by Kraepelin for being the first to point out the characteristic AGE AT ONSET in dementia praecox (schizophrenia). However, in his description of dementia praecox in 1896, Kraepelin does not completely accept Hecker's description of hebephrenia as a disorder in which a depressed state is followed by a manic state, after which mental degeneration quickly follows. Instead, Kraepelin accepts the expanded definition of hebephrenia proposed in a doctoral dissertation by Daraszkiewicz in 1892, which allows for the most severe

cases—including the "depressed forms"—that end in profound mental deterioration.

Kraepelin later referred to hebephrenia as "silly dementia," since often a nonsensical, illogical "silliness" marks the dementia praecox patients with this subtype of the disorder. In the eighth edition (1909–15) of his textbook, *Psychiatrie,* Kraepelin describes this variant of dementia praecox in the following manner:

> That form of dementia praecox which we have called above "silly dementia" is in many respects nearly related to simple insidious dementia. In its clinical picture there appears beside the progressive devastation of the psychic life *incoherence* in thinking, feeling, and action. . . .
>
> The development of the disease is accomplished in almost four-fifths of the cases quite gradually; often an insidious change of the psychic personality precedes the appearance of more distinct morbid phenomena by many years. In the remaining patients the disorder begins in a subacute form; in a few cases it breaks out suddenly. In the preliminary stage there are sometimes nervous troubles, complaints of lassitude, headaches, feeling of giddiness, fainting-fits, irritability, disorders of sleep. The patients become absent-minded, forgetful, negligent; they tire easily, they cannot collect their thoughts any more; they appear lacking in ideas and understanding, they are silly and lazy; they fail in daily tasks, change their occupation, because it is too difficult for them, set aside their work, or give it up entirely.

Kraepelin's description of hebephrenia matches the current diagnostic subtype of schizophrenia known as the DISORGANIZED TYPE that can be found *DSM-IV* (1994). The descriptions of hebephrenia as comprising an insidious onset with the full outbreak of psychotic symptoms in adolescence or early adulthood (usually between ages 15 and 25), and the resulting cognitive disintegration, are all incorporated in modern descriptions of SCHIZOPHRENIA.

Daraskiewicz, L. *Über Hebephrenie, insbesondere deren schwere Form.* Doctoral dissertation, Laakmans, Dorpat, 1892.

Hecker, E. "Die Hebephrenie," *Virchows Archiv für pathologische Anatomie* 52 (1871): 392–449.

Kraepelin, E. *Dementia Praecox and Paraphrenia.* Translated by R. M. Barclay and edited by G. M. Robertons. Edinburgh: E. & S. Livingstone, 1919.

hebephrenic type In the World Health Organization's 10th revision of the *International Classification of Diseases,* or *ICD-10,* this is one of the mental disorders classified under the category of schizophrenic psychoses. It is equivalent to the classical descriptions of HEBEPHRENIA and to current descriptions of the subtype of SCHIZOPHRENIA known as the DISORGANIZED TYPE, which is described in *DSM-IV* (1994).

hemispheric asymmetries in schizophrenia See LATERALITY IN SCHIZOPHRENIA.

hemodialysis treatment of schizophrenia Between the 1930s, when techniques for the CONVULSIVE THERAPIES, COMA THERAPY, and PSYCHOSURGERY were being introduced, and the early 1970s, no new somatic treatment for SCHIZOPHRENIA was introduced. In the 1970s physician R. Cade noticed that the psychotic symptoms of a patient diagnosed with the paranoid subtype of schizophrenia had improved greatly after treatment with hemodialysis for a kidney disease. Cade and colleague J. Wagemaker Jr. theorized that the dialysis might have removed some sort of toxic substance from the blood of the patient that had been responsible for causing the psychotic symptoms. They followed up this observation by submitting to hemodialysis a group of patients who were diagnosed with schizophrenia but who did not have any kidney disease. They were encouraged by seemingly positive results and published them in 1977. However, several attempts at replication by other researchers have failed (most recently in 1983), suggesting that hemodialysis as a treatment for schizophrenia is not very effective and therefore is not recommended.

See also TRANSMETHYLATION HYPOTHESIS.

Carpenter, W. T., et al. "The Therapeutic Efficacy of Hemodialysis in Schizophrenia," *New England Journal of Medicine* 308 (1983): 669–675.

Wagemaker, J., and R. Cade. "The Use of Hemodialysis in Chronic Schizophrenia," *American Journal of Psychiatry* 134 (1977): 684–685.

hemorrhoids, production of as treatment In his 1838 book on *Mental Maladies,* J. E. D. ESQUIROL recommends BLEEDING as a treatment for severe mental illness only if it is performed locally through cupping with leeches. For both the severe forms of depression ("lypemania or melancholy") and of mania, Esquirol recommends the application of leeches to the anus to produce hemorrhoids (varicose veins of the anus). He writes:

> Pursuing the atrabile into the circulation, the humorists deduce from blood-letting a general precept against melancholy … Nevertheless, we may have recourse to local sanguine evacuations; now at the epigastrium, when the stomach is the seat of an active irritation; now, to the vulva, when we wish to reestablish the menstrual flux; or to the anus, when we desire to renew a hemorrhoidal discharge; and finally to the head, when there are signs of cerebral congestion. I have sometimes applied leeches with success to the side of the head, when lypemaniacs complained of a fixed pain in the part.

This form of treatment is a vestige of the type of thinking that resulted from the influence of the HUMORAL THEORY of disease and mental illness, in which an excess of humors in the blood (a condition called *plethora*) needed to be drained off to restore a healthful balance in the patient.

Esquirol, J. E. D. *Mental Maladies. A Treatise on Insanity.* Translated by E. K. Hunt. 1838. Reprint, Philadelphia: Lea & Blanchard, 1845.

heredity See GENETICS STUDIES.

heritability of psychotic disorders Heritability is a quantitative concept from population genetics and is used widely in studies of behavioral genetics. In a given population, heritability is that portion of the variation in a measurable trait (such as IQ, or extraversion-introversion) or a disease (such as SCHIZOPHRENIA) that is due solely to genetic factors. It is expressed as the ratio of the total genetic variance in a population to the phenotypic variance in a population. In the broad sense, then, heritability is a statistic that indicates the degree to which a trait is genetically determined. In the narrow sense, it is the degree to which a trait is transmitted from parent to offspring. If a trait (or a disease) has a heritability estimate of 1.00, that means that 100 percent of the trait or disease is assumed to be caused by the action of genes.

TWINS METHOD AND STUDIES have provided most of the estimates of the heritability of the various psychotic disorders, including estimates for schizophrenia. The most recent estimates are derived from the Maudsley Twin Psychosis Series at Maudsley Hospital in London, England, and were reported in a publication in February 1999. Heritability estimates for schizophrenia, SCHIZOAFFECTIVE DISORDER, and MANIA (BIPOLAR DISORDER) were determined using various diagnostic criteria for each disorder (Research Diagnostic Criteria, *DSM-II-R,* and *ICD-10*). Despite slight differences in the diagnostic criteria for these three disorders, the heritability estimates were all within the same range and were quite high. All were between 82 percent and 85 percent. Thus, it was once again confirmed that genes play a significant role in the origins and development of the psychotic disorders.

Cardno, A. G., et al. "Heritability Estimates for Psychotic Disorders: The Maudsley Twin Psychosis Series," *Archives of General Psychiatry* 56 (1999): 162–168.

high-functioning schizophrenic See AMBULATORY SCHIZOPHRENIC.

high-risk studies Also called the "risk-for-schizophrenia" research, high-risk studies evaluate children who are considered to be at a higher than average statistical risk for developing SCHIZOPHRENIA later in life. These studies hope to clarify several questions that researchers have about the disease process in schizophrenia. For example,

one hope is that by studying children before the onset of the disorder it will be possible to identify the initial, core "warning signs" of the full onset of the disorder and separate them from the later symptoms of the disorder. Furthermore, if specific environmental influences that precede the onset of schizophrenia can be identified, perhaps further research can then tell us whether schizophrenia can be prevented in vulnerable individuals by changing or altering these environmental influences in some way.

Most of the high-risk research has tended to use children with at least one biological parent who has schizophrenia. As the family studies research using the CONSANGUINITY METHOD to find evidence of the genetic transmission of schizophrenia have indicated, children with one schizophrenic parent have a lifetime risk of approximately 12 percent, whereas individuals who have two biological parents diagnosed with schizophrenia have a much higher risk, of 35 percent to 46 percent. Individuals with a schizophrenic biological parent also have a greater risk for developing one of the schizophrenia "spectrum" disorders (e.g., schizotypal personality disorder, schizophreniform disorder, and schizoaffective disorder).

However, it is estimated that 85 percent to 90 percent of all persons diagnosed with schizophrenia do not have a schizophrenic parent. Therefore, high-risk studies that use just the children of schizophrenic parents may not apply to the much larger number of individuals who will develop schizophrenia but who do not have schizophrenic parents. To take this possibility into account, a complementary research strategy using "behavioral markers of risk" has been developed, which defines an individual's risk status based on his or her own specific behavioral disturbances. The ongoing New York High-Risk Project, which is being conducted by researcher L. Erlenmeyer-Kimling of the New York State Psychiatric Institute, has been studying two selected samples since the 1970s consisting of children of schizophrenics. This group periodically undergoes a battery of neuropsychological and psychophysiological tests that measure three primary "biobehavioral domains" of possible predictors of liability to psychopathology: attentional and information-processing capacities, neuromotor functioning, and psychophysiological processes. They theorize that these primary areas of disturbance create problems in social functioning as the child grows older. Their results have indicated greater problems in fine motor coordinations, attentions, and information processing (AIP) in the children of schizophrenics.

Besides the presumed genetic risk factor in schizophrenia, risk factors related to the physical environment have long been explored in the high-risk studies as contributors to the development of schizophrenia. Some of the most suggestive childhood history factors that may increase the risk for developing schizophrenia are: (1) obstetrical complications, (2) the season of birth (a higher percentage of schizophrenics are born in the winter and spring months), (3) prenatal stress of the mother, and (4) early exposure to certain viral infections.

In a major review of the evidence from 24 high-risk studies conducted since 1952, which was published in *Schizophrenia Bulletin* in 1988, researcher Joan Asarnow of the UCLA Neuropsychiatric Institute reaches the following conclusions about the state of our knowledge concerning children at-risk for schizophrenia:

- Some high-risk children can be distinguished from their peers by signs of neurointegrative problems, social impairments, and early symptomatology. Although some abnormalities can be identified as early as infancy, impairments are more pronounced in middle childhood and adolescence.
- Particular deficits in attention-information processing, neuromotor functions, and social behavior may be associated with specific risk for schizophrenia. The form of these deficits may vary with the age of the individual, and future work is needed to clarify developmental patterns within the same individuals. Other deficiencies are shown by children whose parents have other psychiatric disorders, as well as in samples of clinically disturbed children.
- Strong evidence currently exists from the risk-for-schizophrenia and general psychopathology literature that some attributes of the family environment are associated with increased risk for the onset of the disorder. These attributes include: family communication deviance, negative affective

> style, high expressed emotion, and general disturbance in the family environment. It is still unclear whether these family attributes hold specific risk for schizophrenia or are associated with increased risk for a variety of disorders and dysfunctions. However, the current evidence . . . points to the highest rates of schizophrenia spectrum disorders in individuals exposed to both disturbed rearing environments and genetic risk (inferred from the presence of schizophrenia in at least one biological parent). Future studies need to explicate the mechanisms by which environmental attributes, individual attributes and genetic predisposition may interact to influence risk for schizophrenia.

In the 1990s, innovation in the methods of data collection in high-risk studies included advanced techniques for genetic screening and new brain imaging technologies. These neuroimaging studies allow for the long-term assessment of changes in both the structure and the function of children at high-risk for developing schizophrenia as these children age.

Asarnow, J. R. "Children at Risk for Schizophrenia: Converging Lines for Evidence," *Schizophrenia Bulletin* 14 (1988): 613–631.

Cornblatt, B. A., et al. "High-Risk Research in Schizophrenia: New Strategies, New Designs." In *Origins and Development of Schizophrenia: Advances in Experimental Psychopathology,* edited by M. F. Lenzenweger and R. H. Dworkin. Washington, D.C.: American Psychological Association, 1998.

Erlenmeyer-Kimling, L., et al. "Prediction from Longitudinal Assessments of High-Risk Children." In *Origins and Development of Schizophrenia: Advances in Experimental Psychopathology,* edited by M. F. Lenzenweger and R. H. Dworkin. Washington, D.C.: American Psychological Association, 1998.

Hill, Robert Gardiner (1811–1878) English physician who served as the resident surgeon at the Lincoln Asylum in England. Known as a persuasive advocate of nonrestraint policies in the treatment of institutionalized patients, he put such policies into effect at Lincoln in 1838 and is given credit by Wilhelm GRIESINGER for being the first to do so. In an 1838 book he argues that, "in a properly constructed building, with sufficient number of suitable attendants, restraint is never necessary, never justifiable, and always injurious."

See also ABUSE OF PSYCHIATRIC PATIENTS; CHEMICAL RESTRAINT; MECHANICAL RESTRAINT; NONRESTRAINT MOVEMENT.

Hill, R. G. *Lunacy: Its Past and Present.* London: Longman, Green, Reader & Dyer, 1870.

———. *Total Abolition of Personal Restraint in the Treatment of the Insane.* London: Simpkin, Marshall, 1838.

histamines Histamine (HA), a biogenetic amine, is a NEUROTRANSMITTER that has been linked to the regulation of several important functions of the central nervous system. These include arousal, cognition, neuroendocrine regulation, and circadian rhythyms. Animal model research on neurodegeneration conducted by L. Fernandez-Novona and R. Cacabelos of Spain has shown that histamine may have a cytotoxic (cell-poisoning) effect. Histamine has been examined in studies of Alzheimer's disease and SCHIZOPHRENIA. The BIOGENIC AMINE HYPOTHESIS of the cause of schizophrenia has tended to focus on the CATECHOLAMINES (such as DOPAMINE) and the INDOLAMINES (such as serotonin) and not the histamines. An "autointoxication" theory of the cause of dementia praecox first put forth in 1916 by Chicago surgeon and bacteriologist Bayard Taylor HOLMES implicated an overproduction of histamine—or "hyperhistaminia"—in the intestines as a source of poisons carried to the brain, which caused psychotic symptoms.

See also AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX (SCHIZOPHRENIA).

Fernandez-Novona, L., and R. Cacabelos. "Histamine Function in Brain Disorders," *Behavioral Brain Research* 124 (October 2001): 213–233.

Holmes, B. T., and J. Retinger. "The Relation of Cecal Stasis to Dementia Praecox," *Lancet-Clinic* 116 (1916): 145–150.

historical evidence of schizophrenia If SCHIZOPHRENIA is truly a brain disease that has a strong

basis in genetics, then there should be evidence that this severe mental disorder has afflicted people for hundreds, if not thousands, of years. "Madness" has been reported in every society on record to a greater or lesser degree, and descriptions of HALLUCINATIONS, DELUSIONS, and bizarre behavior are often reported in association with ancient mental disorders. In an attempt to trace schizophrenia back to ancient Babylonian accounts (3000 B.C.) or to early Sanskrit texts from India, translations of descriptions of mental illness were collected in articles published in 1985 by D. V. Jeste and his colleagues and in 1984 by C. V. Haldipur. But it is still unclear from this historical evidence that schizophrenia—as we know it, a disease with a particular course that begins in adolescence or early adulthood, with characteristic signs and symptoms and a chronic deteriorating course (at least in the type of schizophrenia that seems to be the most "genetic")—existed in ancient times. This point (and the larger ramifications of this entire issue) has been eloquently argued and documented by psychiatrist E. Fuller Torrey in his book *Schizophrenia and Civilization* (1980).

There are many reasons for this uncertainty. First, ancient descriptions of "madness," which involved delusional, hallucinating, or confused individuals, could be accounts of any number of physical or mental disorders. For example, these symptoms could be produced by head trauma, brain infections, injury due to birth complications, strokes or any number of other known, organic mental disorders. Or, they could be descriptions of the other psychotic disorders, such as bipolar disorder or any of the acute reactive psychoses. What is missing in these ancient accounts are descriptions of the full course of the disease process over time.

Several changes in traditional thought developed in the 1600s (especially in England), which converged to change this state of affairs. First, societies began to incarcerate mentally ill people in central institutions (jails, hospitals), where many of them could be observed together for long periods of time. Secondly, physicians began to be put in charge of the care of the mentally ill in these institutions, as, for example, happened at the BETHLEM ROYAL HOSPITAL in England during the 17th century. And third, the concept of *disease* began to take on a new meaning, largely due to the influence of English physician Thomas Sydenham (1624–89), often referred to as the "English Hippocrates," who emphasized the direct observation of illnesses and suggested their classification according to syndromes or groups of symptoms. This differed from centuries of the identification of diseases usually by a single symptom, as was the case with the mental disorder known as FURY. Throughout the 1700s physicians who doctored to the mentally ill ("mad-doctors," or "lunatic doctors," as their specialty of medical practice came to be known) contributed treatises and textbooks based on their idiosyncratic observations and classifications of the mentally ill.

Eventually, in 1809, the very first clinical descriptions of schizophrenia as we know it appeared in print. Working independently in their respective countries, John HASLAM of the Bethlem Royal Hospital in London and Philippe PINEL of the Salpêtrière asylum in Paris produced expanded second editions of books on mental illness, which had been published previously, that contain the first complete reports of what we now know as schizophrenia in its "chronic" form. The expanded second edition of Pinel's work, *Traité médico-philosophique sur l'aliénation mentale, ou la manie* (first edition, 1801), has never been translated into English. Pinel's description of DÉMENCE in the first edition, which strongly resembles the thought disorder of schizophrenia, was apparently illustrated with case material in the second edition that seemed to confirm this connection. However, the following case history, which is reproduced from Haslam's 1809 *Observations on Madness and Melancholy,* may be the first valid historical evidence in the English language that we have for schizophrenia:

> there is a form of insanity which occurs in young persons; and, as far as these cases have been the subject of my observation, they have been more frequently noticed in females. Those whom I have seen, have been distinguished by prompt capacity and lively disposition; and in general have become the favorites of parents and tutors, by their faculty in acquiring knowledge, and by a prematurity of attainment. This disorder commences, about or shortly after, the period of menstruation, and in

many instances has been unconnected with hereditary taint; as far as could be ascertained by minute enquiry. The attack is almost imperceptible; some months usually elapse before it becomes the subject of particular notice; and fond relatives are frequently deceived by the hope that it is only an abatement of excessive vivacity, conducing to a prudent reserve, and steadiness of character. A degree of apparent thoughtfulness and inactivity precede, together with a diminution of the ordinary curiosity, concerning that which is passing before them; and they therefore neglect those objects and pursuits which formerly proved sources of delight and instruction. The sensibility appears to be considerably blunted; they do not bear the same affection towards their parents and relations; they become unfeeling to kindness, and careless of reproof. To their companions they show a cold civility, but take no interest whatever in their concerns. If they read a book they are unable to give any account of its contents; sometimes, with steadfast eyes, they will dwell for an hour on one page, and then turn over a number in a few minutes. It is very difficult to persuade them to write, which most readily develops their state of mind; much time is consumed and little produced. The subject is reportedly begun, but they seldom advance beyond a sentence or two: the orthography becomes puzzling, and by endeavoring to adjust the spelling the subject vanishes. As their apathy increases they are negligent of their dress and inattentive to personal cleanliness. Frequently they seem to experience transient impulses of passion, but these have no source in sentiment; the tears, which trickle down at one time, are as unmeaning as the loud laugh which succeeds them; and it often happens that a momentary gust of anger, with its attendant invectives, ceases before the threat can be concluded. As the disorder increases, the urine and feces are passed without restraint, and from the indolence which accompanies it, they generally become corpulent. Thus in the interval between puberty and manhood, I have painfully witnessed this hopeless and degrading change, which in a short time has transformed the most promising and vigorous intellect into a slavering and bloated idiot.

Haslam is describing what British psychiatrist T. J. Crow has named Type II schizophrenia or the PINEL-HASLAM SYNDROME: insidious onset, NEGATIVE SYMPTOMS (attention deficits, problems in information processing, apathy, poverty of speech, loss of curiosity in people and activities), and gradual cognitive deterioration. This *démence,* as Pinel called it, was later elaborated upon by French alienist B. A. Morel in his descriptions of mental DEGENERATION, and was used by Morel to coin the term *démence précoce* in 1852. Emil KRAEPELIN borrowed this term to describe our modern clinical picture of DEMENTIA PRAECOX in 1893.

Haldipur, C. V. "Madness in Ancient India: Concepts of Madness in Charaka Samhita (1st century A.D.)," *Comprehensive Psychiatry* 25 (1984): 335–344.

Haslam, J. *Observations on Madness and Melancholy.* London: J. Callon, 1809.

Jeste, D. V. "Did Schizophrenia Exist before the Eighteenth Century?" *Comprehensive Psychiatry* 26 (1985), 493–503.

Pinel, P. *Traité médico-philosophique sur l'aliénation mentale.* 2nd ed. Paris: J. A. Brosson, 1809.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

HIV and schizophrenia Persons with SCHIZOPHRENIA and other psychotic disorders are more susceptible to high-risk behaviors that may lead to HIV infection than persons without any diagnosable mental disorder. Studies have shown that persons with severe psychiatric disorders such as schizophrenia have less knowledge about the dangers of HIV infection and are less concerned about such infection than "healthy" control group members. According to a study conducted in Italy and published in 1997, HIV infection in schizophrenic patients may increase the severity of depression and may reduce tolerability to antipsychotic medication.

See also AIDS AND PSYCHIATRIC PATIENTS.

Gottesman, I. I., and C. S. Groome. "HIV/AIDS Risks as a Consequence of Schizophrenia," *Schizophrenia Bulletin* 23 (1997): 675–684.

Grassi, L., et al. "HIV-Risk Behavior and Knowledge about HIV/AIDS among Patients with Schizophrenia," *Psychological Medicine* 29 (1999): 171–179.

Mauri, M. C., et al. "Schizophrenia Patients before and after HIV Infection: A Case-Control Study," *Encephale* 23 (1997): 437–441.

HIV CNS disease A disease of the central nervous system (the brain and spinal cord) that is due to infection with the human immunodeficiency virus (HIV), implicated in acquired immunodeficiency syndrome (AIDS). The symptoms of such a disease process may resemble many MENTAL DISORDERS, including such psychotic disorders as SCHIZOPHRENIA and BIPOLAR DISORDER. However, the most common symptom is DEMENTIA. The clinical signs and symptoms of the AIDS DEMENTIA COMPLEX were first clearly identified by B. A. Navia and his colleagues in 1986.

Bridge, T. P., A. F. Mirsky, and F. K. Goodwin. *Psychological Neuropsychiatric, and Substance Abuse Aspects of AIDS,* Vol. 44. New York: Raven Press, 1988.

Hoch, August (1868–1919) A Swiss psychiatrist who emigrated to America in 1887 and is best remembered for his posthumously published book *Benign Stupors: A Study of a New Manic-Depressive Reaction Type* (New York: Macmillan, 1921). Hoch had returned to Europe in 1893–94 to train under Emil KRAEPELIN in Heidelberg, Germany. Together they conducted a series of psychological experiments (primarily word-association tests) concerning mental performance under a variety of conditions (fatigue, etc.). Upon arrival in America Hoch first worked at Johns Hopkins Hospital in Baltimore. After returning from Germany, he was a staff psychiatrist at McLean Hospital in Belmont, Massachusetts, from 1895 until 1908. With the help of his friend and fellow Swiss émigré Adolf MEYER, Hoch became a professor of psychiatry at Cornell University Medical College in 1909. In 1910 he replaced Meyer as the chief of the New York Psychiatric Institute at the Manhattan State Hospital on Ward's Island in New York City.

Hoch became a convert to Meyer's view that all mental disorders, including DEMENTIA PRAECOX or SCHIZOPHRENIA, were "reactions" to psychosocial stressors and not caused by heredity (genetics) as Kraepelin and his followers argued. In his last years, poor health forced Hoch to retire to California, where he was the live-in psychiatrist for Stanley McCormick of the wealthy and influential McCormick family of Chicago.

Meyer, A. "August Hoch, MD" (obituary), *Archives of Neurology and Psychiatry* 2 (1919): 576.

Meyer, A., S. E. Jelliffe, and A. Hoch. *Dementia Praecox: A Monograph.* Boston: R. G. Badger, 1911.

Noll, R. "Styles of Psychiatric Practice, 1906–1925: Clinical Evaluations of the Same Patient by James Jackson Putnam, Adolf Meyer, August Hoch, Emil Kraepelin, and Smith Ely Jelliffe," *History of Psychiatry* 10 (1999): 145–189.

holergasia A complete disorganization of mental activity. This was one of the many terms of psychological processes proposed by Swiss psychiatrist Adolf MEYER in the early 20th century that never became really popular and have since disappeared. Holergasia is probably equivalent to the FORMAL THOUGHT DISORDER of the DISORGANIZED TYPE of SCHIZOPHRENIA. Meyer, who came to the United States in 1892, was perhaps the most important figure in American psychiatry from about 1910 to 1940. His new name for schizophrenia, *parergasia,* was never adopted by anyone outside his close circle of followers.

Meyer, A., S. E. Jelliffe, and A. Hoch. *Dementia Praecox, A Monograph.* Boston: R. G. Badger, 1911.

Hollingshead & Redlich See SOCIAL DRIFT THEORY.

hollow wheel See HAYNER'S WHEEL.

Holmes, Bayard Taylor (1852–1924) It is through the psychotic illness in 1905 of Ralph Loring Holmes, his 17-year-old son, that Bayard Taylor Holmes enters the history of psychiatry. Holmes was personally devastated by his son's illness. His anguish was exacerbated by feelings of impotence,

for although his professional life was devoted to improving medical education in Chicago, he had a complete lack of expertise in psychiatry. Holmes, however, had a combative nature and decided to tackle his ignorance and his son's illness head on. Weary of relying on the advice of colleagues and some of the most respected psychiatrists in America while watching his son deteriorate further, Holmes semi-retired from his surgical practice and his position as professor of surgical pathology and bacteriology at College of Physicians and Surgeons in Chicago to care for his son himself. He also vowed to use his scientific expertise to find both a cause and a cure for dementia praecox. He soon became a prominent advocate for reforms in the institutional care of the mentally ill, compiled a bibliographic collection of more than 8,000 international scientific articles, dissertations, and books concerning laboratory studies of dementia praecox, and from 1918 to 1922 was the editor of what is believed to be the first medical journal named after a psychiatric disorder: *Dementia Praecox Studies*.

Using equipment and lab space loaned by medical colleagues, in January 1915 Holmes began his own laboratory studies of dementia praecox. Within a few months, to his satisfaction, he hit upon a viable organic theory of the cause of dementia praecox: an ergotism-like toxemia caused by fecal stasis in the cecum led to an autointoxication process that poisoned the brain. In May 1916, he developed and experimented with a rational treatment based on this theory: abdominal surgery and daily irrigations of the colon as a way to reduce psychotic symptoms. Between May 1916 and January 1918 Holmes and his associates performed cecostomies on at least 22 dementia praecox patients. Holmes tested his surgical procedures, as well as other forms of treatment, on additional patients with DEMENTIA PRAECOX between April 1917 and February 1918 at an experimental inpatient unit he founded: the Psychiatric Research Laboratory of the Psychopathic Hospital, Cook County Hospital, in Chicago, Illinois.

Until recently, Bayard Holmes did not appear in any histories of psychiatry. During his lifetime he was a major critic of just about every prominent figure in American psychiatry. He believed Adolf MEYER was deliberately deceptive in his use of jargon. Freud's psychoanalysis was "a distinctly mystical theory, insusceptible of either proof or refutation," he wrote in 1914. Eugenics was a "pseudoscience," he claimed in 1916. Holmes was especially appalled at the lack of laboratories in mental hospitals. He made it clear in many opinion pieces in medical journals that he detested the psychiatric profession for its lack of interest in laboratory science and for making false claims to the unsuspecting public about scientific knowledge of causes and effective cures. Holmes firmly believed in AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX (SCHIZOPHRENIA) and could not imagine how the followers of Meyer and Freud could ignore the fact that dementia praecox was an organic disease. Holmes died at his vacation home in Fairhope, Alabama, on April 1, 1924, discouraged that he could not convince the medical and psychiatric communities to take up the challenge to find the biological cause and cure of the illness that had so disabled his son.

In May 1916, Ralph Loring Holmes was the very first person in the history of medicine to undergo abdominal surgery as a treatment for dementia praecox. His father, Bayard Taylor Holmes, performed the procedure himself at Lakeside Hospital in Chicago. Ralph died from the procedure four days later.

See also PSYCHOSURGERY.

Beatty, W. K. "Bayard Taylor Holmes—A Forgotten Man," *Proceedings of the Institute of Medicine of Chicago* 34 (1981): 120–123.

Noll, R. "Infectious Insanities, Surgical Solutions: Bayard Taylor Holmes, Dementia Praecox, and Laboratory Science in Early Twentieth-century America," *History of Psychiatry,* 17 (2006): 183–204.

Horn's sack An early German psychiatrist who worked in the Berlin asylum, Ernst Horn (1774–1848) is largely remembered as the inventor of a sack that was put over unmanageable patients in order to calm them down and place them under control. A patient died from suffocation in one of Horn's sacks, and the resulting court case earned Horn considerable notoriety. Horn's sack was a long, wide bag that was reinforced with oilcloth.

Emil KRAEPELIN describes its use in his short historical book, *One Hundred Years of Psychiatry* (1917):

> The bag was pulled over the patient's head and tied beneath his feet. "It restraints the patient," explained Horn. "It shocks him by making him aware of his confinement and causes him to suspect or realize the fruitlessness of any attempt to stir up troubles." He also claimed that many restless, troublesome lunatics—even after other measures had failed to make them obedient, orderly and calm—responded to it by developing a more serene state of mind, by becoming more tractable, and by becoming more responsive to other, indirect, psychic treatments. Many patients who refused to eat were so impressed by the threat of the bag "that they took a new lease on life and began once more to enjoy the food which they had stubbornly refused."

Apparently, Horn was also an advocate of the CRUCIFORM STANCE, a standing form of the BED SADDLE.

Kraepelin, E. *One Hundred Years of Psychiatry.* Translated by W. Baskin. 1917. Reprint, New York: Philosophical Library, 1962.

hospitalism A term for the apathy and loss of ambition or creativity that was first noticed by Emelyn Lincoln Coolidge in 1909 in children who were hospitalized for a long time. Today we would refer to this as the effects of INSTITUTIONALIZATION. It is a type of "learned helplessness" that develops from being too dependent upon a caregiving staff in an institutional setting for too long a time.

In the 1940s the psychoanalyst René Spitz used this term to denote whatever physical or psychological disturbances occur in infants up to 18 months old who undergo a prolonged stay in a hospital or other similar institution where they are completely separated from their mother. Spitz did research in orphanages, nurseries, and other institutions in which infants and young children were separated from their mothers. Spitz thought that when a baby is cared for in an institutional setting in which the caregivers are anonymous and for which no emotional link is established, the child will develop a series of disorders, which are collectively called "hospitalism." These disorders are: (1) retardation of bodily development, (2) retardation of body mastery, (3) retardation of adaptation to the world, (4) retardation of language ability, (5) a reduced resistance to disease, and (6) in the most extreme cases, emaciation and eventual death. Spitz thought the damage caused by this rupture in the earliest mother-child relationship was long-lasting and led to chronic problems, potentially including schizophrenia.

In studies of schizophrenia, the effects of institutionalization must be taken into account and separated from the observable behaviors of the schizophrenic subjects that are caused first and foremost by the disease process. This is the basis of the ACUTE-CHRONIC DISTINCTION in schizophrenia research.

Coolidge, E. L. *Care of Infants Who Must Be Separated from Their Mothers Because of Some Especial Need on the Part of the Child,* Papers of the American Academy of Medicine. Conference on Prevention of Infant Mortality. Washington, D.C.: 1909.

Spitz, R. A. "Hospitalism—An Enquiry into the Genesis of Psychiatric Conditions in Early Childhood," *Psychoanalytic Study of the Child* 1 (1945): 53–74.

Hôtel-Dieu, l' Founded in 1656, l'Hôtel Dieu is the oldest hospital in Paris. In 1660 the French Parliament declared that it should provide special accommodations for "mad men and women." In the early 1790s, during the French Revolution, many of the mentally ill patients were removed from the hospital and transferred to the care of Philippe PINEL at the BICÊTRE Asylum. Prior to this time the patients there were subjected to BLEEDING so often that the technique was commonly referred to by the public as the *traitement de l'Hôtel-Dieu.*

Hoxton madhouses These were private "madhouses" in the Hoxton section of London, England. In the early 1700s practically all mentally ill in London were in one of the Hoxton madhouses. Like "Bellevue" in the United States, the word

"Hoxton" took on the ominous meaning of a place of banishment for the mentally ill, and sometimes was used as a synonym for "madness" or "lunacy" itself.

See also PRIVATE MADHOUSES.

Morris, A. D. *The Hoxton Madhouses.* London: 1958.

humoral theory of mental illness This theory of health and disease is thought to have been formulated by Hippocrates (460–377 B.C.) and expanded upon by Galen (A.D. 129–199). The ancient Greek notion that the universe was comprised entirely of four elements (earth, air, fire, water), which were each associated with a particular quality (dry, cold, hot, moist), formed the basis of Hippocrates' empirical medicine. Hippocrates associated four essential characteristics—the humors (from the Latin word for moisture)—of the human body with combinations of the elemental qualities. These four humors were blood, yellow bile, black bile, and phlegm; their relative quantities in relation to one another led to good health or to disease. Each of these humors was then associated with its ascendancy during a particular season: spring (blood); summer (yellow bile); autumn (black bile); winter (phlegm). Galen later paired combinations of qualities to each of the humors and their seasons of ascendancy: blood was warm and moist, yellow bile warm and dry, black bile cold and dry, and phlegm cold and moist.

Both physical and mental illnesses were considered by Galen to be caused by an excess of humors. What we would call acute diseases tended to be the result of an excess of blood or yellow bile, whereas an excess of black bile or phlegm was associated with more chronic ailments. Black bile in particular caused mental distress, and an excess of it produced MELANCHOLIA or "DEPRESSION," as we know it. Black bile could build up in the blood, the stomach or elsewhere. Therefore Galen recommended what would later become the standard regimen for the institutionalized mentally ill, what PINEL referred to as the "usual treatment" of bleeding, bathing, and purging. These treatments were recommended to either draw off the unwanted excess humor in certain disorders (by BLEEDING or PURGING) or to counteract the effects of the abnormal balance of humors (through temperature-specific baths or douches). Reestablishing the flow of blood in menstruation or from hemorrhoids with the use of leeches was thought by Galen to assist especially in the elimination of the disease-causing humor. Vestiges of the old Galenic humor theory of mental illness can especially be seen in the psychiatric texts of the first half of the 1800s, particularly in J. E. D. ESQUIROL's writings.

See also HEMORRHOIDS, PRODUCTION OF AS A TREATMENT.

Jackson, S. W. "Galen—On Mental Disorders," *Journal of the History of the Behavioral Sciences* 5 (1969): 365–384.

hurry of the spirits A term used popularly in 18th century England for "madness" or "lunacy." William BATTIE uses it in his famous 1758 book, *A Treatise On Madness.*

hydropathic institutions In Europe (especially Germany) in the mid-1800s, special clinics were set up to provide HYDROTHERAPY to mentally ill people as an alternative to commitment to the traditional asylums. These "hydropathic" clinics or institutions could provide outpatient treatment. Thus, people who did not suffer from severe mental disorders did not have to be institutionalized to receive treatment—a very modern concept. However, the established psychiatric authorities of the time—notably Wilhelm GRIESINGER in Germany—strongly criticized these practices as potentially dangerous since they could be performed outside the supervision of the medical profession. In the 1861 second edition of his *Mental Pathology and Therapeutics* (originally published in 1845), Griesinger expresses the following opinions about hydropathic institutions:

> In the first edition of this work, I have already expressed my opinion of the treatment in hydropathic institutions. Since then facts from all quarters have been elicited proving the injury which it generally inflicts on the mentally diseased. Most asylum physicians are in a position to contribute examples of this: Flemming, Erlenmeyer, Dam-

> erow, Sponholz, etc., have expressed themselves decidedly upon this point. This violent procedure seems much to favor the transition to general paralysis. The absurdity of sending patients to cold-water establishments, instead of into lunatic asylums, would be incredible were it not of daily occurrences, still, it is evident that, in certain cases, the occasional use of wet compresses, cold sitzbaths, and, above all, cold washing followed by dry friction, can, under special indications, be beneficially employed.

Despite these criticisms, hydropathic institutions did not disappear, but instead flourished in the 1880s and 1890s as places of treatment for those from the upper classes suffering from the Victorian Age malady of "nervousness" or NEURASTHENIA, the term for this condition coined by physician George Miller Beard (1839–83) of New York in the 1870s. They specialized in a variety of hydrotherapeutic techniques involving both hot and cold bathing, including being wrapped alternately in hot and cold wet sheets, spraying from showering devices, and other such activities. The ancient spas at such places as Baden-Baden, Carlsbad, and Marienbad, which offered natural thermal spring waters, were also popular as forms of hydrotherapy.

Drinka, G. F. *The Birth of Neurosis: Myth, Malady, and the Victorians.* New York: Simon & Schuster, 1984.

Griesinger, W. *Mental Pathology and Therapeutics,* trans. C. L. Robertson and J. Rutherford. New York: William Wood & Co., 1882.

hydrotherapy Literally "water therapy," since the late 19th century the term for the various types of baths or DOUCHES that were one of the primary modes of treatment of the institutionalized mentally ill. It was particularly used for those patients who had become agitated or unmanageable in some way. In the latter half of the 1800s "hydrotherapy" took on the meaning of a particular procedure for a tub bath, which became popular in German psychiatric institutions and then was copied in other places, including the United States. Special treatment rooms were set up that contained large tubs, which would be filled with water and usually heated to between 98 and 102 degrees Fahrenheit. However, cold water baths were sometimes prescribed as well. A thick canvas cover was stretched over the top of the tub and tethered along the rim of the tub, with a hole cut at one end to allow the patient's head to be exposed. A "bathmaster" or "bathmistress" would oversee the treatment sessions, during which a patient would be left immersed in the tub for hours or, in some cases of extreme agitation, days at a time. Not surprisingly, a state of relaxation resulted and behavioral compliance was restored.

While working at the psychiatric clinic at Heidelberg University between 1891 and 1903, Emil KRAEPELIN relied primarily on hydrotherapy for agitated patients, with great success. As he reports in his *Memoirs:*

> By procuring English fireclay tubs and by employing more staff and using the baths during the night, our equipment became more and more complete. The baths were especially successful when they were applied for weeks and months. Slowly, but surely, they became the most important method for dealing with states of agitation, and isolation became completely superfluous.

In the 1890s the primary authority on hydrotherapy in the United States was Dr. Simon Baruch of Bellevue Hospital in New York City. Hydrotherapy equipment was later instituted at St. Elizabeth's Hospital in Washington, D.C., after a visiting physician from there reviewed the hydrotherapy procedures at Bellevue in 1897. When William Alanson White became superintendent of St. Elizabeth's in 1904, he implemented a policy of eliminating the more inhumane forms of physical restraint (straitjackets, bed saddles, etc.) and promoted instead the use of hydrotherapy. By the 1920s, hydrotherapy was the primary mode of treatment for institutionalized patients at St. Elizabeth's, and statistics show that between the summers of 1923 and 1924 a total of 106,816 warm-tub hydrotherapy sessions were prescribed for over 4,000 patients. Hydrotherapy declined in use in the 1930s when the COMA, CONVULSIVE, and ELECTROSHOCK THERAPIES all came into vogue in institutions.

Kraepelin, E. *Memoirs.* Translated by C. Wooding-Deane. Berlin: Springer-Verlag, 1987.

hyperkinesia Excessive movement and restlessness. When accompanied by impulsivity and poor attention span, it is a behavioral sign of a childhood disorder, attention-deficit hyperactivity disorder (ADHD). It is estimated that one-third of children who manifest ADHD (usually before age 4) continue to show signs of the disorder in adulthood. Hyperkinesis is also one of the traditional symptoms of CATATONIC EXCITEMENT.

hypnosis and psychosis In the 19th century a small number of physicians attempted to use hypnotism ("mesmerism") to treat "insanity" in institutionalized patients. For example, in the 1840s in India, British surgeon James Esdaile attempted to cure the mental illnesses of patients of the Calcutta Asylum during a six-month period but was generally disappointed with the results. However, in a few cases, people with less debilitating disorders responded to Esdaile's hypnotic inductions. In one case, a man who had cut his throat during a MANIC EPISODE had emergency surgery performed on him by Esdaile while the patient was under "mesmeric anesthesia." British physician John Elliotson, who largely initiated the explosion of interest in mesmerism in England in 1837 and founded the *Zoist,* a mesmeric medical journal in 1843, recommended the use of hypnotism for HYSTERIA. In Paris, the famous hypnotic experiments (beginning in 1878) of neurologist Jean-Martin Charcot (1825–93) with the institutionalized female patients of the Salpêtrière asylum led to the acceptance of hypnotism by the medical establishment.

In the 20th century there have been many research studies to determine: (1) if people with psychotic disorders can be hypnotized (questionable, due to problems in focusing attention noted particularly in schizophrenia), and (2) whether this may be a beneficial form of treatment. The leading authority on this issue is psychologist Elgin Baker of the Indiana University School of Medicine, who published a review of this issue in 1983. In reviewing the research, Baker found that "psychotics" and "borderlines" were comparable to normal subjects and neurotic subjects in their ability to be hypnotized (hypnotic susceptibility). However, Baker recommends that hypnotism be used as one of many other possible treatment techniques in psychotherapy—and in accordance with an overall treatment plan that may even include ANTIPSYCHOTIC DRUGS, which apparently do not reduce the hypnotic susceptibility of psychotic patients.

Baker, E. L. "The Use of Hypnotic Techniques with Psychotics," *American Journal of Clinical Hypnosis* 25 (1983): 283–288.

Bramwell, J. M. *Hypnotism: Its History, Practice and Theory.* London: Alexander Moring, 1906.

Owen, A. R. G. *Hysteria, Hypnosis and Healing in the Work of J.-M. Charcot.* New York: Garrett, 1971.

hypochondriasis Sometimes called "hypochondria." The contemporary meaning of this disorder is of a preoccupation with the belief and accompanying fear that one has a serious disease; based on a misinterpretation of bodily sensations, when in fact physical examination and medical reassurances to the contrary present proof that one does not have the imagined disease. This belief is not of delusional intensity, so there is no break with reality. It is not known how many people develop this disorder, but the numbers of men and women afflicted seem to be equal, and it seems to follow a chronic course throughout a person's lifetime. Apparent predisposing factors seem to be a past history of an actual serious disease (e.g., a heart attack) in the person's life or in the life of a family member. In *DSM-III-R* this was listed as one of the somatoform disorders, a group of mental disorders that have physical symptoms, which at first seem to have a physical cause.

In the psychotic disorders, particularly schizophrenia, people may report odd physical symptoms in various parts of their bodies (e.g., the head, the genitals), which seems to be more common in the initial stages of the first definite onset of the disorder, or in periodic exacerbations in the first years of the disorder. This is especially true for those diagnosed with one of the three nonparanoid subtypes

of schizophrenia, particularly the DISORGANIZED TYPE OF HEBEPHRENIC TYPE that Emil Kraepelin called the "silly dementia." Although others often interpret these reports by schizophrenics as efforts at malingering or as hypochondriasis, this is generally not the case. Such reports seem to be the experience of genuine effects of the disease process on the nervous system.

"Hypochondria" has been used to describe mental disorders at least since the time of Galen, who may have been the first to use it. *Hypochondrium* is the Greek word for an area just below the lower ribs, and Galen believed this was the place of origin of one of the three forms of *melancholia.* Over the centuries the words *hypochondriasis* and *hypochondria* were used as synonyms for hypochondriacal melancholy, a type of depression accompanied by flatulence and gastrointestinal problems. In the late 1600s, these terms were separated from melancholia (depression) by medical scholars, although hypochondriasis and melancholy were closely related well into the 1800s. However, the connection between an "imaginary illness" and hypochondria was apparent by the early 1600s to some medical scholars. By the 1800s, hypochondriasis differed from other, true forms of mental disorder, such as "hypochondriacal insanity," which were considered a more severe pathological development of "noninsane" hypochondriasis.

Jackson, S. W. *Melancholia and Depression: From Hippocratic Times to Modern Times.* New Haven, Conn.: Yale University Press, 1986.

Kenyon, F. E. "Hypochondriasis: A Survey of Some Historical, Clinical and Social Aspects," *International Journal of Psychiatry* 2 (1966): 308–326.

Savage, G. H. "Hypochondriasis and Insanity." In *A Dictionary of Psychological Medicine,* edited by D. H. Tuke. Philadelphia: P. Blakiston & Son, 1892.

hypofrontality Also referred to as "cerebral metabolic hypofrontality," or "metabolic hypofrontality," it refers to the results of some studies of the patterns of blood flow in the brain, showing that some schizophrenics have a much lower than normal blood flow in the frontal lobe (specifically, the prefrontal regions) of the brain. The original study that discovered this abnormality was conducted by researchers Ingvar and Franzen and published in 1974. They determined this "hypofrontality" by using a then-new BRAIN IMAGING TECHNIQUE known as regional cerebral blood flow (rCBF). In people diagnosed with schizophrenia, the more "hypofrontal" they appeared, the more they were observed to manifest the NEGATIVE SYMPTOMS of schizophrenia (e.g., they were more withdrawn, there was greater "ALOGIA" or poverty of speech, more disturbances in attention). The implication of this research is that this metabolic hypofrontality may be convincing evidence of a primary brain process (a lowered metabolism in the front part of the brain) that produces the observable symptoms of schizophrenia. However, the "hypofrontality" research has been somewhat inconsistent in that all the studies using the rCBF brain imaging technique seem to replicate Ingvar and Franzen's original finding, but studies that use PET SCANS (positron emission tomography) to measure cerebral metabolism have been much less consistent.

Despite the inconsistencies across studies, by 1995 the finding of hypofrontality in schizophrenia had reached the status of a "paradigm." Most researchers accepted it as a major truth about the abnormal brains of persons with schizophrenia. This success was due, primarily, to the vigorous promotion of this hypothesis by two National Institute of Mental Health researchers, Daniel Weinberger and Karen Faith Berman, in the late 1980s. However, the claim that hypofrontality was a "trait-like" pathophysiologic characteristic of schizophrenia has been weakened considerably by other studies. These additional studies suggest that the images of lower metabolic activity in the prefrontal cortex of the brain (hypofrontality) may depend on the specific cognitive demands of the experimental task employed in the study (in other words, they are task-dependent or state-specific), and may therefore not be due to any continuous abnormality in the around-the-clock operation of a brain addled by schizophrenia. By 2005 references to a static "hypofrontality" have virtually disappeared in the literature on schizophrenia.

The hypofrontality controversy in schizophrenia is a useful case study in the history of science, for in it we see how quickly a scientific "finding" that

seems so certain and true can be just as quickly overturned by more carefully designed and controlled research.

Curtis, V. A., et al. "Attenuated Frontal Activation in Schizophrenia May Be Task Dependent," *Schizophrenia Research* 37 (1999): 35–44.

Gur, R. C., and R. E. Gur. "Hypofrontality in Schizophrenia: RIP," *Lancet* 3 (June 1995): 1,383–1,384.

Weinberger, D. R., and K. F. Berman. "Prefrontal Function in Schizophrenia: Confounds and Controversies," *Philosophical Transactions of the Royal Society of London. B. Biological Sciences* 351 (1996): 1,495–1,503.

hypomanic episode This is a less serious version of a fully developed MANIC EPISODE that is indicative of a MOOD DISORDER, particularly BIPOLAR DISORDER. The predominant mood in a hypomanic episode is usually described as expansive, elevated, or irritable. A hypomanic episode is not serious enough to cause impairment in social and occupational functioning, and it does not develop into the sometimes psychotic features (delusions, hallucinations) that may accompany a manic episode. "Hypomania" was first described by Berlin psychiatrist Emanuel Ernst Mendel (1839–1907) in 1881.

hysteria *Hysteria* is the Greek word for uterus. From ancient times, a significant number of mental and physical disorders in women were believed to be caused by the wandering of a restless womb in the female body. Thus, there has always been a connection between hysterical symptoms and sexuality in women. Hysteria was initially identified by the Hippocratic school in the fifth century B.C. A large number of symptoms have been attributed to hysteria, many of which have survived into today's diagnostic manuals. Among the most ancient and most often reported symptoms have been spasms or convulsions, and feelings of choking due to the rise of an "hysterical ball" from the womb to the throat. In the 1700s and 1800s, other symptoms indicative of an hysteric were added, such as the "vapors" (fainting, dizziness), paralysis of the limbs, loss of sensation in the skin (anesthesias), a deep suggestibility or gullibility and dissociative "trance-like" states of *absences* (as it was termed in France). The symptoms were often very changeable, alternating or appearing and disappearing without warning. Sometimes hysterics would also develop psychotic symptoms such as hallucinations, delusions, and poor REALITY TESTING, leading 20th-century psychiatric manuals to refer to this as "hysterical psychosis."

"Hysteria" was generally an uncommon diagnosis in psychiatric institutions until the last quarter of the 19th century. The explosion of interest in this disorder was perhaps first evident in France, but soon spread to Germany, England, and the United States. In a book on the French psychiatric profession in the 19th century, historian Jan Goldstein reports that at the SALPÊTRIÈRE asylum for women in Paris, only 1 percent of the admissions for the two-year period 1841–42 were given "hysteria" as a diagnosis, but in the period 1882–83 a full 20.5 percent received that diagnosis. Also in this later period, two males were admitted to the Bicêtre asylum for men with this diagnosis, revealing a change in thinking about this "female malady."

The work of J. M. Charcot at the Salpêtrière in the 1870s legitimized hysteria as a distinct diagnostic category, and he identified four successive stages or "periods" that marked the fundamental nature of a "grand" hysterical attack *(grande hystèrie):* developing from physical rigidity, to spasmodic movements *(grands mouvements),* to a vividly dramatic, almost theatrical acting out of intense emotional states *(attitudes passionnelles),* and then to a final delirious period in which the afflicted person laughed, cried, and was otherwise highly labile until he or she returned to a more reasonable state. Charcot eventually recognized that hysteria was not a form of severe insanity *(aliéne)* but was instead a mental disorder that fell into a borderline area of partial normality *(demi-fou).* This also reflects the distinction, largely coming into vogue at about this time, between a PSYCHOSIS and a NEUROSIS. Sigmund FREUD studied with Charcot in Paris in the winter of 1885–86, and as a result of his exposure to Charcot's hypnotic treatment of hysterics he and his mentor Joseph Breuer began to treat "hysterical neurosis" in

their private practice patients in Vienna. In 1895 they published their famous book of such case histories, *Studien Über Hysterie (Studies on Hysteria)*. Freud's theories about the causes of hysteria in sexuality formed the basis of his "psychoanalysis" in the decades to come.

Due to the sometime psychosis-like symptoms in hysteria (disturbances in attention, "dreamy" or "indifferent" quality in interactions with others, delusions, and hallucinations), there was much discussion at the turn of the century as to how it was related to KRAEPELIN's dementia praecox. One of the most important contributions made by Swiss psychiatrist and psychoanalyst C. G. JUNG was his detailed analysis of the similarities and differences between these two disorders in his 1907 monograph, *Über die Psychologie der Dementia praecox: Ein Versuch (The Psychology of Dementia Praecox)*, particularly in his chapter on "Dementia Praecox and Hysteria." He pictured dementia praecox as the far more serious disorder and the one that was probably organic in origin.

In the 20th century, "hysteria" survived as a diagnosis as one of the "neurotic disorders" of the World Health Organization's *ICD-9* (1978); and in *DSM-III-R* (1987) it was split up into no less than four different types of somatoform disorders.

Goldstein, J. *Console and Classify: The French Psychiatric Profession in the Nineteenth Century.* Cambridge: Cambridge University Press, 1987.

Micale, M. S. "On the Disappearance of Hysteria: A Study in the Clinical Deconstruction of a Diagnosis," *Isis* 84 (1993): 496–526.

I

ICD-10 This is the acronym for the periodically revised manual produced by the WORLD HEALTH ORGANIZATION entitled: *The International Statistical Classification of Disease, Injuries, and Causes of Death.* It is usually revised at 10-year intervals; the very first edition appeared in 1900 and the most recent—*ICD-10*—in 1992. A more detailed revision of *ICD-10* by major medical organizations in the United States, to make it more useful to clinicians, researchers, epidemiologists, and others, is the *Clinical Modification* (or *ICD-10-CM*). With the growing importance of mental disorders, WHO produced in 1978 a special publication that included the chapter on mental disorders from *ICD-9* and a glossary and classification guide; it is perhaps the most useful summary of the *ICD-9* position on mental disorders.

Although *DSM-IV* may be more widely used in clinical practice and research around the world, together with *ICD-10* these two manuals have become the standard classification systems for mental disorders in the 20th century.

Commission on Professional and Hospital Activities. *The International Classification of Disease, 10th Revision, Clinical Modification.* Ann Arbor, Mich.: Commission on Professional and Hospital Activities, 1992.

World Health Organization. *Mental Disorders: Glossary and Guide to their Classification in Accordance with the 10th Revision of the International Classification of Diseases.* Geneva: World Health Organization, 1992.

id The Freudian "unconscious." Sigmund FREUD borrowed the term Das Es from a colleague, Georg Groddeck. Psychosis was viewed by Freud as the result of the ego's inadequate defenses against the id, thereby resulting in a flood of irrational, instinctually based "primary process" material—as appears, for example, in dreams. *Id* is Latin for "IT" (Das Es).

ideas of reference One of the most common symptoms of the psychotic disorders. It is an idea that certain events or people in a person's immediate environment have a magical "special meaning" for that person. For example, a song heard on the radio may be interpreted by a psychotic person as having been specifically played at that time to convey a special message to him or her. Ideas of reference are not as strong as DELUSIONS, nor are they as long-lasting. They tend to be transient and specific to the immediate situation the psychotic person finds him- or herself in at the moment.

idiot savant See AUTISTIC SAVANTS.

idiot's cage The name for an iron cage used to confine severely mentally ill and mentally retarded people for public display, usually as entertainment. Such cages were used well into the 1700s and had variations such as the BELGIAN CAGE that were used in the 1800s.

illusion This is a mistaken perception of an *actual* object or event in the environment. Illusions are different from HALLUCINATIONS, which do not have actual external stimuli for the sensory experience.

illusion des sosies See CAPGRAS SYNDROME.

illusion of intermetamorphosis See INTERMETAMORPHOSIS SYNDROME.

illusion of negative doubles See CAPGRAS SYNDROME.

illusion of positive doubles See FREGOLI'S SYNDROME.

immediacy hypothesis This is the hypothesis that the behavior of people with schizophrenia is controlled primarily by stimuli immediate in their environment. "Normal" people are "controlled" by much wider and less immediate (i.e., not in the immediate environment) stimuli, according to this hypothesis, which is largely based on a radical behavioral interpretation of COGNITIVE STUDIES OF SCHIZOPHRENIA. This hypothesis was first put forth by Kurt Salzinger in 1966.

See also ATTENTION, DISORDERS IN.

Salzinger, K. *Schizophrenia: Behavioral Aspects.* New York: Wiley, 1973.

immersion therapy See BATHS; HYDROTHERAPY.

immune system alterations in schizophrenia Research on mental disorders such as schizophrenia has always been directly influenced by new concepts and technologies that have emerged in other medical sciences. By the end of the 19th century, a time when most physicians had little or no formal training in medical schools, a "laboratory revolution" in medicine was well underway that would change the practice of medicine forever. Instead of relying on the training of apprentice physicians by master physicians through the relating of clinical anecdotes and the shadowing of the day-to-day medical practicing of the master by the apprentice, many physicians in Europe and North America called for the application of new knowledge gained through basic research in laboratories to everyday medical practice. Laboratory-based knowledge of human physiology and especially the potential causes of disease were especially valued. This revolution in medicine was eventually won by the physicians who sought to make medicine a science based on objective, quantitative, and replicable laboratory findings, and less an art based on subjective personal experiences.

The discovery of "microbes" or "bacteria" and the demonstration that these "germs" either directly caused disease or were secondarily involved in the deteriorating effects of disease was an idea finally accepted by the medical elites by 1880. The "germ theory of disease" led to the medical science of bacteriology, and many diseases that were thought to be caused by heredity, such as tuberculosis and syphilis, were found to be caused by bacteria. The rise of bacteriology (starting in the 1880s), and the emergence of endocrinology from general physiology (starting in earnest after 1890), led to various theories of AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX (SCHIZOPHRENIA).

The immune response (the 1890s) By 1890 the discovery of "reactions" in the blood to foreign organisms or substances ("antigens", as evidenced by the production of detectable "antitoxins," "defensive ferments," or "antibodies," led to the rise of immunology in medicine. Originally, immunology was named immunochemistry in 1904 by the noted Swedish chemist and physicist Svante Arrhenius (1859–1927). The focus on the identification and investigation of the antigen-antibody reaction dominated early research in immunology from 1890 to 1910, as historian A. M. Silverstein has documented. From about 1910 to about 1940 knowledge of the "immune response" was applied to the development of *serum therapy* (the production of vaccines and other therapies to prevent or cure various diseases, based on antibodies present in the blood of ill persons). Starting in 1940, immunology was revitalized by the introduction of techniques and concepts from molecular biology, and a great deal of attention was focused on the lymphocytes (white blood cells produced in the lymph glands) as an important aspect of the immune response. In 1949 the Australian researcher MacFarlane Burnet (1899–1965) added an important dimension to the definition of immunity when he proposed that animal bodies had some sort of mechanism of

biological memory for distinguishing "self" from "not-self." Antigens present in the body before birth were accepted as "self." No antibodies were made in response to them.

The immune system (the mid-1960s) Theories of immune reactions, how such reactions may relate to one another, and their connection to the nervous system and endocrine system, were not viewed as comprising aspects of a comprehensive functional system until the mid-1960s. The first reference to the immune system was to the lymphoid system in 1963. As historian of science Anne Marie Moulin has documented, it was only during that decade that the first modern concept of an integrated "immune system" came into being in connection with the development of *cellular immunology.* Cellular immunology arose as a reaction to purely chemical interpretations of immune reactions (*humoral immunology*) that became popular in the mid-20th century. The immune system was conceptualized in terms of its function, not its structure, and focused on a set of autonomous cells involved in all immune reactions. These cells were imagined as freely wandering throughout the whole body, unrestricted by any internal organ.

All that had been known for most of the 20th century was that immune responses (such as the activation of lymphocytes, the production of antibodies, the development of immunity to a disease through exposure to it, allergic reactions, and so on) defended the body against infectious organisms such as bacteria and viruses as well as against toxins manufactured within the body, or entering from outside the body. Each immunity response came from a separate place in the body (the bone marrow produced granulocytes and macrophages, plasma cells produced antibodies, and the lymph nodes produced lymphocytes), but how all these different places in the body were connected, if at all, was not understood. Nor were the presumed connections between immune responses, the endocrine system, and the nervous system. The new concept of a "system" of "restless cells" roaming the entire body at all times took the focus away from immunity being localized only in specific areas of the body (such as in "central" organs like the spleen versus "peripheral" organs like the lymph nodes).

Historian of science Anne Marie Moulin identified four essential main features of the immune system concept that emerged from the mid-1960s to the mid-1970s:

(1) Immunity is a permanent function of the entire body.
(2) The representation of immunity requires anatomical and histological knowledge of its parts.
(3) Knowledge of immunity, beyond this morphological description, refers to a logical category—the so-called immunocompetence of cells—whatever their localization.
(4) All immunological phenomena can be described and explained in terms of the immune system.

The rise of psychoneuroimmunology in the 1970s, led by the work of Robert Ader, focused attention on the interconnections of the immune, endocrine, and nervous systems and their possible relevance to mental disorders such as schizophrenia.

Immunology and the understanding of neurosyphilis The success story of the linkage of the clinical symptoms, cellular pathology, and etiology (underlying cause) of syphilis in an astonishingly brief six-year period had a major impact on biological psychiatrists looking for the cause of schizophrenia in the early 20th century. This story is told in detail in classic books on the Wasserman reaction test by Ludwig Fleck (1935) and Felix Plaut (1911). In 1905 the spiral-shaped bacterium that caused syphilis was discovered by two German researchers. By the following year, antibodies created as a defense against the syphilis bacterium were identified, leading directly to the development of the famous Wasserman blood test for syphilis in 1906. Finally, in 1913, the syphilis bacterium was found in the brain tissue of persons in asylums suffering from the degenerating psychotic disorder known as GENERAL PARALYSIS OF THE INSANE (GPI). GPI, which accounted for more than 20 percent of the inpatients committed to asylums, was thereby proven to be a syndrome caused by the tertiary stage of syphilis and was therefore soon renamed neurosyphilis. Hopes were raised for the discovery of similar bacterial organisms that may be involved in dementia praecox (schizophrenia). If specific infectious

organisms could be found for the psychotic disorders, then antibodies could be located in the blood or cerebral spinal fluid and a diagnostic BLOOD TEST FOR SCHIZOPHRENIA could be developed. As a result, starting in the first decade of the 20th century, a great deal of research—all ultimately fruitless—was aimed at finding immune system alterations in dementia praecox (schizophrenia).

Immunological studies of dementia praecox Changes in the numbers of white blood cells in "lunatics" or "insane persons" had been observed through primitive microscopic examinations throughout the latter half of the 19th century. We now know that such changes in white blood cells—leukocytes—might be an indication of altered immune functions, although the linkage of immune response and white blood cell count did not become apparent until the early 20th century.

One of the first promising immunity findings involved injecting persons with dementia praecox and manic depression with cobra venom and looking for the antibodies created as an immune response. In 1909 two German researchers from Eppendorf created a minor sensation when they injected patients with cobra venom and found that all the dementia praecox patients and a portion of the manic-depressive subjects invariably reacted to the toxin (by producing antibodies to fight it that were detectable in the blood), while other psychiatric patients and normals did not. The excitement over the "Much-Holzmann psycho-reaction" was over within two years. Although the "Much-Holzmann psycho-reaction" was quickly discredited by other researchers, it was the first promising immune response finding for dementia praecox and manic-depressive insanity.

In an era in which autointoxication theory influenced medical and psychiatric cognition, researchers posited that bacteria in the intestines spread throughout the body and caused damage to internal organs. These damaged organs would release debris such as "toxic albumins" into the bloodstream, which would then be carried to the brain and cause the symptoms of insanity. Immune responses to such foreign materials were eagerly sought in countless laboratory studies. Such theories were many and varied, as were the hypothetical substances that could be detected in the blood or cerebral spinal fluid of the insane. Between 1912 and 1918 several prominent dementia praecox researchers relied heavily on a test known as the Abderhalden defensive ferments reaction test, first developed in 1909 by Swiss biochemist Emil Abderhalden as a pregnancy test. It was thought that this blood test could differentially diagnose dementia praecox from other mental disorders and from the blood of persons with no mental disorders. The problem with this test, as many researchers discovered by 1914, was that Abderhalden's reaction test was highly subjective and not quantitative (the identification of a particular deep blue or violet color was evidence of a "reaction"—not a measurement of any sort), resulting in enormous experimenter bias and error. Furthermore, there was no other corroborating evidence of an immunity response such as "defensive ferments," and soon it was apparent that Abderhalden's defensive ferments simply did not exist.

Throughout the 20th century, searches for specific and replicable evidence for immune system abnormalities or dysfunction in dementia praecox (schizophrenia) produced wildly conflicting results. Most of the research focused on lymphocytes and immunogobulins, yielding confusing and contradictory results. Diagnostic criteria for identifying subjects with dementia praecox or schizophrenia were not standardized, so the comparison of groups across studies and the generalizing of findings were not possible with any degree of accuracy. Also, much of the confusion regarding immunity was due to a general lack of knowledge about the complexities of the immune system (until the 1960s) and the lack of powerful computer-aided technologies to study them properly (until the 1980s). Even well into the 1990s very few researchers were looking into the role of the immune system in schizophrenia, and chapters reviewing this area of research disappeared from major volumes on the disease. For example, not only is there no chapter on immune system functioning in schizophrenia in the important 2003 volume *Schizophrenia,* 2nd ed., by Steven Hirsch and Daniel Weinberger, nowhere in the volume is such a research literature even acknowledged as existing. However, with further advances in technology and a more sophisticated view of the "immune

system," the latter half of the 1990s brought new researchers to this very old problem in schizophrenia research. The most prominent of the new generation of researchers on the role of immune function in schizophrenia—Norbert Mueller and his colleagues, Markus Schwarz, Manfred Ackenheil, and Michael Riedel—are located at the Psychological Clinic at Ludwig Maximilian University in Munich, Germany.

The concept of the immune system in the early 21st century At the beginning of the 21st century, the relatively primitive "immune system" concept of the 1960s had given way to a highly complex and still somewhat mysterious notion of a mechanism of involving at least two functionally different immune systems. The first, sometimes called the innate immune system, is a more primitive and, assumedly, older immune system in terms of the evolutionary development of life on this planet. This "phylogenetically older" immune system is the first line of defense in many organisms, including humans. The second immune system, assumed to be of more recent origin in the evolution of life on this planet, is known as the adaptive immune system. It is found in "higher" organisms, including humans. This second line of defense includes higher functions such as "memory" and can be conditioned. It is the adaptive immune system's mysterious memory ability that can "recognize" an enemy (e.g., a virus) upon re-exposure to it (that is, a second exposure to the antigen of the intruder), and it can initiate a specific immune response.

The innate and adaptive immune systems are further broken down into two other components. The first, known as cellular immunity, refers to the direct actions of immune cells (such as lymphocytes, macrophages, and leukocytes) and the products they secrete (cytokines) on substances recognized as foreign ("not-self"). In the older innate immune system, cellular immune structures include monocytes, macrophages, granulocytes, and NK (natural killer) cells. In the more recent adaptive immune system, cellular immune structures are T (thumus) and B (bone marrow) cells.

The second, known as humoral immunity, refers to the production of proteins known as antibodies or immunoglobulins that act on some of the other cells in the immune system. Humoral productions of the innate immune system include complement, APP, and mannose binding lectin (MBL). Humoral productions of the phylogenetically more-recent adaptive immune system are the antibodies. A special class of antibodies, known generally as autoantibodies, directs its actions against the body, mistaking "self" for "not-self" and thereby causing the inflammation of cells and eventually disease (cellular pathology). Such diseases are known as autoimmune diseases.

Although the findings of immune system alterations in schizophrenia are varied, inconsistent, and difficult to interpret, two patterns of immune system alterations have been repeatedly noted. The first involves elevated interleukin-6 (IL-6) production. IL-6 is an important cytokine that initiates the immune system response to foreign intruders and especially activates the B-cell system, activating B-cells to synthesize antibodies. IL-6 is released from different cell types in the blood (macrophages, monocytes, and T and B cells). IL-6 may be involved in the exacerbation of symptoms in autoimmune disorders in the central nervous system (brain and spinal cord). IL-6 has also been shown, in vitro, to stimulate neurons to secrete neurotransmitters such as dopamine and probably other catecholamines as well. Several studies have found elevated levels of IL-6 in schizophrenia, perhaps indicating an activation of the innate immune system in schizophrenia. One possible mechanism for this is the activation of the monocyte/macrophage system, leading to an overproduction of IL-6 by the innate immune system. IL-6 levels also increase when the T-Helper-2 cell system is activated (see below). Some studies have found that treatment with ANTIPSYCHOTIC DRUGS significantly lowers levels of IL-6. Hence, at present, the role of IL-6 in the pathophysiology of schizophrenia is suggestive.

A second finding in several studies indicates T-Helper-2 cell activation in schizophrenia. There is a functional balance between the TH-1 system and TH-2 system in the body. In schizophrenia, the activation of the TH-2 system has been coupled with evidence of a lack of activation of the TH-1 system. A lack of activation of the TH-1-related cellular immune system blunts immune system response to exposure to various antigens. In schizophrenia, additional suggestive evidence that there may be

a blunted answer of the cellular mediated (TH-1) response is found in publications prior to the introduction of antipsychotic drugs. Antipsychotic drugs mainly stimulate the TH-1 system to action.

It has been noted for decades that there may be an increased antibody production in persons with schizophrenia. This observation led to the theoretical speculation that schizophrenia is an autoimmune disease. However, although about 20 to 35 percent of persons with schizophrenia were estimated in these studies to show evidence of an autoimmune response, the effect of antipsychotic drugs in producing this effect was not taken into account. It has been known since at least the late 1970s that treatment with phenothiazines increases the production of antibodies that can be detected in the blood and cerebral spinal fluid of persons with schizophrenia. We now know that antipsychotic medications may activate not only TH-1 cell production but also the production of antibodies by activating B cells. Activated B cells produce antibody cells.

The immune system alterations associated with treatment with antipsychotic drugs indicate that both arms of the more recent adaptive immune system may be activated. The cellular immunity arm of the adaptive immune system evidences alterations in the activity of the TH-1 system and the activation of the B cell system. The activation of B cells produces a humoral immunity response, the production of antibodies. This is the second arm of the adaptive immune system. Future studies of the phylogenetically older innate immune system—which is still not well understood—may indicate this system is activated in persons with schizophrenia who are not medicated. Such a definitive finding may demonstrate that such innate immune system alterations may be part of the underlying natural disease processes of schizophrenia and may give us a better idea of the involvement of the immune system in this disorder. Immune system alterations in schizophrenia may therefore be found to be due to a dysfunction in the oldest part of the immune system, the phylogenetically-older innate immune system.

At present, the elevations of IL-6 and the shift from TH-1 blunting to TH-2 activation—the firmest findings of immune system alterations in schizophrenia—may be artifacts of treatment with antipsychotic drugs and have little or no connection to any involvement of the immune system in the etiology (cause) or the pathophysiology of the disease. The theory that schizophrenia may be an autoimmune disease is therefore based on evidence tainted by the effect of antipsychotic drugs on persons with schizophrenia and has little to support it. This situation may change. In a review of the autoimmune hypothesis by Amanda Jones and colleagues published in *Immunology and Cell Biology* in 2005, the discovery that some autoantibodies are directed specifically against neurotransmitter receptors in the brain may give a new perspective on the cause of schizophrenia. The first to propose a similar theory, that schizophrenia is caused by autoantibodies attacking dopamine receptor sites in the brain, was first put forth by J. G. Knight in 1982. The first study to report the detection of "anti-brain antibodies" in persons with schizophrenia was published by Lehmann-Facius in 1939.

Currently, the interdependence of the immune system, the nervous system, and the endocrine system is not well understood in human beings. All three are highly complex systems in the body, each ancient and mysterious in its own right. Nonetheless, the search for immune system alterations continues to this day in schizophrenia research, with not only the blood but also the cerebral spinal fluid examined for antibodies to possible pathogens. Evidence connecting schizophrenia to allergic reactions to foods, viruses transmitted from cats to humans (toxoplasmosis), and a lengthy list of other possible pathogens is still rather weak. Maternal exposure to viruses early in pregnancy has long been suspected to be a RISK FACTOR involved in the etiology of some forms of schizophrenia and bipolar disorder, although no confirmatory antibodies have yet been detected (Yolken and Torrey, 1995). Thus, at present, neither of the two main theories of immunological involvement in the cause and pathophysiology of schizophrenia—the autoimmune hypothesis and the viral infection hypothesis—have much scientific support.

Lymphocytes as a neutral probe into brain functioning and gene expression In 2004 a research group from Groningen, The Netherlands, led by Anatoliy Gladkevich proposed the hypothesis that

lymphocytes—which make up about 20 percent of all white blood cells—might carry information that reflects the metabolism of brain cells and might be utilized as an indirect probe of a limited number of cellular functions, including gene expression. They proposed focusing on the T (thymus-derived) cell, B (bone marrow–derived) cell, and NK cell subpopulations of lymphocytes. This suggestion was recently put into practice by noted schizophrenia researcher Ming T. Tsuang and colleagues and used to develop a genetic diagnostic blood test for schizophrenia and bipolar disorder. Lymphocytes were used to extract mitochondrial RNA from the blood of persons with schizophrenia and bipolar disorder for the purpose of genetic microarray analysis. The assumption was that the switching on of certain genes would leave identifiable mRNA traces in lymphocytes, thus giving an indication of brain functioning. Eight candidate genes were identified as possible biomarkers that could differentially diagnose schizophrenia from bipolar disorder and from normal controls. Both schizophrenia and bipolar disorder were found to have unique blood-based gene expression profiles. The procedure had an overall estimated accuracy of 95 to 97 percent. The preliminary report appeared in the *American Journal of Medical Genetics* in January 2005. However, this study has not yet been replicated, and the results remain tentative.

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impulsive character See BORDERLINE SCHIZOPHRENIA.

incidence of schizophrenia See EPIDEMIOLOGY.

incipient schizophrenia An older term for that phase of the schizophrenic disease process when signs of the impending disorder first clearly make their appearance. This usually involves a clear deterioration in functioning before the active phase of the disorder. This is now called the PRODROMAL PHASE.

incoherence Uncomprehensible speech. This term is applied when a person's speech is marked by ILLOGICAL THINKING, excessive use of incomplete sentences, tangential or irrelevant

statements, or abrupt changes in the topic of conversation. Grammar may be distorted and word usage may be bizarre or idiosyncratic. Incoherence may be a sign of FORMAL THOUGHT DISORDER. It is commonly found in schizophrenia (particularly the DISORGANIZED TYPE) and in the atypical PSYCHOSES. Incoherence does not apply to an identifiable speech or language disorder such as an aphasia.

incomplete penetrance In GENETICS STUDIES, the likelihood that a particular genetically transmitted abnormality (such as a disease) will be expressed depends on the degree of penetrance of that disorder. For example, with SCHIZOPHRENIA it may be that close biological relatives (such as MONOZYGOTIC TWINS) will carry the genetic predisposition to developing the disease, but the genetic abnormalities that may produce the disease may not be expressed equally in the psychological and physiological development of these persons. For example, although the CONCORDANCE RATE for schizophrenia between monozygotic or "identical" twins is suggestively high, nonetheless one twin will often develop schizophrenia and the other will not, rendering them discordant for schizophrenia. This is an example of incomplete penetrance—the genetic defect does not fully "penetrate" or influence later "expressed" psychological and physiological development (in this case, in the genetically "identical" twin that does not develop schizophrenia). Because the modes of GENETIC TRANSMISSION for mental disorders are presently unknown, incomplete penetrance continues to be a major problem in genetics studies of these disorders.

Inderal See PROPRANOLOL.

index case In GENETICS STUDIES of schizophrenia, particularly the "family studies" using the CONSANGUINITY METHOD, the index case is the person who is diagnosed with the disorder. Such information as the possible risk for SCHIZOPHRENIA in relatives of a schizophrenic person are made by analyzing the relationships between the index case and other family members. Another term for the index case is the PROBAND.

India The prevalence rates for schizophrenia in India have been found to range from 2.2 to 5.6 per 1,000. India is unusual in that the greater rates for schizophrenia have been found in the higher socioeconomic groups, which is unlike the pattern for most of the rest of the world, in which the higher rates are found in the lowest socioeconomic strata of society.

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indolamines A group of biogenic amines including the NEUROTRANSMITTER SEROTONIN. The biogenic amines are implicated in the development of certain mental disorders, including SCHIZOPHRENIA, BIPOLAR DISORDER, and DEPRESSION.

See also BIOGENIC AMINE HYPOTHESIS.

induced delusional disorder See FOLIE À DEUX.

infantile autism See AUTISM, INFANTILE.

infectious agent hypothesis See FOCAL INFECTION AS CAUSE OF PSYCHOTIC DISORDERS; VIRAL THEORIES OF SCHIZOPHRENIA.

infectious insanity See FOLIE À DEUX.

influenced psychosis See FOLIE À DEUX.

information processing in schizophrenia By employing metaphors and concepts derived from the computer sciences, COGNITIVE STUDIES OF SCHIZOPHRENIA have attempted to demonstrate the differences in the processes of thinking between

people who are diagnosed with schizophrenia and those who are not. These studies examine the stages of information processing—essentially defined as the encoding, transformation, storage, and retrieval of information for the purpose of regulating behavior—to determine at what stage or stages defects occur in schizophrenics that are unlike those found in most normals.

A comprehensive review of the literature of schizophrenia studies, conducted from an information-processing approach and compiled and analyzed by Canadian psychologists Leonard George and Richard Neufeld, appeared in *Schizophrenia Bulletin* in 1985. They conclude that the following traditional schizophrenic symptoms have the accompanying interpretations according to information processing theory.

Sensory and perceptual anomalies Hallucinations may occur in conjunction with an interaction of several defects in information processing: a disruption in sensory processing, leading to the spontaneous retrieval of information in long-term memory; a predisposition toward representing this information as mental imagery; and the misattribution of these products of internal processing to external sources.

Body-image distortions These may be misperceptions based on the result of a general sensory analysis dysfunction.

Loosening of associations This anomaly may be related to studies that show a schizophrenic deficit in the implementation of the network of semantic relations in long-term memory.

Delusions A large body of evidence indicates cognitive and perceptual differences between paranoid and nonparanoid schizophrenics, with the paranoid characterized by a "premature judgment" or "jump to conclusions" response set.

Movement abnormalities These may be due to inadequate or inaccurate feedback information, or may reflect strategies for coping with attentional dysfunction.

See also ATTENTION, DISORDERS IN; NEUROPSYCHOLOGICAL STUDIES.

George, L., and R. W. J. Neufeld. "Cognition and Symptomatology in Schizophrenia," *Schizophrenia Bulletin* 11 (1985): 264–285.

informed consent Before any medical procedure is performed, physicians must legally obtain the informed consent of the patient to perform the procedure. This involves an explanation of the purpose of the procedure, how it is done, and the potential risks involved for the patient that may result from the procedure. If the patient agrees, the consent is then given in writing. Although obtaining informed consent usually presents no problem in most people who are about to undergo a medical procedure or treatment (e.g., surgery), for individuals who are suffering from a psychotic disorder there are dilemmas. Can a person who is having problems remaining in contact with "reality" and is unable to think clearly and comprehend difficult information truly give informed consent?

This is an ethical and legal issue that is continually debated not only in the psychiatric profession but also in the legal system. For example, all the present medical treatments for the psychotic disorders (ANTIPSYCHOTIC DRUGS, electroconvulsive therapy, etc.) have side effects that effect either the immediate functioning of the individual (e.g., loss of memory after ECT) or his or her long-term health (e.g., TARDIVE DYSKINESIA caused by years of treatment with antipsychotic drugs). Most studies confirm the obvious: psychotic patients may say that they understand what is being explained to them, but in fact when they are given an objective examination afterward, they reveal that they did not. The "lack of informed consent" before administering treatment to patients is one of the most common causes of legal action against psychiatrists.

Cohen, R. J., and W. E. Mariano. *Legal Guidebook in Mental Health.* New York: Free Press, 1982.

Irwin, M., et al. "Psychotic Patients' Understanding of Informed Consent," *American Journal of Psychiatry* 142 (1985): 1,351–1,354.

inheritance, modes of See GENETIC TRANSMISSION.

input dysfunction hypothesis This is one of the early "cognitive" interpretations of the behavior of schizophrenics that was put forth to explain defi-

cits in attention. In 1964, British psychologist Peter Venables proposed that schizophrenics suffer from an "input dysfunction" in their ability to focus attention. Essentially, he postulated that the ability to focus attention was related to levels of internal "arousal" in the nervous system. It is a well-known fact that for most of us, when we are nervous about performing some activity (such as public speaking, a job interview, or taking a test), our ability to focus our attention may be affected. Venables proposes that in chronic nonparanoid schizophrenics there is a heightened arousal of the brain and nervous system (termed "cortical arousal"), which leads to an oversensitivity. Thus, when stimuli from the outside confronts the schizophrenic (even simple social interactions, for example), the person finds this to be "too intense," and he or she "shuts down." They may withdraw, become apathetic, and feel a restriction in their range of feelings (these are now called NEGATIVE SYMPTOMS). The field of attention is then narrowed in these people. In contrast, acute schizophrenics suffer from a lowered level of cortical arousal when compared to normals, resulting in an expansion of attention that is so broad that they feel that they cannot shut anything out of awareness. Everything hits them at once, and they report feeling "flooded."

Venable's "input dysfunction theory" is only one of the many theories put forth in the 1960s about deficits in the ability of schizophrenics to focus attention. An excellent summary of these detailed theories, and of the research on all areas of "schizophrenic cognition," can be found in a classic volume by Loren J. and Jean P. Chapman, *Disordered Thought in Schizophrenia*.

See also ATTENTION, DISORDERS IN.

Chapman, L. J., and J. P. Chapman. *Disordered Thought in Schizophrenia.* Englewood Cliffs, N.J.: Prentice Hall, 1973.

Venables, P. H. "Input Dysfunction in Schizophrenia." In *Progress in Experimental Personality Research.* Vol. 1, edited by B. A. Maher. New York: Academic Press, 1964.

insane A word derived from the Latin *insanus,* for "unsound (in mind)."

insanity Originally termed "insanity of mind," this refers to the state of being insane. Presently, it has only a legal meaning (not a psychiatric one) relating to the soundness of mind of a person when involved in actions that have legal consequences. More generally, it has come to mean that a psychosis was present when a person committed such a legally consequent act. Throughout most of the 18th and 19th centuries, "insanity" was a generic term for all mental illnesses and was used in the same way that we rely on the term "mental disorders" today. Until the latter part of the last century, "lunacy" was a synonym also used by the psychiatric and legal professions to refer to mental illness. In 19th-century France, the distinction made was between *aliéne* and *demi-fou,* roughly our present distinction between a "psychosis" and "neurosis." Although a vast literature has existed since the early 1800s on the legal issues raised by acts committed by mentally ill offenders ("insane" offenders), the word "insanity" was still being used in a quasi-psychiatric sense (at least in the United States) in the 1920s. In 1923 William Alanson White, the superintendent of St. Elizabeth's Hospital in Washington, D.C., and the foremost forensic psychiatrist in the country, argued forcefully in a book that the word "insanity" was entirely to be considered a legal term and had no medical meaning. White, as the president of the AMERICAN PSYCHIATRIC ASSOCIATION at that time, was also instrumental in changing the name of the *American Journal of Insanity* to the *American Journal of Psychiatry* in 1922.

See also FEIGNED INSANITY; M'NAUGHTEN RULES.

Hughes, J. S. *In the Law's Darkness: Isaac Ray and the Medical Jurisprudence of Insanity in Nineteenth-Century America.* New York: Oceana Publications, 1986.

Quen, J. M. "Isaac Ray and the Development of American Psychiatry and the Law," *Psychiatric Clinics of North America* 6 (1983): 527–537.

White, W. A. *Insanity and the Criminal Law.* New York: Macmillan, 1923.

insanity by contagion See FOLIE À DEUX.

insanity defense This is the legal defense in which a person may plead that he or she is not

guilty for committing an alleged crime by reason of insanity. It apparently dates back to 13th-century English constitutional law, when it was popularly known as the "wild beast test," i.e., if people act like wild beasts they cannot be held accountable for their actions. Over the centuries the concept that a person could not be responsible for criminal acts because he or she was *non compos mentis* (mentally incompetent), usually due to being an "idiot" since birth or a "lunatic" thereafter, has undergone many changes. Our modern concepts of the insanity defense date back to the famous trial of Daniel M'Naughten in England in 1843 in which he was acquitted of a criminal act on the grounds of insanity. The judges in that trial relied primarily on the opinions in a book by American physician Isaac RAY, *A Treatise on the Medical Jurisprudence of Insanity* (1838), in which he advocated many reforms in the then-standard criminal laws and in the incompetency and commitment laws. The famous M'NAUGHTEN RULES, which later resulted from the trial, became the established criterion of "knowing right from wrong" for judging insanity.

The insanity defense has been disputed in the 1980s due to the "not guilty by reason of insanity" verdict against John Hinckley Jr., who attempted to assassinate President Ronald Reagan. Some states have abolished it completely, and many others have instituted major modifications that restrict its use. Some states have passed legislation allowing a variation on the verdict in the form of "guilty but insane."

Lewinstein, S. R. "The Historical Development of Insanity as a Defense in Criminal Actions," *Journal of Forensic Science* 14 (1969): 275–293, 469–500.

Oppenheimer, H. *The Criminal Responsibility of Lunatics: A Study in Comparative Law.* London: Sweet & Maxwell, 1909.

insight Family members of persons with schizophrenia insist that the worst symptom of their loved one's disease is "lack of insight" or "poor insight" into their own illness and the need for medication to treat it. Lack of insight is one of the most common features of psychotic disorders. Many persons simply are not aware, or do not acknowledge, that they are "delusional" due to an illness that needs treatment. The very meaning of the term "insanity" since antiquity is bound to this notion. Throughout the history of PSYCHIATRY, lack of insight has been viewed as a willful act of opposition requiring that a person be "flogged into reason," or as an unconscious psychological defense mechanism (Freudian PSYCHOANALYSIS), an adaptive coping strategy to avoid a painful awareness of truths about oneself, or—the current view—as the result of a neurocognitive deficit caused by abnormal brain functioning. This last interpretation was perhaps first proposed by the noted British psychiatrist Aubrey Lewis (1900–75) in 1934.

It has only been relatively recently, since the early 1990s, that correlational and experimental studies of insight in PSYCHOSIS have been conducted. Poor insight or unawareness of illness is directly correlated with medication noncompliance, making this a vital issue of concern for the treatment of BIPOLAR DISORDER, SCHIZOPHRENIA, and the other psychotic disorders. In studies conducted by Xavier Amador and colleagues, lack of insight in schizophrenia has not been found to be highly correlated to the severity of symptoms but instead is related to the type of symptoms. Poor insight is associated with the presence of NEGATIVE SYMPTOMS. Lack of insight is far more common in schizophrenia than in any other psychotic disorder. It is speculated that this may tie in with BRAIN ABNORMALITIES IN SCHIZOPHRENIA associated with the frontal lobe. Second in severity to schizophrenia, however, is the lack of insight manifested by persons experiencing a MANIC EPISODE.

See also BIPOLAR DISORDER; NEUROPSYCHOLOGICAL STUDIES OF SCHIZOPHRENIA.

Amador, X. F. *I Am Not Sick I Don't Need Help! Helping the Seriously Mentally Ill Accept Treatment.* Peconic, New York: Vida Press, 2000.

Amador, X. F., and A. S. David. *Insight and Psychosis: Awareness of Illness in Schizophrenia and Related Disorders.* 2nd ed. Oxford: Oxford University Press, 2004.

Lewis, A. J. "The Psychopathology of Insight," *British Journal of Medical Psychology* 14 (1934): 332–348.

institutionalization It has long been observed that many people who are diagnosed with SCHIZO-

PHRENIA and spend most of their time in institutions tend to get worse as the years go on. Patients become apathetic, submissive, resigned, emotionally flat, and lose their sense of appropriateness in social behavior. But is this due to the disease process or is it due to the experience of being involuntarily (usually) hospitalized in an institution?

There have been many theories about the effects of hospitalization on the course of schizophrenia, and the ACUTE-CHRONIC DISTINCTION in schizophrenia research is partly designed to "control" for such institutionalization effects. For example, Erving GOFFMAN pictures the "inmates" of "total institutions" (mental hospitals, prisons, etc.) as undergoing a degrading devaluation of any sense of self-worth or identity, as being, essentially, brainwashed into the "role" of career mental patient. Others have viewed a hospitalized schizophrenic patient as holding a unique privilege—not responsible for his actions. Therefore, there may be every incentive to be sexually or aggressively inappropriate with others and to abdicate responsibility for self-care (feeding oneself, hygiene, etc.). Therefore, according to this view, patients are "rewarded" for acting "crazy" and manipulatable and remaining in the hospital—which may be more like a vacation resort than anything else. This latter position reflects the "impression management" theory of the effects of the institution on schizophrenics proposed by Braginsky and Braginsky in the late 1960s.

Controlled studies of the effects of institutionalization (chronicity) on schizophrenic patients have generally found that there is little evidence of intellectual deterioration that cannot be attributed to the disease process. Furthermore, the "zombie-like" appearance of some severe schizophrenics in institutions cannot entirely be attributed to the influence of ANTIPSYCHOTIC DRUGS, since these behaviors match clinical descriptions of schizophrenics in institutions before the advent of this form of treatment. Some early studies of these effects, as well as a summary of the above theories, can be found in a 1973 book by Chapman and Chapman. However, given the often emotionally intense, noisy, and frequently violent "holding-tank" environments of most large psychiatric institutions, it is difficult to see how living in such a setting could not have a negative effect on the mental health of the patient.

See also HOSPITALISM.

Braginsky, B. M., and D. D. Braginsky. *Methods of Madness: The Mental Hospital as a Last Resort.* New York: Holt, Rinehart & Winston, 1969.

Chapman, L. J., and J. P. Chapman. *Disordered Thought in Schizophrenia.* Englewood Cliffs, N.J.: Prentice Hall, 1973.

insulin coma (or shock) therapy This was the most popular—and most consistently effective—form of treatment for ACUTE SCHIZOPHRENIA from 1933 to the late 1950s, when treatment with ANTIPSYCHOTIC DRUGS became dominant. This technique was invented by an Austrian psychiatrist, Manfred Joshua Sakel (1906–1957), who was working at the Lichterfield Hospital in Berlin with patients recovering from morphine addiction, between 1927 and 1933. To diminish the agitation and psychotic symptoms due to withdrawal, Sakel began giving them experimental doses of insulin, a relatively new drug—isolated and used for the treatment of diabetes only in 1922—whose full range of effects were not yet well known. He discovered that the higher doses did indeed relieve the agitative withdrawal symptoms. When he found that high doses would induce a coma in patients—particularly in those patients who were also diagnosed with SCHIZOPHRENIA—he began to experiment in 1933 with induced insulin comas as a treatment for schizophrenia.

This therapy essentially regarded the induction of a hypoglycemic (abnormally low blood sugar) coma as a form of "shock" to the system of a schizophrenic patient. The modified procedure, which eventually came into use after Sakel published his results in 1934, required several months of treatments on an inpatient unit with a highly trained staff, since inattentiveness could lead to the death of the patient. In his book, *Interpretation of Schizophrenia* (1974), Silvano Arieti described the usual procedure for insulin treatment:

> It consists of administration of insulin in progressively larger doses. One starts initially with 10 to 15 units and increases the dosage until the patient

undergoes severe hypoglycemic shocks, which are characterized by comas and, less frequently, by epileptic seizures. The average coma producing dose is 100 to 150 units. The state of coma used to be terminated in the fourth or fifth hour by administration of an adequate amount of carbohydrates. Sugar was given orally if the patient was able to drink, or through tube feeding, or through an intravenous injection of a glucose solution. Now termination is obtained through the use of glucagon, in doses of 0.33 to 1 mg intravenously or intramuscularly. Small amounts generally awaken the patient, who is then able to drink a sugar solution. From a minimum of twenty to a maximum of eighty comas are generally produced, usually at a frequency of at least three times a week.

Sakel's theoretical explanation for why insulin coma therapy worked with acute schizophrenics was never considered adequate and was rejected by most. Nonetheless, the treatment seemed to be the first one that was consistently successful with people who were undergoing their very first episodes of psychosis. Chronic schizophrenics did not benefit at all from the treatment. Critics of this method have pointed out that most people undergoing their very first schizophrenic episodes respond to just about any form of treatment (or go into spontaneous remission anyway). Sakel immigrated to the United States in 1937, where insulin coma therapy became a prominent treatment for schizophrenia for the next two decades.

Sakel, M. "New Treatment of Schizophrenia," *American Journal of Psychiatry* 93 (1937), 829–841.

———. *The Pharmacological Shock Treatment of Schizophrenia.* New York: Nervous and Mental Diseases Monographs, 1936.

intermetamorphosis syndrome One of the rarest of the psychotic MISIDENTIFICATION SYNDROMES, the intermetamorphosis syndrome involves the delusional belief that certain persons or objects have been interchanged. Rather than insisting that related persons are alien "impostors" (as in CAPGRAS SYNDROME), or that these strangers are, in reality, known persecutors who are inhabiting their bodies (FREGOLI'S SYNDROME), this delusion involves the belief that known persons have been interchanged or replaced by other known persons. For example, such a delusional person may insist that one's mother has been replaced by one's first-grade teacher, and so on. In the very first published case of the intermetamorphosis syndrome—by French psychiatrists P. Courboun and J. Tusques in 1932—a depressed woman with paranoid delusions of persecution insisted that her new coat had been replaced by a shabby, older one; that her two young hens had been replaced by older ones; and that various women had been metamorphosed into men, and the young into old. As with the other misidentification syndromes, intermetamorphosis syndrome may be the result of an ORGANIC MENTAL DISORDER or be found within the delusional systems of those diagnosed with the paranoid subtype of schizophrenia.

Courbon, P., and J. Tusques. "L'illusion d'intermétamorphose et de charmes," *Annales Medico-Psychologique* 90 (1932): 401.

interpersonal functioning In any of the psychotic disorders, but particularly in SCHIZOPHRENIA, there is a marked deterioration in the ability to sustain relationships with other people. In fact, social withdrawal, emotional detachment, and occupational problems often mark the beginning of the first full onset of schizophrenia. Since psychotic disorders, by their very definition, involve a disturbed relationship with the external demands of reality, this invariably leads to problems with others. Sometimes people may find themselves becoming preoccupied with bizarre ideas and fantasies and will therefore shut out relationships. Other afflicted people may instead do the opposite: They may begin to cling to others, becoming almost child-like in their dependence on them. Or they may begin to intrude upon strangers in public, demanding their attention and becoming physically too close to them, obviously making the strangers uncomfortable. These "inappropriate behaviors"—as the phrase is so often used in the psychiatric institutions of today—are often quite troublesome for the family members of schizophrenics and people with other psychotic

disorders, and often leads the family finally to seek help for the individual.

introversion A term coined by Swiss psychiatrist and psychoanalyst C. G. JUNG for a pervasive "attitude" toward the world in which one's "psychic energy" or "libido" is primarily directed inward toward the self and the internal world of one's own fantasies. Jung believed all people fit along a continuum from introversion to extroversion with, usually, one or the other as a dominant mode of approaching the world. Although introverted people were often very individualistic and were supposed to have a close relationship with the unconscious, they were often uncomfortable in groups or in social situations. In its extreme pathological form, introversion was thought to describe the withdrawal of many schizophrenic patients from the external world.

involuntary commitment See COMMITMENT.

involutional psychosis Also referred to as "involutional melancholia," this is a severe depression that has developed into a psychosis. Agitation, delusions, mood-congruent hallucinations, and somatic preoccupations characterize this disorder. It is also characterized by a loss of interest in activities, early morning awakenings, worse depression in the morning, significant weight loss or anorexia, and psychomotor retardation or agitation.

ipsity disorder See SUBJECTIVE EXPERIENCE IN SCHIZOPHRENIA.

Ireland Along with parts of Croatia and northern Sweden, western Ireland has one of the highest prevalence rates of SCHIZOPHRENIA in the world. Proportionately, Ireland has three times more people diagnosed with schizophrenia in psychiatric hospitals and three times more first admissions for schizophrenia than England. The schizophrenia first-admission rate is even three times that of the United States. Western and southwestern Ireland, which contain the poorer counties, have the highest schizophrenia rates. In these areas there is a one in 25 chance that a person will be hospitalized for schizophrenia at some point in their lives, making these rates the highest in the world. The counties most affected are Mayo, Kerry, Sligo, Roscommon, Galway, Clare, Cork, and Waterford. Northern Ireland, which is part of the United Kingdom, has always maintained a lower rate of schizophrenia than in the south. Studies in the United States and Canada have consistently found that immigrants from Ireland have very high first-admission rates to psychiatric hospitals when compared to other ethnic groups.

Torrey, E. F. "Prevalence Studies of Schizophrenia," *British Journal of Psychiatry* 150 (1987): 598–608.

isolation Isolating agitated or violent people who are psychotic has long been a method of preventing them from harming themselves or others. It has been considered by many, over the centuries, as a more humane form of restraint than either physical or chemical methods. The famous "padded rooms" invented by the German physician Ferdinand AUTENREITH (1772–1835), which were lined with cork and rubber, were widely copied throughout European asylums in the 19th century as places to isolate patients. Many institutions today still have isolation or "time-out rooms" for their more active patients.

In his 1838 classic, *Des Maladies Mentale,* ESQUIROL devotes many pages to a discussion of "isolation," but he uses the word in much the same way we use "hospitalization" today. His use of the term was to denote the isolating of the mentally ill person from his family by commitment in an institution for the "insane." Esquirol felt that the novelty of the new situation would have therapeutic value: "The first effect of isolation is, to produce new sensations, to change and break up the chain of ideas, from which the patient could not free himself. New and unexpected impressions strike, arrest, and excite his attention, and render him more accessible to those councils, that ought to bring him back to reason." Yet, after listing more virtues of commitment to an

asylum for the insane, Esquirol also expresses some words of caution about "isolation":

> But, it may be said, that there are insane persons who are cured at home. This is true. These cures, however, are rare, and cannot impair the general rule. They prove only, that isolation, like all other curative means, ought always to be prescribed by a physician. I will say more, – that isolation has been fatal to some persons. And what shall we conclude from this? That we should recommend it with caution; especially when it is to be prolonged; and also, that it is the nature of the best and most useful things, not to be always exempt from inconveniences. To the wise, judicious and experienced physician does it belong, to foresee and prevent them.

A more commonly used term in the 20th century for isolating patients in separate rooms is *seclusion.*

Esquirol, J. E. D. *Mental Maladies, A Treatise on Insanity.* Translated by E. K. Hunt. 1838. Reprint, Philadelphia: Lea & Blanchard, 1845.

Israel Israel is a nation of immigrants. Since studies of SCHIZOPHRENIA prevalence rates in immigrant groups are subject to errors in statistical measurement because of the large number of variables to take into consideration, it has been difficult to determine reliable prevalence rates for schizophrenia in Israel.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

Italy It has been noted at least since 1862, when W. Charles Hood published his book *Statistics of Insanity,* that the rates of "insanity" in southern European countries were much lower than those in northern European countries. In fact, Hood found Italy to have the lowest rates in all of Europe. Although no conclusive prevalence rates have been calculated for Italy, it has been noted that, well into the 20th century, Italy had low hospitalization rates for SCHIZOPHRENIA as compared to other countries. Also, it has been found that the first-admission hospitalization rates for Italian immigrants in England and the United States are far lower than for other ethnic groups.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

J

Janet, Pierre (1859–1947) A French philosopher and psychiatrist whose research on the nature of the unconscious mind and on psychotherapy makes him one of the most important figures in the history of psychology and PSYCHIATRY. He was appointed to teach philosophy at the Liceum of Le Havre in 1881 (at the age of 22) and did volunteer work at the local asylum, where he conducted research for his doctoral dissertation. His studies of the highly hypnotizable hysterical female patients there led to observations about the workings of the unconscious mind, which he incorporated into his dissertation and his classic book *L'Automatisme Psychologique (Psychological Automatisms)* (1889). He is best remembered for his descriptions of the psychological process known as DISSOCIATION and how it worked in people under hypnosis, in those with hysteria, and in those with multiple personalities. About 1980, when multiple personality disorder once again began to attract serious interest, the work of Janet likewise found new students. Janet wrote voluminously (in French) on a wide range of psychiatric, psychological, and philosophical topics, but only a few of these works have ever been translated into English. There are many papers on paranoid schizophrenia that Janet produced in the 1930s and 1940s that still await translation.

Janet, P. *L'Automatisme psychologique.* Paris: Félix Alcan, 1889.

Perry, C., and J. R. Laurence. "Mental Processing Outside of Awareness: The Contributions of Freud and Janet." In *The Unconscious Reconsidered,* edited by K. S. Bowers and D. Meichenbaum. New York: John Wiley, 1984.

Van der Hart, O., and B. Friedman. "A Reader's Guide to Pierre Janet on Dissociation: A Neglected Intellectual Heritage," *Dissociation* 2 (1989): 3–16.

Japan Japan and Sweden are the two countries in which the best data on the prevalence rates for SCHIZOPHRENIA have been collected. In Japan, the prevalence rates for schizophrenia have ranged from 2.1 to 2.3 per 1,000. The lowest socioeconomic level in Japan has been found to have prevalence rates for psychotic disorders that are three to five times higher than the highest socioeconomic levels.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

jealous type One of the variants of delusional disorder as listed in *DSM-IV* (1994). It is a persistent, usually "nonbizarre" DELUSION in which a person is convinced that his or her spouse is being unfaithful—without any rational grounds for the suspicion. As this delusion can take on psychotic dimensions, such a person may take extraordinary measures to intervene and dissolve the fantasized relationship. He or she may keep the spouse locked in the house or may restrict that person's activities in other ways. The person with the delusional jealousy may secretly follow the spouse or have that person followed. In some cases the person with the psychotic delusion may physically harm the spouse. Although the delusion itself is so out of line with reality that it renders the person psychotic at times, no other FORMAL THOUGHT DISORDER or other sign of a psychosis is present. In its pure form, this delusion of jealousy has been called the OTHELLO SYNDROME.

jealousy, delusional See DELUSIONAL JEALOUSY.

Jung, Carl Gustav (1875–1961) A Swiss psychiatrist and psychoanalyst who formulated his own unique "analytical psychology" (first called "complex psychology") after breaking with his mentor, Sigmund FREUD, in 1913. The son of a Protestant pastor in Basel, Switzerland, the young Jung originally wanted to become an archaeologist. After a vividly symbolic dream, he decided instead to pursue medicine, which was an offshoot of his fascination with the natural sciences. During his medical school years (specifically, in 1896), Jung became interested in the unusual trances and hypnotic phenomena of his 15-year-old cousin, who was a medium. In an attempt to analyze her behavior, he read widely in philosophy and spiritualism. In 1902, he based his doctoral dissertation on this work with her. In 1900, during his final examinations, he came across a PSYCHIATRY textbook written by German psychiatrist and neurologist Richard von Krafft-Ebing that convinced him he should study psychiatry—commonly regarded at the time as an "inferior" medical discipline. Jung passed his medical examinations and won a position at the BURGHÖLZI HOSPITAL under the direction of Eugen BLEULER in 1900.

From the beginning, Jung was interested in pursuing the psychological and symbolic meaning behind the psychotic disorders and not just their classification, which was the traditional occupation of psychiatry in those days. As Jung tells it in a lecture given in 1925:

> I told nobody that I intended to work out the unconscious phenomena of the psychoses, but that was my determination. I wanted to catch the intruders in the mind—the intruders that make people laugh when they should not laugh, and cry when they should not cry.

Jung remained at the Burghölzi for nine years. During this time he developed a worldwide scientific reputation for his famous "word-association test" experiments and for his 1907 monograph on the psychological processes involved in dementia praecox (*Über die Psychologie der Dementia Praecox*). It was likewise during these years that Bleuler was developing his ideas on "schizophrenia" (a term Bleuler first used in print in 1908), and Bleuler acknowledges the contributions of his assistant Jung in the preface to his famous book, *Dementia Praecox, Or the Group of Schizophrenias* (1911). Jung's later psychology was based largely on the dissociative experiences of his mediumistic cousin and his nine years of daily clinical work with institutionalized psychotic patients. He was particularly interested in the story-motifs and structures of schizophrenic hallucinations and delusions and how they seemed to correspond to the myths and fairy tales of centuries past. These organizing structural dominants of all psychological life, conscious and unconscious, he called "archetypes." In contrast, Freud (whom Jung was associated with from 1907 to 1913) based his theories of the structure and dynamics of the psyche on the neurotic patients he saw in the Viennese consulting room of his home and had only minimal contact with institutionalized patients.

Jung is famous for proposing that a "toxin" may be the actual cause of many of the seriously debilitating psychological symptoms of SCHIZOPHRENIA, although this toxin was first produced by the intense emotions of a psychological disturbance (i.e., a complex). He is also remembered for being perhaps the first to conduct individual psychotherapy with institutionalized schizophrenics; in his descriptions of his pre-psychoanalytic-period cases, he revealed a psychoeducational and rehabilitative approach rather than an insight-oriented one—an approach that is recommended for use with schizophrenics today. Although in his writings Jung sometimes refers to the successful treatment of "dementia praecox" in some patients, he later admitted that these were BORDERLINE CASES that did not develop into the full picture of this disorder. In a September 24, 1926, letter to an American psychiatrist who had asked about Jung's successful treatment of dementia praecox, Jung admits the limitations of his success:

> I suppose the news you heard of my successes in the treatment of Dementia praecox is greatly exaggerated. As a matter of fact I only treated a limited number of cases, and these were all what one might call in a liquid condition, that is, not yet congealed. I avoid the treatment of such cases as much as possible. It is true they can be treated,

> and even with the most obvious success, but such a success costs almost your own life. You have to make the most stupendous effort to reintegrate the dissociated psychic entities, and it is by no means a neat and simple technique which you can apply, but a creative effort with a vast knowledge of the unconscious mind.

Even in the face of the growing evidence for the organic basis of schizophrenia, until the end of his life Jung maintained that it may have an equally important psychological cause. His final statement on the issue was a letter sent to the chairman of a Symposium on Chemical Concepts of Psychosis (held in September 1957), clarifying his views on the issue; it was published in 1958. Jung asserts that the cause of schizophrenia is a "dual one: namely, up to a certain point psychology is indispensable in explaining the nature and the causes of the initial emotions which give rise to metabolic alterations. These emotions seem to be accompanied by chemical processes that cause specific temporary or chronic disturbances or lesions."

See also ABAISSEMENT DU NIVEAU MENTAL; BIOCHEMICAL THEORIES OF SCHIZOPHRENIA; BIBLIOTHERAPY; COMPLEX; DISSOCIATION.

Jung, C. G. *Letters. 1:1906–1950.* Princeton, N.J.: Princeton University Press, 1973.

———. *The Collected Works of C. G. Jung.* 20 vols. Princeton, N.J.: Princeton University Press, 1953–1979.

———. *Analytical Psychology: Notes of the Seminar Given in 1925.* Princeton, N.J.: Princeton University Press, 1989.

K

Kahlbaum, Karl Ludwig (1828–1899) In 1863 German psychiatrist Karl Kahlbaum of Prussia published his Habilitation (the equivalent of a second doctoral dissertation in Germany, necessary for becoming a university professor), *Die Gruppirung der psychischen Krankheiten* (*The Classification of Psychiatric Diseases*). In this book, Kahlbaum described a class of progressively degenerating psychotic disorders that he grouped under the term *Vesania typica* (typical insanity). This example, and numerous others in his textbook, indicated Kahlbaum's distate for those advocating that all the insanities were really manifestations of one underlying insanity (a concept termed the *EINHEITSPSYCHOSE* or "unitary psychosis"). In 1866 Kahlbaum became the director of a private psychiatric clinic in Goerlitz, Prussia, a small town near Dresden. He was accompanied by his younger assistant, Ewald Hecker (1843–1909), and together they conducted a series of research studies on young psychotic patients that would eventuate in a major influence on the development of modern psychiatry. Kahlbaum and Hecker were the first to describe and name such syndromes as dysthymia, cyclothymia, PARANOIA, CATATONIA and HEBEPHRENIA. These are just the diagnostic labels that survived into history. In an attempt to overthrow the confusion of the past, including the inclination of physicians since pagan antiquity to group all mental disorders as forms of either "MANIA" or "MELANCHOLIA" (terms that were not distilled down to their present meanings until the period between 1850 and 1900), Kahlbaum made the mistake of coining new names for just about every syndrome. Though acknowledged as a major psychiatric thinker in the 19th century, perhaps second only to Emil KRAEPELIN, his classification system was too novel and idiosyncratic to be widely adopted, and thus Kahlbaum receded into the shadows of history.

Perhaps their most lasting contribution to psychiatry was the introduction of the "clinical method" from medicine to the study of mental diseases, a method which is now known as psychopathology. Other than Benedict-Augustin MOREL's claims about mental illness in his DEGENERATION THEORY, the element of time had largely been missing from definitions of mental disorders. Psychiatrists made pronouncements about prognosis that were not based on careful observations of the changing symptoms of patients over time. MAD-DOCTORS, ALIENISTS, and other physicians who wrote about the insane arbitrarily invented names for insanities and described their characteristic signs and symptoms based on a short-term, cross-sectional observation period of their lunatic patients. When the element of time was added to the concept of diagnosis, a diagnosis became more than just a description of a collection of symptoms: diagnosis now also defined prognosis (course and outcome). An additional feature of the clinical method was that the characteristic symptoms that define syndromes should be described without any prior assumption of brain pathology (although such links could be made later as scientific knowledge progressed). Karl Kahlbaum first made his appeal for the adoption of the clinical method in PSYCHIATRY in his 1874 book on catatonia. Without Kahlbaum and Hecker there would be no dementia praecox.

See also DEMENTIA PRAECOX; NOSOLOGY.

Kahlbaum, K. *Die Gruppierung der psychischen Krankheiten und die Eintheilung der Seelenstorungen.* Danzig: 1863.

———. "The Relationships of the New Groupings to Old Classification and to a General Pathology of Mental Disorder," *History of Psychiatry* 7 (1999): 167–181.

Lanczik, M. "Karl Ludwig Kahlbaum and the Emergence of Psychopathological and Nosological Research in German Psychiatry," *History of Psychiatry* 3 (1992): 53–58.

Kallman, Franz J. (1897–1965) Kallman was a German-Jewish psychiatrist and researcher who, from 1928, directed neuropathology laboratories for psychiatric hospitals in Berlin. In 1936 he immigrated to the United States and brought his research on the genetics of MENTAL DISORDERS with him. A translated version of his manuscript was published in 1938, and it is considered by many contemporary scholars to be the first true starting point for the GENETICS STUDIES of schizophrenia. He also later became interested in the genetics of manic-depressive psychosis.

Kallman, F. J. *The Genetics of Schizophrenia.* New York: J. S. Augustin, 1938.

Kandinsky-Clérambault syndrome This is the type of delusional experience in which a person feels his or her mind is being controlled or influenced in some way by outside forces. It is a commonly reported experience in people diagnosed with SCHIZOPHRENIA. It was first described in 1890 by Viktor Chrisanfovich Kandinsky (1825–89) and Gaétan Gaitian de Clérambault (1872–1934).

Kanner, Leo (1894–1981) An Austrian-born psychiatrist who immigrated to the United States and became the "father of child psychiatry." He did research on INFANTILE AUTISM and CHILDHOOD SCHIZOPHRENIA, which he thought, based on psychoanalytic theory, were caused by disturbances in early mother and child relationships. Kanner separated infantile autism from childhood schizophrenia in 1943, believing them to be two separate types of childhood disorder. Because of his pioneering work in this area, infantile autism is also called Kanner's syndrome.

Kanner, L. *Child Psychiatry.* Springfield, Ill.: Charles Thomas, 1942.

Kanner's syndrome See AUTISM, INFANTILE.

karyotype This is a chromosome that has been stained with a special substance and prepared so that it can be identified. Only since the early 1960s, when it was developed, has the process of karyotyping chromosomes made it possible to identify and study specific chromosomes.

katatonia See CATATONIA.

Kirkbride, Thomas Story (1809–1883) An American physician from Philadelphia and one of the original 13 founders of the AMERICAN PSYCHIATRIC ASSOCIATION. Kirkbride was the superintendent of the psychiatric section of the Pennsylvania Hospital for more than four decades (from 1840 until his death)—so long, in fact, that the institution became known by Philadelphia locals as simply "Kirkbride's." He became interested in the effects on the patients of the institutional environment's construction and of staff management styles; he firmly believed that, by designing and building pragmatic institutions, mental illness could be cured. His 1847 textbook on this issue (second edition, 1880), considered one of the most important American psychiatric textbooks of the 19th century, is divided into two primary parts: the first concerning the physical details of the ideal institution and the second detailing administrative procedures.

Kirkbride, T. *On the Construction, Organization, and General Arrangements of Hospitals for the Insane, with some Remarks on Insanity and its Treatment.* Philadelphia: Blakiston, 1880.

Tomes, N. *A Generous Confidence: Thomas Story Kirkbride and the Art of Asylum Keeping, 1840–1883.* Cambridge: Cambridge University Press, 1984.

Kitsune-Tsuki psychosis This is an unusual psychotic disorder native to Japan in which a person maintains the DELUSION that he or she has been possessed by a fox. Kitsune-Tsuki psychosis is an

example of a "culture-bound syndrome." A European variation of this is LYCANTHROPY, in which a person believes he or she has been transformed into a wolf. Some psychiatric authorities on this syndrome have likened it to an atypical psychotic disorder marked by the "fox" delusion, and others have noted that it is similar to a POSSESSION SYNDROME.

Furukawa, F., and M. Bourgeois. "Délires de possession par le renard au Japon (ou délire de Kitsune-Tsuke)," *Annales Médico-Psychologiques* 142 (1984): 677–687.

Korsakov's psychosis More commonly known as Korsakov's syndrome, this syndrome of amnesia is due to the deficiency of thiamine in the body caused by chronic alcoholism. In *DSM-IV* (1994) it is called alcohol amnestic disorder. Once it appears, this syndrome follows a chronic course, and impairment may be so severe as to require lifelong custodial care. When thiamine is administered during a detoxification process before the syndrome is evident, it does not develop. Prior to the discovery that thiamine could reverse some of the other neurological signs that precede the amnesia of this syndrome, it routinely developed into its most severe forms. The syndrome is named after Sergei Sergeievich Korsakov (1853–1900), who was largely responsible for founding the discipline of psychiatry in Russia. He first described this syndrome in 1887 but called it *cerebropathia psychica toxemica*.

Kraepelin, Emil (1856–1926) Emil Kraepelin is now universally recognized as the most important figure in the history of psychiatry in the 20th century. Certainly he is the most important figure in the history of research on schizophrenia and the other psychotic disorders. Kraepelin was a German neurologist, psychiatrist, professor, and experimental researcher who understood (a) that mental disorders were caused by biological processes affecting the brain and (b) that heredity (genetics) played a significant role in the origins and development of DEMENTIA PRAECOX (SCHIZOPHRENIA). Kraepelin's biological outlook and his diagnostic classification of mental disorders remain the foundation of our understanding of schizophrenia today. Contemporary biological psychiatry and the diagnostic criteria for the psychotic disorders found in *ICD-10* (1992) and *DSM-IV* (1994) are thoroughly Kraepelinian.

Biographical history Kraepelin was described by one observer in 1916 as "a small stocky man with yellowish skin and a full, dark beard." He was an intense, driven man who characterized himself as having a "firm and persevering will." He was first and foremost a scientist and had no religious creed, although he was tolerant of other faiths. Like many German scientists in the 19th and early 20th centuries, he had a fascination with the religions of India and an attraction for pantheism. Kraepelin was a well-known activist with strong political views (monarchist and German nationalist, anti-socialist) and strong social views on a variety of issues (criminality, alcoholism, syphilis, mental illness, eugenics). Kraepelin also strongly opposed the anti-hereditarian, anti-laboratory science views of psychoanalysts Sigmund FREUD and Carl JUNG. Because of his utter disregard for the pseudoscience of psychoanalysis, throughout most of the 20th century Kraepelin has not been treated kindly by historians of psychiatry, as many of them were psychoanalytically trained American psychiatrists and uncritical disciples of Sigmund Freud. It is only now, with psychiatry's return to its biological and experimental roots, that Kraepelin is receiving the recognition that is his due.

Kraepelin's hereditary roots were in the Mecklenberg region of Germany. After earning his medical degree, Kraepelin taught medicine in the Baltic region of the Russian Empire at the university in Dorpat from 1866 to 1891. At Dorpat, Kraepelin conducted research on the effects of drugs on intellectual capacity and motor functions, examining the psychological effects of tea, alcohol, and other drugs. It was during this time that Kraepelin began his lifelong interest in conducting psychological experimentation on both normal and psychiatric populations, often using variations of the word-association test. During his tenure in Dorpat, Kraepelin wrote and published the very first edition of his famous textbook, *Psychiatrie* (1883),

which would undergo multiple revisions as he defined his ideas until the four-volume eighth and final edition (1909–15).

After sharpening his expertise in neurological and psychiatric problems, he moved to the University of Heidelberg, Germany, in 1891 and occupied himself with both clinical and research duties. Horrified by high percentage of alcoholism-related admissions to the psychiatric clinic at the university, in 1895 Kraepelin himself became abstinent and remained so for the rest of his life. Like August FOREL, Eugen BLEULER and many other major figures in medicine at the end of the 1800s, Kraepelin became an activist in the anti-alcohol movement. It was believed that chronic alcoholism caused hereditary DEGENERATION and therefore future generations would be permanently damaged (biologically) by the "sins of the fathers [and mothers]." During his tenure in Heidelberg, Kraepelin continued the psychological experiments he had learned in Leipzig from his beloved master Wilhelm WUNDT (1832–1920) and began the serious neuropathological search for the causes of psychotic disorders with colleagues Franz NISSL (1860–1919) and Alois ALZHEIMER.

In 1903 Kraepelin moved to Munich and became director of the Institute of Hygiene at the University of Munich. Alzheimer accompanied him. Together they continued their brain dissections and neurohistological research to find the cause of neurodegenerative and psychotic disorders. Besides his continuing efforts to refine his classification system of mental disorders, which was quickly becoming the world standard, Kraepelin continued the neuropathological, psychological, and serological research on the psychotic disorders and continued to compile statistics on the familial inheritance of mental disorders. His anthropological interests led him to do fieldwork in such places as India and Java. He visited the United States twice, in 1908 and 1925, both times as a consultant to the wealthy McCormick family of Chicago, who wanted his assessment of Stanley McCormick (1874–1947). On both occasions Kraepelin found him to be suffering from the catatonic subtype of dementia praecox. Kraepelin remained in Munich until his death at age 70 in 1926, although in his later years he often vacationed at a villa he and his wife owned in Italy.

Dementia praecox and manic-depressive psychosis Kraepelin first described and coined the terms for the two major FUNCTIONAL PSYCHOSES in successive revisions of his textbook: DEMENTIA PRAECOX was first discussed in the fourth edition (1893), and manic-depressive psychosis in the sixth edition (1899). He separated the two based on their outcomes: manic-depressive psychosis had a relatively good outcome, with many patients experiencing remissions; dementia praecox had a poor prognosis, following a chronic, degenerating course. In his fifth edition he puts forth the idea that it is a brain disease that is perhaps metabolic in origin, one in which the brain "autointoxicates" itself.

Kraepelin's influence on the practice of psychiatry was felt everywhere, as his classification system helped to unify the profession. In his memoirs, William Alanson White, one of the major figures in American psychiatry in the first third of the 20th century, tells of the confusing state of affairs in psychiatry in the 1890s prior to Kraepelin's work:

> Of course we systematically labeled each patient according to the diagnosis that we thought best fitted him, but I am quite sure that nobody felt that he had accomplished much in so doing. The fact that whenever a physician from another institution visited the hospital one of the first questions was "What classification do you use?" indicates to my mind the very serious discontent with this state of affairs . . . When, therefore, Kraepelin's classification, based upon a new descriptive symptomatology and the course and outcome of the disease process, came to be known, it was hailed everywhere with joy. Here was a new lease on life for all of us, a new interest in psychiatry, new points of view. The whole subject was revivified and made more alive, and the patients correspondingly became more interesting.

German Research Institute for Psychiatry As early as 1911 Kraepelin had official support from the Kaiser-Wilhelm Gesellschaft for his vision of a single, multidisciplinary institute where laboratory research could be conducted to find the causes and cures of mental illness. Funds were raised through donations by two Americans of German descent, Dr.

James Loeb and Alfred Heinsheimer, and in April 1918 the Deutsche Forschungsanstalt fuer Psychiatrie, or German Research Institute for Psychiatry, was officially opened within one of the buildings of the Munich University Psychiatric Clinic. With the end of World War I in November, riots on the streets of Munich, and a socialist revolution in Bavaria in 1919, the German economy collapsed. The donated money for the institute quickly evaporated during a period of extraordinary inflation. Kraepelin's institute survived from 1920 until 1927 on yearly donations from Dr. Loeb. In the last years of his life much of Kraepelin's energy was taken up with the search for funds. Finally, in 1927, the year after Kraepelin's death, a sizable grant from the Rockefeller Foundation allowed for the construction of a four-story-high building "with decorations in bright red and green" (according to a report in a Cologne newspaper) near the Schwabing Hospital in Munich. On June 13, 1928, the dedication ceremony to mark the opening of the Forschungsanstalt fuer Psychiatrie, Kaiser-Wilhelm-Institut took place. A marble bust of the late Kraepelin (a gift of Dr. Loeb) was placed in the lobby near the grand staircase. The street outside the institute was named after Kraepelin, as it still is today. However, the building itself was destroyed by American bombs during World War II, but the site on *Kraepelinstrasse* is now the home of the Max Planck Institute for Psychiatry.

During the years that Kraepelin was alive, the institute could manage only four divisions: laboratories for anatomy, serology, and psychology, and a fourth division for the collection of statistics on the hereditary transmission of dementia praecox and other mental disorders. Upon rededication in 1928, the institute housed six independent research divisions under one roof, adding a clinic archives division to keep track of the patients in the psychiatric wards at the nearby Schwabing Hospital, and a chemistry division.

The NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH) in the United States was directly modeled on Kraepelin's institute when the National Institutes of Health was created after World War II. NIMH is now where most of the world's cutting-edge research on the biological causes of schizophrenia takes place. Kraepelin's vision lives on.

Brink, L., and S. E. Jelliffe. "Emil Kraepelin—Psychiatrist and Poet," *Journal of Nervous and Mental Diseases* 77 (1933): 277–288.

Engstrom, E. "Emil Kraepelin: Psychiatry and Public Affairs in Wilhelmine Germany," *History of Psychiatry* 2 (1991): 111–132.

Kraepelin, E. *Memoirs.* Berlin: Springer-Verlag, 1987.

———. *One Hundred Years of Psychiatry.* New York: Philosophical Library, 1962; first published, 1917.

———. "The Manifestations of Insanity (1920)." Translated by Dominic Beer. *History of Psychiatry* 3 (1992): 509–529.

Noll, R. "Styles of Psychiatric Practice, 1906–1925: Clinical Evaluations of the Same Patient by James Jackson Putnam, Adolf Meyer, August Hoch, Emil Kraepelin, and Smith Ely Jelliffe," *History of Psychiatry* 10 (1999): 145–189.

Rüdin, E. R. "Historical Record. Forschungsanstalt für Psychiatrie, Munich, (Institute for Psychiatric Research), 1925–1928," (1928). Unpublished manuscript in the files of the Rockefeller Archives Center, New Tarrytown, New York.

White, W. A. *William Alanson White: The Autobiography of a Purpose.* Garden City, N.Y.: Doubleday, 1938.

lactation psychoses It was commonly believed by the ancients and by physicians well into the 1800s that the severe mental disorders suffered by women shortly preceding and especially directly following childbirth were related to the production (or lack of production) of milk. It had been thought for centuries that milk was diverted from the breasts to other areas of the body, especially the brain, causing these MENTAL DISORDERS. This process was sometimes called lacteal metastasis. J. E. D. ESQUIROL found these disorders to be so common that he devoted an entire chapter to them in his *Des Maladies Mentales* (1838), entitled "Mental Alienation of Those Recently Confined, and of Nursing Women." "Confinement" or "to be confined" is an 18th-century term for the period during which a woman was "confined" to her "child-bed" before and after giving birth. "The number of women who become insane after confinement, and during or after lactation, is much more considerable than commonly supposed," according to Esquirol. He noted that he was not talking about the much more common "milk fever," the transient delirium that takes place after confinement, but instead the more serious postpartum depressions and psychotic episodes that can occur.

Esquirol, after observations made during autopsies, asserted that no milk was ever found in the brain tissue of deceased women who suffered from postpartum psychoses. Although it was commonly observed that the suppression or diminution of milk production after birth was sometimes associated with the onset of the psychosis, Esquirol denied that the cause was related to milk being diverted to the brain. "Finally, it would be strange to find milk in the brain after confinement or lactation, when there was suppression of this secretion, as to find menstrual blood in the cavity of the cranium, in females who have become insane after the suppression of the menses." Esquirol admitted, however, that many of these women responded well to treatment, particularly when it was designed to reestablish lactation or menstruation following childbirth. He recommended enemas, emetics, warm hip-baths, and, in the more extreme cases, to restore menstruation, the application of leeches to the vulva and cupping glasses to the thighs.

By the 20th century, however, the idea that psychoses occurring in women at about the time of birth were related to the lack of production of milk had been disregarded. Instead, the stress of pregnancy, and childbirth in particular, was thought to exacerbate an already existing underlying mental disorder such as schizophrenia or manic-depressive psychosis. This is the argument made by Eugen BLEULER in the fourth edition (1923) of his famous textbook *Lehrbuch der Psychiatrie* (first edition, 1916), in the section "Causes of Mental Diseases" in the English translation of 1924. Bleuler thus concludes: "The *lactation psychoses* have little practical significance."

See also BLEEDING; POSTPARTUM PSYCHOSIS; PUERPERAL INSANITY.

Bleuler, E. *Textbook of Psychiatry.* 4th ed. Translated by A. A. Brill. 1916. Reprint, New York: Macmillan, 1924.

Esquirol, J. E. D. *Mental Maladies: A Treatise on Insanity.* Translated by E. K. Hunt. 1838. Reprint, Philadelphia: Lea & Blakiston, 1845.

Laing, Ronald David (1927–1989) One of the most controversial psychiatrists of the 20th century, R. D. Laing, is best remembered as a critic of the profession of psychiatry and a strong advocate of the often-neglected human rights of psychotic

people. He was born and educated in Glasgow, Scotland, where he trained as a physician and a psychiatrist and served at the Glasgow Royal Mental Hospital. In 1957 he joined the famous Tavistock Clinic in London. However, by this time he had developed serious doubts about the profession of psychiatry. He felt there was a large gap between physicians and patients, and the meaning of people's lives was lost in dehumanizing clinical terms that placed them in an inferior position. Laing believed that society gave psychiatrists special powers over others that often led to abuse. His many books, starting with *The Divided Self* (1960), are thoughtful and provocative critiques of the present state of psychiatry. Beginning in June 1965 at Kingsley Hall, a community center in London, Laing and his colleagues began an experiment in which they lived with severely disturbed psychotics who would otherwise be locked up in mental institutions. There was no staff per se, no locked doors, no psychiatric treatment—just a group of people living together and trying to come to terms with one another. The atmosphere was described as being more like a "hippie commune" than a mental hospital ward. The Philadelphia Association, as this charitable organization was called, ended its experimental program at Kingsley Hall in May 1970.

Laing was often more criticized than applauded during his lifetime. His views were often regarded as mystical or downright dangerous for schizophrenics and others who, it was felt, might be led astray by Laing's antimedical, overly optimistic view of psychosis and its successful outcome. However, many of those sympathetic to his work introduced his radical ideas into practice and were collectively known as the "anti-psychiatry movement," a term that Laing says in his 1985 memories he never approved of. It was, however, invented by a colleague of Laing's, psychiatrist David Cooper, who set up an "anti-psychiatry ward" in a large mental hospital near London in 1962. Laing, however, was obviously sympathetic to the thesis of antipsychiatry, namely, that the role of psychiatry is to exclude and repress those persons that society wants excluded and repressed.

Boyers, R., and R. Orrill, eds. *R. D. Laing and Anti-Psychiatry.* New York: Harper & Row, 1971.

Cooper, D. *Psychiatry and Anti-Psychiatry.* London: Tavistock Publications, 1967.

Laing, R. D. *Wisdom, Madness, and Folly: The Making of a Psychiatrist.* New York: McGraw-Hill, 1985.

language abnormalities in schizophrenia One of the most distinctive signs of schizophrenia is a disturbance in language. Odd phrasing, loosening of associations, bizarre content of speech and the use of nonexistent words ("word salad") can all mark the person suffering from schizophrenia. To the extent that our spoken language reflects our thought processes, most studies of schizophrenic language are incorporated in research on FORMAL THOUGHT DISORDER, usually in the form of COGNITIVE STUDIES OF SCHIZOPHRENIA. One of the first books to appear on the subject of language abnormalities in schizophrenia was edited by J. S. Kasanin and published in 1944. Although abnormalities in language occur as a result of many mental disorders, studies by researcher Nancy Andreasen and colleagues at the University of Iowa suggest that alogia, the diminished capacity to think or express thoughts (also known as the NEGATIVE SYMPTOM of schizophrenia called poverty of speech), may be an especially important identifying indicator of schizophrenia and may also point to a poor prognosis. Because language ability is largely governed by the left hemisphere of the brain, there has been much speculation that schizophrenia may be the result of abnormalities in this area of the brain.

See also BRAIN ABNORMALITIES IN SCHIZOPHRENIA; LATERALITY AND SCHIZOPHRENIA.

Andreasen, N. C., R. E. Hoffman, and W. M. Grove. "Language Abnormalities in Schizophrenia." In *New Perspectives in Schizophrenia,* edited by M. N. Menuck and M. V. Seeman. New York: Macmillan, 1985.

Kasanin, J. S., ed. *Language and Thought in Schizophrenia.* Berkeley: University of California Press, 1944.

Lasègue's disease A rarely used 19th-century term for "persecution mania," the paranoid delusion that one is being deliberately persecuted by others when in fact there is no evidence to support this. It was initially described by Ernest Charles

Lasègue (1816–83) in 1852. Lasègue is more commonly remembered, however, for an article he published with J. P. J. FALRET in 1877 that identified another psychotic delusional syndrome—FOLIE À DEUX.

lashing See FLOGGING.

latent psychosis This terms refers to the idea that a person has an underlying psychotic process that can break out into a full overt psychosis under the right circumstances. References to latent psychoses are found in the older psychiatric literature, but the idea is now generally subsumed under such terms as the *incipient* or *prodromal phases* of a psychotic disorder, particularly schizophrenia.

latent schizophrenia This term refers to people who exhibit odd or eccentric behavior, perhaps even with transient hallucinations and delusions, but who never develop the full symptomatology of schizophrenia. In *DSM-IV-TR* (2000), latent schizophrenia is called SCHIZOTYPAL PERSONALITY DISORDER—one of the "schizophrenia spectrum" disorders (including, for example, SCHIZOID PERSONALITY DISORDER and SCHIZOPHRENIFORM DISORDER) that seem to be related in some way to schizophrenia. "Latent schizophrenia" is still a valid diagnostic category in *ICD-10* (1992), but it is not recommended for general use. *ICD-9* suggested that this label replace such previously used terms as *latent schizophrenic reaction*, *borderline schizophrenia*, *prepsychotic schizophrenia*, *prodromal schizophrenia*, *pseudoneurotic schizophrenia*, and *pseudopsychopathic schizophrenia*. The pre-1980 psychiatric literature speaks of "prepsychotic symptoms," which are summarized in a review by Docherty et al. (1978).

Eugen BLEULER, who coined and first used the term *schizophrenia* in a publication in 1908, also refers to "latent schizophrenia" for the first time in this same seminal classic. In his 1911 classic, *Dementia Praecox, Or the Group of Schizophrenias*, Bleuler notes in the introduction to his discussion of the "symptomatology" of schizophrenia that the symptoms can only be described when defining the clear-cut cases of the disorder and that "the milder cases, latent schizophrenics with far less manifest symptoms, are many times more common than the overt, manifest cases." He later emphasizes just how important the "subgroup" of schizophrenia known as latent schizophrenia is when compared with the other "schizophrenias":

> There is also a latent schizophrenia, and I am convinced that this is the most frequent form, although admittedly these people hardly ever come for treatment. It is not necessary to give a detailed description of the various manifestations of latent schizophrenia. In this form, we can see in *nuce* all the symptoms and all the combinations of symptoms which are present in the manifest types of the disease. Irritable, odd, moody, withdrawn or exaggeratedly punctual people arouse, among other things, the suspicion of being schizophrenic.

People with latent schizophrenia may very well be those who are genetically predisposed for developing schizophrenia but never manifest the full symptoms of the disorder.

See also BORDERLINE CASES; BORDERLINE SCHIZOPHRENIA; INCOMPLETE PENETRANCE.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenias.* Translated by Joseph Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

———. "Die Prognose der Dementia Praecox—Schizophreniegruppe," *Allgemeine Zeitschrift für Psychiatrie* 65 (1908): 436–464.

Docherty, J. P., et al. "Stages of Onset of Schizophrenic Psychosis," *American Journal of Psychiatry* 135 (1978): 420–426.

late-onset schizophrenia Since the time of Emil KRAEPELIN, who relied on Ewald Hecker's description of the youthful age of onset of HEBEPHRENIA to help define his concept of DEMENTIA PRAECOX, schizophrenia has often been regarded as a disease that shows its first serious signs in late adolescence or early adulthood. Cases of persons developing schizophrenia after the age of 40, for

example, were considered relatively uncommon. However, a comprehensive review of the research on this issue by M. J. Harris and D. V. Jeste suggested that late-onset schizophrenia may be more common than originally thought. Although they were careful to point out the possible faults in the more than 30 studies (mainly from Europe) they review, they nonetheless found that persons who develop late-onset schizophrenia (that is, after age 40) have the following characteristics: (1) they tend to have predominant paranoid symptoms, (2) 66 to 87 percent are female, (3) more instances of hearing loss or eye disease seem to occur among this group, (4) prior to the full outbreak of the active phase of schizophrenia, these persons tend to have personalities that have strong "paranoid" or "schizoid" traits, (5) the disease tends to follow a chronic course, and (6) there is some alleviation of symptoms with ANTIPSYCHOTIC DRUGS.

Harris, M. J., and D. V. Jeste. "Late-Onset Schizophrenia: An Overview," *Schizophrenia Bulletin* 14 (1988): 39–55.

laterality and schizophrenia Most people are familiar with the media versions of the popular-psychology interpretations of "right brain" versus "left brain" functioning. It is roughly true that the left hemisphere of the brain is responsible for performing the more analytic, sequential, verbal, and temporal sequencing functions, whereas the right hemisphere tends to serve more visual and spatial functions. The term *laterality* refers to the scientific evidence for this phenomenon. Since the 1960s, researchers have found that the two hemispheres of the human brain are not identical in many areas: Their respective structures (morphology) and biochemistry (proportions of various neurotransmitters) are not alike, and the two sides of the brain seem to serve different psychological functions. Laterality is found not only in humans but also in other primates and mammals (such as rats).

Since Paul Broca (1824–80) published his famous report in 1861 of the autopsy of a male patient from the BICÊTRE asylum in Paris that localized the speech center of humans in the left hemisphere (now called "Broca's area"), language ability has commonly been assumed to be in this area of the brain. Furthermore, because approximately 93 percent of humans are right-handed, and speech has long been observed to be controlled by areas located in the hemisphere of the brain that is contralateral ("opposite-sided") to the dominant hand—the left hemisphere—it was thought that the language center could always be determined by handedness. However, although in the vast majority of cases expressive language is largely centered in Broca's area in the left hemisphere, this is not always the case, particularly for left-handed people who prove to be right-hemisphere dominant. Many people seem to have functions such as language and handedness distributed in unique patterns between the two hemispheres, and language and handedness may not even be related at all in some people. There are many differences in laterality between the sexes as well, with females appearing to be more like left-handed people in general, with more functions such as speech distributed in areas in both hemispheres. This is why it is thought that women and left-handed people in general can recover more completely from strokes (cerebral vascular accidents) than right-handed men.

Given the hypothesis that schizophrenia and, perhaps, the other psychotic disorders are brain diseases, is there evidence that they can be localized according to laterality in the brain?

The first evidence that laterality may be a factor in the psychotic disorders was found by neurologist P. Flor-Henry in 1969. Flor-Henry noticed in a study of temporal-lobe epilepsy (which can have many psychotic symptoms) that when the focal point of the seizure was in the left hemisphere, schizophrenia-like psychotic features would appear, whereas when the seizure focus was in the right hemisphere, the psychotic symptoms resembled those found in affective psychoses. When the epileptic patient had "bilateral foci," the psychotic symptoms seemed to be "schizo-affective" in nature. Based on Flor-Henry's initial study, there have been many other such neurophysiological studies of the psychotic disorders trying to link schizophrenia with the left hemisphere and bipolar disorder with the right hemisphere.

There have been many published reviews of the evidence suggesting that laterality may be related to schizophrenia, although not all the evidence points conclusively to the left hemisphere as the source of dysfunction. This may be due to the fact that much of the research does not take schizophrenic subtype differences or gender differences into account. For example, paranoid schizophrenics are often distinguished from schizophrenics diagnosed with one of the nonparanoid subtypes on the basis of many perceptual and cognitive tasks in tests, but few studies take these subtype differences into account in laterality studies, generally only comparing generic "schizophrenics" with "normals" or other groups. This is true in the many neuropsychological studies, as well as those neurophysiological studies using measurements with the EEG and evoked potentials, regional cerebral blood flow (rCBF), position emission tomography (PET SCANS), and measurements of neurochemical differences to detect asymmetry between the hemispheres in the activity of certain NEUROTRANSMITTERS such as DOPAMINE. However, an informed review of the major research into the issue of laterality and schizophrenia by psychiatric researcher Henry A. Nasrallah in 1986 provides the following cautious conclusion: "Overall the evidence for left hemisphere dysfunction and over-activation appears to be relatively better documented than other types of dysfunction, although it is by no means definitive."

Because schizophrenia seems to be characterized by language abnormalities, the left hemisphere is thought to be a prime candidate for the localization of the disease process. However, a number of studies point to the possibility that schizophrenia may be related to an "interhemispheric dysfunction," that is, it may be the result of disturbances in the way messages are passed and interpreted between the two hemispheres of the brain. A minority of studies even point to the right hemisphere as the source of dysfunctions in schizophrenia. Until more is understood about the importance of laterality in the functioning of the human brain, it may be difficult to conclusively resolve the question of laterality in the psychotic disorders.

Broca, R. "Remarques sur la siège de la faculté du langue articule," *Bull. Soc. Anat.* 6 (1861): 330–357.

Flor-Henry, P. "Psychosis and Temporal Lobe Epilepsy: A Controlled Investigation," *Epilepsia* 10 (1969): 363–395.

Nasrallah, H. A. "Is Schizophrenia a Left Hemisphere Disease? In *Can Schizophrenia Be Localized in the Brain?* edited by N. C. Andreasen. Washington, D.C.: American Psychiatric Press, 1986.

Wexler, B. E. "Cerebral Laterality and Psychiatry: A Review of the Literature," *American Journal of Psychiatry* 137 (1980): 279–291.

lazar house (lazaretto) See LEPER HOUSES.

leeches and leeching See BLEEDING.

legal issues in schizophrenia See COMMITMENT; CONFIDENTIALITY; INFORMED CONSENT; INSANITY DEFENSE; RIGHT TO REFUSE TREATMENT; RIGHT TO TREATMENT.

leg-locks A form of MECHANICAL RESTRAINT used in Europe until the mid-19th century. These were heavy iron clasps around each ankle or shin, linked by a chain or a thick metal ring.

leper houses Also known as lazar houses or lazarettos (particularly in Italy), these were asylums for lepers. After a drop in the incidence of leprosy in the 1500s, these places were used to contain the poor, the sick, and the mentally ill—in other words, they were places of exile for all society's undesirable elements. Many European asylums arose out of these former places of banishment for the lepers. According to French historian Michael Foucault, until about 1650 the mentally ill were not considered a "threat" to the existing "sane" society in Europe. After that time, the Age of Reason was on the rise, and for the first time the mentally ill were rounded up into institutions called hospitals to contain the socially displaced: the mentally ill, the poor, the disabled, the elderly, criminals, those with venereal diseases, and political dissidents. These "hospitals" largely had no medical function but were essentially places of confinement. Foucault argues

that the creation of these institutions was inspired by the older tradition of banishing lepers to leper houses and colonies.

Foucault, M. *Madness and Civilization: A History of Insanity in the Age of Reason.* New York: Random House, 1965.

leucotomy The name given by Portuguese neurologist António Egas Moniz for his intrusive PSYCHOSURGERY procedure in which the skull of a person is opened and the white fibers connecting the frontal lobe to the rest of the brain are severed. It is derived from two Greek words meaning "white" and "to cut." Egas Moniz performed the first leucotomy on a human subject (a chronically depressed female patient from a local mental hospital in Portugal) on November 15, 1935. The first leucotomy performed in the United States was completed on September 14, 1936, in Washington, D.C., by American neurologists Walter FREEMAN and James Watts. In 1936, Freeman began to refer to the procedure as a "lobotomy" to separate himself from the shadow of Egas Moniz and create an international reputation of his own. A leucotomy was a form of major surgery that involved opening the skull, whereas a technique devised by Freeman in 1946, the "trans-orbital lobotomy," only involved the penetration of an "ice pick" or similar instrument into the eye socket (the "orbit of the eye"), behind the eye and into the brain.

licensed houses A 19th-century British term for those "private madhouses" that had obtained a license to house and provide limited care to the mentally ill. Licenses were obtained by petitioning the College of Physicians. These private madhouses generated a hefty profit for their operators, for their overhead could be kept quite low by providing the absolute minimum in food and custodial care for their mentally ill residents. This brisk and lucrative "trade in lunacy" finally degenerated to such inhumane conditions that a regulative body, the COMMISSIONERS IN LUNACY, was established in 1845 to monitor the private madhouses and ensure that they met minimum standards.

See also HOXTON MADHOUSES.

Jones, K. *Lunacy, Law, and Conscience, 1744–1845: The Social History of the Care of the Insane.* London: Routledge & Kegan Paul, 1955.

Parry-Jones, W. *The Trade in Lunacy: A Study of Private Madhouses in England in the Eighteenth and Nineteenth Centuries.* London: Routledge & Kegan Paul, 1972.

life expectancy of schizophrenics See MORTALITY.

limbic system In most research on the areas of the brain that seem to be implicated in the disease process in SCHIZOPHRENIA, the one characteristic that does seem to unite them (even more than laterality) is the fact that most of these areas are interconnected in the brain according to what has been identified as the "limbic system." The limbic system (also sometimes called the visceral brain), which involves a number of structures that lie deep below the surface of the brain (the cortex), was long considered to be one of the oldest parts of the brain and the one that governs many of the primitive, instinctual functions. Recent neurological research now considers the limbic system to be a major integrative system, where raw sensations are selected and integrated and sent to sites throughout the brain. The limbic system is composed of such subcortical structures as the hippocampus, amygdala, hypothalamus, mammillary bodies, the olfactory area, and bordering areas of the frontal and temporal lobes. Much of the work that identified the role of the limbic system as this large integrated network was conducted by neurologist Paul MacLean in the 1940s.

The evidence that schizophrenia involves abnormalities in the limbic system and its connections come from a wide variety of areas. EEG studies have shown abnormalities in the limbic areas of the brain, and brain structure abnormalities and neurochemical disturbances have been found in these areas. Because there is still much more to be learned about the functions of the brain as a whole, more research needs to be conducted to understand exactly how the limbic system is involved in the organic disease process of schizophrenia and to determine the meaning of these disparate research findings from many different areas when taken as a whole.

In his 1988 book, psychiatrist E. Fuller Torrey writes that one of the "four established facts" about the causes of schizophrenia is that "the limbic system and its connections are primarily affected."

MacLean, P. D. "Psychosomatic Disease and the 'Visceral Brain,'" *Psychosomatic Medicine* 11 (1949): 338–353.

Torrey, E. F. *Surviving Schizophrenia: A Family Manual.* 2nd ed. New York: Harper & Row, 1988.

Torrey, E. F., and Peterson, M. R. "Schizophrenia and the Limbic system," *Lancet* 2 (1974): 942–946.

linkage In genetics, "linkage" refers to the tendency of two ALLELES at different places (loci) on the same CHROMOSOME to be inherited together. The closer they are together, the lesser the chances of a genetic recombination occurring between them. Therefore, there is a greater probability that they will be inherited together. For example, in the search for the gene or genes that predispose to schizophrenia, it may well be that the abnormal gene responsible for a BIOLOGICAL MARKER OF SCHIZOPHRENIA (for example, eye movement abnormalities) may be "linked"—because of its physical closeness—to the actual disease gene that produces schizophrenia.

linkage analysis See GENETICS STUDIES.

linked markers See GENETIC MARKERS OF VULNERABILITY; MOLECULAR MARKERS.

lithium Lithium is the most commonly used drug for the treatment of recurrent affective (or mood) disorders such as BIPOLAR DISORDER or recurrent unipolar depression, MANIC EPISODES or acute HYPOMANIC EPISODES. A naturally occurring salt, lithium was discovered in 1817 by Swedish chemist John A. Arfvedson (1792–1841). Medical uses began to be applied in 1858 for the treatment of such conditions as gout and urinary calculi. It was later combined with bromides and used as a sedative. In 1940 lithium chloride was administered to cardiac patients as a salt substitute, but the severe toxic reactions they developed strongly discouraged researchers from conducting further studies on this drug. However, psychopharmacologist J. F. J. Cade continued research with lithium and in 1949 published the first scientific report of the antimanic effects of lithium. In a study of agitated psychotic patients, Cade found that 10 manic patients responded favorably to lithium, six schizophrenic and chronically depressed psychotic patients did not, and one patient's symptoms reappeared after the lithium was stopped. Its use for the treatment of affective disorders was not approved in the United States until 1970.

It is not clearly understood how lithium works to produce its results in behavioral changes. However, it is estimated that between 70 percent and 80 percent of people with "typical" bipolar disorder respond favorably to lithium therapy. This means, however, that 20 percent to 30 percent of people experiencing mania do not respond to lithium. Lithium may take one to two weeks to be fully effective, but after the acute symptoms of a disorder lessen, lithium maintenance therapy can reduce the number, severity, and frequency of episodes. The side effects of long-term lithium therapy may cause various endocrine abnormalities (thyroid problems, diabetes mellitus), kidney damage, cardiac reactions, skin problems, gastrointestinal problems, and some central nervous system problems such as fine hand tremors and other neuromuscular problems. Because lithium can be lethal at toxic levels, blood levels of the substance must be assessed regularly to avoid dangerous concentrations.

Baldessarini, R. J. *Chemotherapy in Psychiatry: Principles and Practice.* Cambridge, Mass.: Harvard University Press, 1985.

Cade, J. F. J. "Lithium—Past, Present, and Future." In *Lithium in Medical Practice,* edited by F. N. Johnson and S. Johnson. Baltimore: University Park Press, 1978.

———. "Lithium Salts in the Treatment of Psychotic Excitement," *Medical Journal of Australia* 11 (1949): 349–352.

lobectomy A form of extreme surgery in which an entire lobe of the brain is removed. Although this procedure was sometimes performed to remove tumors and halt their spread in the brain, in the 1930s it was suggested that it might be an effective

form of PSYCHOSURGERY for some mentally ill persons, specifically if the frontal lobe of the brain was removed. A full lobectomy was first performed on the chimpanzees Becky and Lucy in June 1934 at the Yale primate research laboratory by John Fulton and Carlyle Jacobsen. The entire frontal mass of the brain was extracted and a cottonoid (a sterile, oil-soaked cotton wad) was put in its place to fill in the space left in the skull and to support the remaining sections of the brain. At an international conference in London in August 1935, Fulton and Jacobsen reported on the behavioral changes that were observed in these animals as a result of the lobectomy. They inspired Portuguese neurologist António EGAS MONIZ to suggest at their presentation that lobectomies be performed on humans. The horrified response of most of the participants caused him to modify his views, but on his return to Portugal after the conference he devised a less radical procedure, the LEUCOTOMY, which merely severed the connections of the frontal lobe to the rest of the brain, and performed the first psychosurgery on a human subject in November 1935.

See also FREEMAN, WALTER; TRANSORBITAL LOBOTOMY.

lobotomy The term that American neurologist Walter FREEMAN invented to replace LEUCOTOMY, the name given by Portuguese neurologist António EGAS MONIZ for his famous psychosurgical procedure that severed the white fibers connecting the frontal lobe to the rest of the brain. Freeman suggested the name change at a meeting of the Southern Medical Association in Baltimore in November 1936, and it was first used in a published article in 1937. Because leucotomy referred to the severing of specific fibers, "lobotomy" was suggested as a more general term for any psychosurgical procedure that involved the cutting of the nerve fibers of a lobe of the brain.

Freeman, W. J., and J. Watts. "Prefrontal Lobotomy in the Treatment of Mental Disorders," *Southern Medical Journal* 30 (1937): 23–31.

lock hospitals A term popular in England for LEPER HOUSES and later asylums for the mentally ill in which persons would be involuntarily "locked in."

locus In genetics research, the word *locus* (plural, *loci*) is often used to refer to the place where a particular gene (or genes) is located.

lod score See LINKAGE ANALYSIS.

longitudinal studies These are also known as "long-term follow-up" studies. Particular groups of patients, or cohorts, are identified and followed throughout the course of their lives. The best studies follow patients from childhood (such as the HIGH-RISK STUDIES), although most have simply followed patients diagnosed with a particular illness. The purpose of these studies is to provide a picture of the natural course of a disease, identifying its characteristics throughout the life cycle of an individual. A special issue of *Schizophrenia Bulletin* devoted to a comprehensive review of such studies appeared in 1988 (vol. 14, no. 4).

See also COURSE AND OUTCOME OF SCHIZOPHRENIA.

loosening of associations This is one of the primary symptoms of the major psychotic disorders, particularly schizophrenia. It is considered a sign of FORMAL THOUGHT DISORDER. Loosening of associations refers to the verbal expression of thoughts that are disjointed and jump from one subject to another without any relationship whatsoever; in addition, the speaker demonstrates no awareness of the disconnection of these thoughts. When loosening of associations is severe, the person may be perceived as speaking nonsense or gibberish and may be incoherent.

Eugen BLEULER thought that such ASSOCIATION DISTURBANCES were one of the "primary symptoms" of schizophrenia that uniquely characterized it when compared with other mental disorders. He recognized the importance of loosening of associations in his first publication (1908) that introduced the concept of schizophrenia and its divergence

from Kraepelin's notion of DEMENTIA PRAECOX. Bleuler writes:

> On the psychological side the most fundamental disorder appears to be a change in associations. In schizophrenia it is as if the physiological inhibitions and pathways have lost their significance. The usual paths are no longer preferred, the thread of ideas very easily becomes lost in unfamiliar and incorrect pathways. Associations are then guided by random influences, particularly by emotions, and this amounts to a partial or total loss of logical function. In the acute stages associations are broken up into little fragments, so that in spite of constant psychomotor excitement, no kind of action is possible because no thought is followed through, and because a variety of contradictory drives exist side by side and cannot be synthesized under one unitary or affective point of view.

Disturbances in associations are also related to disturbances in attention and are more commonly found in the nonparanoid subtypes of schizophrenia that are characterized by such NEGATIVE SYMPTOMS. However, loosening of associations can also sometimes appear in MANIC EPISODES or in the ACUTE AND TRANSIENT PSYCHOTIC DISORDERS.

See also PRIMARY SYMPTOMS OF SCHIZOPHRENIA; the FOUR A'S.

Bleuler, E. "The Prognosis of Dementia Praecox: The Group of Schizophrenias" (1908). In *The Clinical Roots of the Schizophrenia Concept: Translations of Seminal European Contributions On Schizophrenia,* edited by J. Cutting and M. Shepherd. Cambridge: Cambridge University Press, 1987.

loxapine See ANTIPSYCHOTIC DRUGS.

Loxitane See ANTIPSYCHOTIC DRUGS.

lunacy, lunatic Derived from the Latin word for moon—*luna*—these terms were used for centuries to reflect the belief that mental disorders were caused by the influence of the moon. Both terms were in common usage until the mid- to late 19th century, when the term *INSANITY* replaced them as a generic reference to "mental illness" or "mental disorders," as we would term them today. The mentally ill were called lunatics, and the physicians who administered aid to them were sometimes called lunatic-doctors. Whereas *lunacy* was a term used in medical and legal texts and organizations (e.g., COMMISSIONERS IN LUNACY), the popular term *madness* was not used in these official capacities.

lunacy trials Beginning with Illinois in 1867, many states passed "jury trial commitment" laws that entitled a person to be judged insane by a body of his or her peers before being involuntarily committed to an institution. These began as the result of the influence of Elizabeth Packard, whose husband had her committed to the Illinois State Asylum at Jacksonville for three years simply for disagreeing with him on philosophical issues. Although Illinois repealed its "lunacy trial" bill in 1892, many states still had such laws on the books well into the 20th century. There were many critics of the lunacy trials, who felt that they caused unnecessary public embarrassment to the patient and that they cast the mentally ill person into the role of a criminal. The First International Congress of Mental Hygiene, a congregation of the organizations of the Mental Hygiene Movement founded by Clifford BEERS, condemned the practice of lunacy trials in 1930. A long transcript of such a lunacy trial and a description of the events that transpired, including the incarceration of a Philadelphia businessman who was eventually set free by the jury, can be found in the 1869 autobiographical account by Ebenezer Haskell.

See also COMMITMENT.

Haskell, E. *The Trial of Ebenezer Haskell, in Lunacy and His Acquittal before Judge Brewster, in November, 1868, together with a Brief Sketch of the Mode of Treatment of Lunatics in Different Asylums in This Country and in England, with Illustrations, including a Copy of Hogarth's Celebrated Painting of a Scene of Old Bedlam, in London, 1635.* Philadelphia: E. Haskell, 1869.

lycanthropy Described since ancient times as a form of "MELANCHOLIA," lycanthropy is a mental disorder in which an individual believes that he or she has been transformed into an animal, especially a wolf. This disorder has also been referred to as "werewolfism," in reference to the Anglo-Saxon term (literally, a "man-wolf"). Lycanthropy was long thought to be an extinct disorder, but at least 18 individual cases have been reported since 1975. Most of these cases concern people who have been diagnosed with one of the psychotic disorders, usually PARANOID SCHIZOPHRENIA, DEPRESSION with psychotic features, or BIPOLAR DISORDER. In the past century, such terms as *insania zoanthropica, zoanthropy* and *cyanthropy* have been used occasionally in psychiatric texts to refer to this exotic disease of the mind.

Jackson, S. W. *Melancholia and Depression: From Hippocratic Times to Modern Times.* New Haven, Conn.: Yale University Press, 1986.

Keck, P. E., et al. "Lycanthropy: Alive and Well in the Twentieth Century," *Psychological Medicine* 18 (1988): 113–120.

Noll, R. *Vampires, Werewolves and Demons: Twentieth Century Reports in the Psychiatric Literature.* New York: Brunner/Mazel, 1991.

Verdoux, H., et al. "La Lycanthropie: Une pathologie contemporaine?" *Annales de Psychiatrie* 4, no. 2 (1989): 178–179.

lypemania This is J. E. D. ESQUIROL's term for MELANCHOLIA, a group of disorders that we now refer to as depression. Depressed or "melancholic" persons were referred to as "lypemaniacs."

M

mad-business This was the 17th- and 18th-century term used for any profession that dealt with "mad-people" or "madmen." This included physicians, apothecaries, and others who were responsible for the custodial care of the mentally ill, as well as the entire system of private "mad-houses" (after 1845 called LICENSED HOUSES) in England.

mad-doctor Also known as lunatic doctors, mad-doctors were physicians who provided medical care to the mentally ill. This term was popular in the late 1600s and colloquially, into the 1800s. Our current usage of the term is different, referring instead to representations of psychotic scientists or physicians in literature and in motion pictures. For example, the profane experiments of the grandiose Dr. Victor Frankenstein, as described in the book *Frankenstein, Or, the Modern Prometheus* by Mary Shelley in 1816, may be the first such depiction of this image, and it has been carried into this century in many films, notably in the many roles played with such zeal by actor Lionel Atwill in the 1930s and 1940s.

Mad Hatter, mad as a hatter The "Mad Hatter" was a popular character in Lewis Carroll's *Alice in Wonderland* (1865), and it is because of this book that we are familiar with this term today. However, the expression "mad as a hatter" predates this book, although there are conflicting views as to how it originated. Some have argued (namely William Hazlitt) that the expression comes from a 17th-century eccentric named John Hatter. Another view is that a 17th-century hatter by the name of Robert Crab is the original "mad hatter," since he developed grandiose religious delusions and proclaimed himself a prophet after receiving head wounds in 1642 during the English civil war. However, modern interpretations suggest that the profession of hatmakers may have had more than its share of psychotic individuals due to the toxic effect of a substance they all commonly employed in making felt hats—mercuric nitrate—which may have induced an ORGANIC MENTAL DISORDER that included such psychotic symptoms as delusions and hallucinations.

Spalding, K. "Poisoning from Mercurous Nitrate Used in the Making of Felt Hats," *Modern Language Review* 46 (1951): 442.

madness An Old English word first appearing in the 1300s, "mad" or "madness" has always referred to mental disorder, extreme foolishness or folly or an insane rage or fury. It has always been used as part of everyday conversation, but with the rise of the profession of PSYCHIATRY in the 1800s the terms *lunacy* and then *insanity* were almost exclusively used in the official sense. Hence, there were more often commissions on "lunacy" or journals of "insanity," but no such uses seem to have been made of the coarser term *madness.* The word is still used today (as is its 16th-century synonym, *crazy,* which is derived from a French word meaning "cracked") in this coarse sense.

Dalby, J. T. "Terms of Madness: Historical Linguistics," *Comprehensive Psychiatry* 34 (1993): 392–395.

mad-shirt A sacklike garment that was used as a form of mechanical restraint for unmanageable patients. It is described as a close-fitting cylindrical garment, usually made of canvas or other

strong material, which was pulled down over the head of the individual and fastened tightly below the knees. It is reported to have been in use at the Pennsylvania Hospital in Philadelphia in the early 19th century.

See also HORN'S SACK; STRAITJACKET.

magical thinking This refers to the unusual belief that some people may have in which they feel that their thoughts, words, or actions can influence other people or events in the physical world in such a way that defies our known physical laws of cause and effect. Sometimes this can reach delusional proportions and become a fixture of the person's belief system about him- or herself and the world. For example, a person with grandiose paranoid delusions may insist that he or she personally caused the 1989 San Francisco earthquake and will do so again if he or she is not immediately released from involuntary commitment to a hospital. Loren J. Chapman and Jean P. Chapman, two noted schizophrenia researchers from the University of Wisconsin in Madison, theorize that magical ideation in undiagnosed people in the general population is a strong indicator of "psychosis-proneness," particularly to schizophrenia. They have developed a 30-item Magical Ideation Scale with such items as "I think I could learn to read other people's minds if I wanted to" (keyed true), and "The hand motions that strangers make seem to influence me at times" (keyed true). They are conducting long-term studies to test their hypothesis that magical thinking in undiagnosed persons may be a sign of later schizophrenia. These persons may in fact be the type referred to with the labels LATENT SCHIZOPHRENIA, SCHIZOTYPAL PERSONALITY DISORDER, OR BORDERLINE SCHIZOPHRENIA.

Chapman, L. J., and J. P. Chapman. "Psychosis-Proneness." In *Controversies in Schizophrenia,* edited by M. Alpert. New York: Guilford Press, 1985.

magnetic resonance imaging One of the BRAIN IMAGING TECHNIQUES currently used in research on the psychotic disorders, particularly schizophrenia. In MRI (its common acronym), a high-strength magnetic field works on the hydrogen atoms located in the brain. Once "oriented," radio frequency pulses are bounced off the hydrogen atoms. The resonant echoes are detected and, with the aid of computer analysis, can be constructed into an image of the inner structure of the brain. MRI has advantages over the use of the CT SCAN in that it can better identify the differences between gray matter and white matter in the brain. The first published study of schizophrenia using MRI was reported by R. C. Smith and colleagues in 1984.

A comprehensive review (by R. W. McCarley and colleagues) of 118 MRI studies of schizophrenia published between 1987 and May 1998 reported BRAIN ABNORMALITIES that tended to be supported by other neuropathological, neuroimaging, and neuropsychological evidence. The authors of the study also argue that the MRI studies suggest that structural abnormalities differ in bipolar (manic-depressive) psychosis and in schizophrenia—just as Kraepelin predicted in the beginning of the 20th century.

McCarley, R. W., et al. "MRI Anatomy of Schizophrenia," *Biological Psychiatry* 45 (1999): 1,099–1,119.

Smith, R. C. "Nuclear Magnetic Resonance in Schizophrenia: A Preliminary Study," *Psychiatry Research* 12 (1984): 137–147.

magnetic resonance spectroscopy imaging (MRSI) A BRAIN IMAGING technique that measures certain chemical characteristics in living brains to determine the integrity of specific populations of nerve cells. This is one of the new technologies for studying NEURAL CIRCUITRY IN SCHIZOPHRENIA. Many MRSI studies use the technique of proton magnetic resonance spectroscopic imaging (abbreviated as 1H-MRSI in the scientific literature). MRSI has largely focused on one potential BIOLOGICAL MARKER of schizophrenia, N-acetylaspartate, or NAA. NAA is a measure of the health of certain populations of nerve cells. When compared to healthy, non-schizophrenia controls, NAA has been found to be reduced in certain areas of the brain in persons with schizophrenia and in their family members. Children with CHILDHOOD-ONSET SCHIZOPHRENIA also seem to have

NAA reductions, lending support to the neurodevelopmental model of schizophrenia that claims a continuity of disease process from childhood into adulthood. Although promising, one drawback to this form of neuroimaging is that the spatial resolution of MRSI is poor compared with either magnetic resonance imaging and position emission tomography scans, and therefore it is more difficult to pinpoint exact locations in the brain that may be dysfunctional.

Bertolino, A., et al. "Reproducibility of Proton Magnetic Resonance Spectroscopic Imaging in Patients with Schizophrenia," *Neuropsychopharmacology* 18 (1998), 1–9.

Brooks, W. M., et al. "Frontal Lobe of Children with Schizophrenia Spectrum Disorders: A Proton Magnetic Resonance Spectroscopic Study," *Biological Psychiatry* 43 (1998): 263–269.

Mahler's syndrome See SYMBIOTIC PSYCHOSIS.

malaria therapy See FEVER THERAPY.

malingering The intentional faking of psychological or physical symptoms for some ulterior motive (e.g., to receive worker compensation instead of returning to work, or to avoid military duty). It is quite common for many relatives and friends of mentally ill persons—particularly those with schizophrenia or severe depression—to unjustly accuse them of malingering to avoid the responsibilities of life. Strongly expressed sentiments of this sort by family members of schizophrenics can actually worsen the person's very real condition and increase the probability of relapse. However, with more education about mental illness, such misconceptions will hopefully diminish.

See also FEIGNED INSANITY.

malvaria A new subtype of schizophrenia proposed by psychedelic researcher Abram Hoffer in 1963 that was supposedly characterized by a "mauve factor." The idea never took hold and was never seriously considered by mainstream psychiatry.

See also TRANSMETHYLATION HYPOTHESIS.

Hoffer, A. "Malvaria: A New Psychiatric Disease," *Acta Psychiatrica Scandinavica* 39 (1963): 335–366.

mania One of the two ancient categories of insanity (along with MELANCHOLIA). *Mania* was the term used by the ancient Greeks for "madness." From ancient times until the second half of the 19th century, all forms of mental illness were interpreted as either forms of melancholia or mania, and these terms had a variety of meanings that do not correspond to our contemporary psychiatric definitions of the clinical syndromes of mania and depression. From the time of the Greeks, mania referred to states in which a person was highly energized, excitable, euphoric, "possessed," talkative, frenzied, enraged, irritable, grandiose, and hallucinating. In ancient times as now, "maniacs" sometimes went through periods were they did not sleep for days or weeks at a time. Until the late 19th century, "mania" almost always referred to an elevation or an increase in intensity of moods, thoughts, and behaviors (as opposed to melancholy, where there was a decrease in intensity in these areas). From antiquity until the time of KRAEPELIN, perhaps hundreds of different forms of insanity were labeled as special forms of mania, sometimes with a single symptom dominating the picture (e.g., kleptomania).

Starting in the 1850s with the proposal that states of mania and melancholy (depression) could alternate in the same person as aspects of a single underlying disease process (the CIRCULAR INSANITY of French psychiatry), attention was turned to carving out the core clinical concepts of mania and melancholia (depression) and thereby separating them from their ancient, varied, and confusing meanings. All the confusing forms of mania (and melancholia, except one form, involutional melancholia) were grouped under the concept of MANIC-DEPRESSIVE ILLNESS (*das manisch-depressive Irrsein*) by Emil Kraepelin in 1899. The two great and ancient insanities of mania and melancholia were now replaced by manic-depressive illness and dementia praecox. By the end of the 20th century,

manic-depressive illness became the AFFECTIVE DISORDERS or mood disorders, and dementia praecox became schizophrenia and other psychotic disorders.

Although Kraepelin identified numerous forms of mania and "mixed states" (dysphoric states in which depression and mania were mixed), and changed these diagnostic categories until his death, for the rest of the 20th century mania was still largely viewed as a state of euphoric intensity that, over time, might devolve into irritability, rage, and psychotic delusions. Prior to 1980, when the diagnostic concept BIPOLAR DISORDER was introduced to replace manic-depressive illness, anyone experiencing depressive episodes with no history of mania was often labeled manic-depressive. After 1980, a person must experience at least one MANIC EPISODE to be diagnosed as bipolar.

Current research on mania indicates there are three primary forms: the classical form of euphoric mania, dysphoric mania (known as MIXED STATES), and psychotic mania. Only the first, euphoric mania, responds well to treatment with LITHIUM. The other dysphoric (or mixed) mania responds to treatment with ANTIPSYCHOTIC DRUGS, particularly olanzapine (Zyprexa). Psychotic mania may respond to either lithium or olanzapine (Zyprexa). In clinical practice, without knowing the medical history of a patient, a person experiencing mania with psychotic features (particularly delusions) is indistinguishable from someone experiencing an acute episode of schizophrenia (particularly paranoid schizophrenia).

See also FUNDAMENTAL STATES OF MANIC DEPRESSIVE INSANITY.

Cassidy, F., et al. "Signs and Symptoms of Mania in Pure and Mixed Episodes," *Journal of Affective Disorders* 50 (1998): 187–201.

Diethelm, O. "Mania: A Clinical Study of Dissertations Before 1750," *Confina Psychiatrica* 13 (1970): 26–49.

Suppes, T., et al. "Report of the Texas Consensus Conference Panel on Medication Treatment of Bipolar Disorder 2000," *Journal of Clinical Psychiatry* 63 (April 2002): 288–299.

mania sine delirio Literally, "mania without delirium." This refers to a MANIC EPISODE in which the consciousness of the afflicted person is not clouded (see DELIRIUM), nor is thinking permanently impaired. This is perhaps the most ancient definition of MANIA that exists. Sometimes in the older psychiatric literature, the word *delirium* means a disturbance in the rational thinking processes (e.g., delusions) and may not refer specifically to our modern concept of delirium as an organic disease of the brain. Philippe PINEL devoted an entire section to this "species of mental derangement" in his 1801 classic textbook, *Traite médico-philosophique sur l'aliénation mentale, ou la manie,* in which he referred to it in French as *manie sans délire.* According to Pinel, this type of mania "may be either continued or intermittent. No sensible change in the functions of the understanding; but perversion of the active faculties, marked by abstract and sanguinary fury, with a blind propensity to acts of violence." Due to the problems in institutional management created by such agitated "maniacs," it is not surprising that they frequently received the more extreme "treatments," such as extensive BLEEDING, the CAUTERY TREATMENT, the BATH OF SURPRISE, and DOUCHING with cold water. J. E. D. ESQUIROL describes the treatment of a typical maniac in the following passage from his 1838 textbook:

> A maniac becomes furious during the night, and utters frightful howls. At two o'clock in the morning, I order the douche, and whilst the cold water is falling upon his head, inundating his body, he appears to be greatly pleased and thanks us for the kindness we have shown him; becomes composed; and sleeps remarkably well the rest of the night.

Esquirol, J. E. D. *Mental Maladies: A Treatise on Insanity.* Translated by E. K. Hunt. 1838. Reprint, Philadelphia: Lea and Blanchard, 1845.

Pinel, P. *A Treatise on Insanity.* Translated by D. D. Davis. 1801. Reprint, Sheffield, England: W. Todd, 1806.

manic-depressive illness One of the two comprehensive categories of insanity that have dominated psychiatry since 1899. Throughout the 20th century, and into the 21st century, all disorders of emotion, affect, or mood have been defined

under, or in relation to, manic-depressive illness or its successor, BIPOLAR DISORDER (1980). All major psychotic disturbances of intellectual functioning, on the other hand, have been subsumed under, or related to DEMENTIA PRAECOX (1893) or SCHIZOPHRENIA (1908). Manic-depressive illness and schizophrenia have been the two anchors of modern psychiatric diagnostic manuals since 1899.

Historical background From Greek and Roman antiquity until the latter half of the 1800s, the two great forms of insanity were mania and melancholia. Hundreds of various manias or forms of melancholy (including syndromes we might term delusional or paranoid) were defined in terms of these two anchors. Much of the times these disorders were seen to be mutually exclusive, but by the 1800s some "mad-doctors" or "alienists" began to see certain disorders as first starting off as a form of melancholy then morphing into a form of mania, or vice versa. Mania and depression in their modern sense were not defined until the late 1800s.

Descriptions of persons who suffered from bouts of recurring and alternating depression and mania have existed since the first century A.D. The clearest description of what may have been manic-depressive illness can be found in the second-century A.D. works of Aretaeus of Cappadocia. The description of euphoric mania turning into irritable mixed states with psychotic features is a familiar one to clinicians even today:

> If mania is associated with joy, the patient may laugh, play, dance night and day, and go to the market crowned as if a victor in some contest of skill. . . . The ideas the patient has are infinite . . . believing they are experts in astronomy, philosophy or poetry. . . . The patient may become excitable, suspicious, and irritable . . . his hearing may become sharp . . . some get noises and buzzing in the ears . . . or may have visions . . . bad dreams and his sexual desires may get uncontrollable . . . if aroused to anger, he may become wholly mad and run unrestrainedly, roar aloud . . . kill his keepers, and lay violent hands upon himself.

It was not until 1854 that French *alienists* Jean-Pierre Falret and Jules-Gabriel-François Baillarger independently described CIRCULAR INSANITY (Falret) or "double formed insanity" (Baillarger). This is the first time that the two very distinct phases were viewed as expression of one underlying chronic illness. In Prussia, German psychiatrist Karl Kahlbaum coined the term *cyclothymia* for a less severe form of circular insanity that was primarily a disorder of emotion and not intellectual functioning and that did not progress into terminal dementia, unlike the more severe form of circular insanity that affects cognitive functioning and the will and that leads to mental confusion, dementia, and "complete mental degeneration." Kahlbaum's distinction between cyclothymia and what we now call bipolar disorder is still reflected today in *DSM-IV-TR* (2002). Kahlbaum is perhaps second only to Kraepelin in terms of his influence on our current methods and categories of mental disorder classification.

manic episode According to *DSM-IV-TR* (2000), the experience of a diagnosable manic episode, whether currently or in the past, is the essential criterion of being given a diagnosis of BIPOLAR DISORDER (technically, Bipolar I Disorder). However, as clinicians well know, the idea that someone who is "bipolar" or "manic-depressive" alternates between manic episodes and depressive episodes is simply untrue. In fact, manic-depression in its classic form is rare. Indeed, there are many persons who experience manic episodes and/or MIXED EPISODES who never experience an episode of major depression. Whether the presence of a manic episode really means a "bipolar" disorder is present remains doubtful.

In *DSM-IV-TR,* a manic episode is defined in the following way:

(1) There is a distinct period of abnormality and persistently elevated, expansive, or irritable mood, lasting at least one week (or any duration if hospitalization is necessary).
(2) During the period of mood disturbance, three or more of the following symptoms must have persisted (four if the mood is only irritable):
    (a) inflated self-esteem or grandiosity
    (b) decreased need for sleep

(c) more talkative then usual or pressure to keep talking
(d) flight of ideas or subjective experience that thoughts are racing
(e) distractibility (attention too easily drawn to unimportant or irrelevant external stimuli)
(f) increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
(g) excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

Emil Kraepelin first proposed the "nosological dichotomy" of the endogenous psychoses manic-depressive illness (*manisch-depressive Irresein*) and the so-called *"Dementia-praecox Gruppe"* in a public lecture delivered in Heidelberg, Germany, on November 27, 1898. These ideas were reflected in print a few months later, beginning the process that would change psychiatric classification up to the present day. In 1899 the 6th edition of Emil Kraepelin's book, *Psychiatrie,* grouped all the affective disorders described by previous generations of psychiatrists (all the simple manias, periodic or circular insanities and their mixed forms, and the affective melancholias, except involutional melancholia) and grouped them under a major class of insanity, manic-depressive illness (*das manisch-depressive Irresein*).

> ". . . we are definitely in a position to class within the large framework of manic-depressive insanity even the smallest fragment of a pathological process belonging here; there are no bridges leading over to the other groups of mental disorders, except perhaps for degenerative psychosis. For all of these reasons, I feel bound to take the clinical circle of forms of manic-depressive insanity as a homogenous whole, and to depict the individual pictures and types of course as special forms of the one, common, pathological process.
>
> As its name suggests, manic-depressive insanity takes place in single attacks which present either the signs of so-called *manic excitation,* flight of ideas, elated mood, and urge to be active, or those of a particular *psychic depression with psychomotor inhibition,* or finally a *mixture of the two states* (p. 273).

The "attacks" of manic-depressive illness (or insanity) were relatively short-lived (days or weeks at the most, sometimes months in the case of depressive attacks) but always eventually remitted. Patients between episodes returned to full normal functioning without any deterioration or degeneration of cognitive functioning (which was, instead, the essential feature of diseases like dementia praecox). In the short term, therefore, prognosis was good. However, Kraepelin noted that this disorder lasted a lifetime in most people. The number of attacks, the type of attack (manic, depressive, or mixed states), and the period of relative health between attacks were variable. Kraepelin also noted that some persons experienced only manic attacks, or periodic mania, and some only bouts of depression or periodic melancholia (both of which would be termed *unipolar* today), but that both were still aspects of the same disease and should be diagnosed as manic-depressive (*bipolar* in our terms today). Kraepelin noted that in about 60 percent of the cases the disease started with a depressive episode. Two-thirds of all his patients with manic-depressive disorder were female. In two-thirds of the total cases (both men and women), the age of onset was before age 25. The attacks come and go without external causes (hence, they are endogenous, or generated from within).

Delusions, illusions, and hallucinations are common during attacks, particularly in manic attacks. In "mixed forms," the manic excitement and irritability are combined with the low spirits and negative thoughts of depression. The identification of mixed states was an important element in linking mania and depression together as two aspects of the same underlying disease, and Kraepelin's descriptions of such states came from the work of one of his assistants at the University of Heidelberg, Wilhelm Weygandt. Weygandt's monograph on this topic, *Uber die Mischzustande des manisch-depressive Irreseins (On the Mixed States of Manic-Depressive Insanity)* also appeared in 1899.

In 1899 Kraepelin was clear on the distinction between manic-depressive illness and dementia

praecox. The clinical pictures were distinct and, he believed, they were caused by very different underlying disease processes (dementia praecox being a degenerative disorder). However, by the end of his career, he was not so sure that these two great insanities were so distinct. In 1920 he wrote: "We must, then, accustom ourselves to the idea that the phenomena of illness which we have hitherto used are not sufficient to enable us to distinguish reliably between manic-depressive illness and schizophrenia in all cases." This lack of clarity between the two great psychotic disorders resulted in geographical and national differences in diagnosis. Books and articles appearing in the 1970s reported that schizophrenia was overdiagnosed in the United States and manic-depression underdiagnosed compared to Europe, particularly the United Kingdom, where the reverse was true. As schizophrenia researcher Nancy Andreasen (1938–) pointed out in a 1994 article examining this issue, such evidence of cultural style differences in diagnosis cast doubt on the idea of dementia praecox or schizophrenia as an "ahistorical" disease entity like physical diseases such as cancer or diabetes. History, tradition, and culture have always played an important role in shaping our concepts of mental disorders. Manic-depression and schizophrenia are no exceptions.

Cause "We are completely in the dark about the nature of manic-depressive insanity," Kraepelin wrote in 1899 when addressing the issue of etiology (cause). He devoted exactly two paragraphs to this topic, stressing the "periodic" nature of the illness and how such cycling resembles metabolic processes and epileptic attacks. "This could indicate a chemical theory, all the more so as we now seem to be coming close to postulating an autointoxication in the case of epilepsy too, which likewise is periodic. . . . Still, we can probably expect this matter to be clarified some day by metabolic investigations" (p. 309). At this time Kraepelin held to the theory of AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX, and so it was a natural speculation on his part that autointoxication may also play a role in manic-depressive insanity. In later writings on manic-depression, Kraepelin stressed the fact that heredity may be involved, noting that the disease ran in families.

Research Manic-depressive illness never captured the attention of biological psychiatrists the way that dementia praecox did. Volumes reviewing the experimental literature on dementia praecox and schizophrenia have appeared with great regularity since the 1920s, with Leopold Bellak editing such compilations each decade from the late 1940s to the late 1970s. The most recent series seems to be the successive editions of *Schizophrenia* by Steven R. Hirsch and Daniel Weinberger (2nd ed., 2003). However, only two such comprehensive reviews of manic-depressive illness have appeared in the last 50 years—*Manic-Depressive Disease: Clinical and Psychiatric Significance* (1953) by John D. Campbell, and *Manic-Depressive Illness* (1990) by Frederick K. Goodwin and Kay Redfield Jamison. This relative inattention by researchers to manic-depressive insanity since 1899 reflects the fact that persons with this disorder undergo long periods of normal functioning with only cyclic episodes that may require institutionalization and hence is not as disabling a disease as schizophrenia. Additionally, pharmacological treatments for bipolar disorder have been effective in controlling the illness and allow most persons to live productive lives, whereas the medications for schizophrenia have been far less successful in restoring social and occupational functioning. Research conducted since the introduction of the RESEARCH DIAGNOSTIC CRITERIA (1978) and *DSM-III* (1980) have studied this mental disorder according to the criteria given to it under its new name, BIPOLAR DISORDER.

Andreasen, N. "Changing Concepts of Schizophrenia and the Ahistorical Fallacy," *American Journal of Psychiatry* 1 (1994): 355–362.

Campbell, J. D. *Manic-Depressive Disease: Clinical and Psychiatric Significance.* Philadelphia: JB Lippincott, 1953.

Goodwin, F. K., and K. R. Jamison. *Manic-Depressive Illness.* Oxford: Oxford University Press, 1990.

Kraepelin, E. *Psychiatry: A Textbook for Students and Physicians,* Volume 2*: Clinical Psychiatry,* translated by Sabine Ayed, edited by Jacques Quen. Canton, Mass.: Science History Publications, 1990. [Originally published in two volumes in 1899 as the sixth edition of *Psychiatrie: Ein Lehrbuch für Studirende und Aerzte.* Leipzing: Verlag von Johann Ambrosius Barth.]

Salvatore, P., et al. "Weygandt's *On the Mixed States of Manic-Depressive Insanity:* A Translation and Commentary on

Its Significance in the Evolution of the Concept of Bipolar Disorder," *Harvard Review of Psychiatry* 10 (2002): 255–275.

Weygandt, W. *Uber die Mischzustande des manisch-depressiven Irreseins.* Munich: Verlag von J. F. Lehmann, 1899.

MAO activity See ENZYME DISORDER HYPOTHESIS.

marital schism See FAMILY INTERACTION THEORIES.

marital skew See FAMILY INTERACTION THEORIES.

marital status of schizophrenics It has long been observed that most people with severe mental disorders that are admitted to psychiatric hospitals are unmarried. For example, even in 1812, American physician Benjamin RUSH could conclude, based on the patient statistics of the Pennsylvania Hospital in Philadelphia, "Single persons are more predisposed to madness than married people." Almost all studies of the first admission rates of psychiatric hospitals in recent decades have likewise shown that more unmarried than married people have serious psychiatric illnesses, and that this unmarried rate is consistently higher among males than females. In schizophrenia, these high rates are related to the age of onset of illness (it is generally earlier than in bipolar illness) and the subtype of schizophrenia (the unmarried rate is higher for the nonparanoid subtypes). According to a comprehensive review by Letten Saugstad of Norway published in 1989, the single to married ratio in SCHIZOPHRENIA is 7.7:1 for males, and 4.5:1 for females, and for manic-depressive psychosis (bipolar disorder) the ratios were a far lower 1.5:1 for males and 1.3:1 for females. The likelihood of a schizophrenic person remaining married is directly related to the severity and course of illness, with those people with the worst prognosis obviously having the greater marital disruptions and divorces. Thus, in schizophrenia, being single or divorced is associated with a poor prognosis for the illness.

Eaton, W. W. "Marital Status and Schizophrenia," *Acta Psychiatrica Scandinavica* 52 (1975): 320–329.

Saugstad, L. F. "Social Class, Marriage, and Fertility in Schizophrenia," *Schizophrenia Bulletin* 15 (1989): 9–43.

masturbation Masturbation (also known as self-pollution, onanism, or chiromania) was first proposed as a cause of physical and mental disease in a pamphlet published in England in 1710 entitled *ONANIA, or the Heinous Sin of Self-Pollution and All Its Frightful Consequences in Both Sexes, Considered.* The author was anonymous, but it is suspected to be the work of a clergyman. Although masturbation had long been known as a sin since biblical times, this pamphlet is the first place where direct biological effects are connected with this practice. With the rise of DEGENERATION THEORY in the mid-1800s, the direct mental and physical weaknesses caused by this practice were not only harmful to its practitioners, but also to future generations. Seminal loss in men depleted the vitality and the potentially good heredity of males. The shocks to the "spinal marrow" produced by masturbation in both men and women also led to hereditary taint that could be passed on to the next generation. Physical diseases like tuberculosis and insanities such as epilepsy might also result from such practices.

In French alienist J. E. D. ESQUIROL's 1838 textbook, *Mental Maladies,* a chart of the "physical causes" of MANIA in males and females in separate asylums in Paris lists masturbation as the cause of insanity in 16 cases. As he put it later in his book, "Masturbation, that scourge of human kind, is more frequently than is supposed, the cause of insanity, especially among the rich." Treatments for chronic masturbation included the application of ice or leeches to the scrotum or vulva, cold sitz baths, cold enemas, or confinement in MECHANICAL RESTRAINTS such as STRAITJACKETS or MUFFS. Major medical authorities continued to link masturbation with the development of "neurasthenia" and even psychotic disorders at least until the 1930s.

Englehart, H. T. "The Disease of Masturbation: Values and the Concept of Disease," *Bulletin of the History of Medicine* 48 (1974): 239–248.

Gilbert, A. N. "Doctor, Patient, and Onanist Diseases in the Nineteenth Century," *Journal of the History of Medicine,* July 1975, pp. 217–234.

Hare, E. H. "Masturbation and Insanity," *Journal of Mental Science* 108 (1962): 16.
Macdonald, R. "The Frightful Consequences of Onanism: Notes on the History of a Delusion," *Journal of the History of Ideas* 28 (1967): 423–431.

Maudsley, Henry (1835–1918) A British psychiatrist, editor of the *Journal of Mental Science* and the benefactor and founder of the famous Maudsley Hospital in London, Henry Maudsley was perhaps the most important figure in British psychiatry from the 1870s until his death. He was married to the daughter of the man who had previously dominated psychiatry in Britain, John CONOLLY, the leader of the NONRESTRAINT MOVEMENT. Like his contemporary Wilhelm GRIESINGER in Germany, Maudsley believed in the physiological basis of all mental disorders and particularly emphasized the role of heredity in transmitting these disorders. His first book, *The Physiology and Pathology of Mind* (1867), was considered a turning point in British psychiatry due to this biological perspective. In this book he proposed that there were "two great divisions" in the "varieties of insanity," namely *"Affective* and *Ideational,"* and these were distinguished on the basis of whether or not a person had delusions (delusions being a sign of an ideational insanity). He was much criticized for his chapter in that book entitled "Insanity in Early Life," because it was not generally accepted in those times that children could develop psychotic disorders. Although he recommended the earliest possible treatment of people with mental disorders in settings that removed them from their families, he also believed that the most chronic mental patients should be discharged from asylums and cared for at home. As treatment, Maudsley recommended baths, emetics, and purgatives, a good diet and the use of opium.

Unlike his cheerful and emphatic father-in-law, John Connolly, Maudsley was often described as arrogant, aloof, somewhat mean-spirited, and bitter. In 1896, at the age of 60, Maudsley's rather pessimistic view of life was reflected in this confessional passage about his career:

> A physician who had spent his life in administering to diseased minds might be excused if, asking at the end of it whether he had spent his life well, he accused the fortune of an evil hour which threw him on that track of work. He could not well help feeling something of bitterness in the certitude that one-half the diseased he had dealt with never could get well, and something of the misgiving in the reflection whether he had done real service to his kind by restoring the other half to do reproductive work. Nor would the scientific interest of his studies compensate entirely for the practical uncertainties, since their revelation of the structure of human nature might inspire a doubt whether, notwithstanding impassioned aims, paeans of progress, endless pageants of self-illusions, its capacity of degeneration did not equal, and might someday exceed, its capacity of development.

Maudsley, H. "Insanity in Relation to Criminal Responsibility," *Alienist and Neurologist,* April 17, 1896.
———. *The Physiology and Pathology of Mind.* New York: D. Appleton, 1867.

mechanical restraint Throughout history, the mentally ill have been abused and generally mistreated, both before and after the rise of institutional care in the late 1700s and especially during the early 1800s. More often than not, the human needs of the mentally ill (who were viewed as wild, like beasts) were met with FLOGGINGS and lashings, placement in cages, or restraint by chains. Masks and gags that would keep talkative patients silent were perfected by Ferdinand AUTENREITH in Germany in the late 1700s. Various machines based on the CIRCULATING SWING or the GYRATOR were used to spin patients into obedience, as would the "hollow wheel" (HAYNER'S WHEEL) treadmill. Another 17th-century invention, by MacBride in England, was the "straight-waistcoat," later known as the STRAITJACKET, and this in turn inspired other variations by other asylum keepers, including the sacklike mechanical restraints known as HORN'S SACK or the MAD-SHIRT that would be placed over the unmanageable patient's head in order to subdue him or her. Despite the widespread influence of the NONRESTRAINT MOVEMENT in Europe beginning in the 1840s, many such inhumane devices

of mechanical restraint as the straitjacket, MUFFS or the BED SADDLE survived into the 20th century.

Part of the reason that the use of mechanical restraints was so common in the treatment of the mentally ill was due to the prevailing belief in those days that mental illness was incurable. According to Emil KRAEPELIN in his book *One Hundred Years of Psychiatry* (which is actually an excellent history of the use of mechanical restraints), it was only about 1820 that the idea took hold in Europe (and presumably the United States) that some cases of mental illness might be treatable and that some patients could be rehabilitated. Mechanical restraints, although often portrayed as "treatments" that led to "cures," were in fact merely coercive methods to subdue difficult patients during periods of crisis. Philippe PINEL made the first steps to correct the torturous treatment of the mentally ill by freeing dozens of patients from their chains on May 24, 1789 (with his male nurse, Pussin), and by advocating the practice of "moral medicine." Yet rehabilitative treatment for these patients was not begun until two decades later.

When Emil Kraepelin served at the Heidelberg Clinic from 1891–1903, he used no coercion with his patients—a standard philosophy of the time that was not everywhere practiced to the letter. To demonstrate to his medical students how much had changed in the institutional treatment of the mentally ill, he set up a small museum of mechanical restraints. Kraepelin relates in his memoirs:

> The revolution caused by the systematical introduction of bed rest, the frequent use of baths, and finally the newer narcoleptics and tranquilizers was striking. To give the students an idea of these advances, I began collecting means of mechanical restraint, for example, straightjackets, chairs, footcuffs, muffs, gloves, and so on with corresponding illustrations from the old asylums and made a little museum, which I showed the students during the semester. I managed to get some chains, which had once been used to chain a patient.

Perhaps the only form of mechanical restraint still in use today is the FOUR-POINT RESTRAINT or FIVE-POINT RESTRAINT used for brief, supervised periods. Seclusion or isolation rooms are still used in some institutions as well. However, many patients and patient advocates charge that the modern equivalent of these mechanical restraints is in reality the use of ANTIPSYCHOTIC DRUGS as a form of CHEMICAL RESTRAINT to keep patients manageable in an institutional setting.

Illustrations of almost all the forms of mechanical restraint ever used are reproduced in a useful book by A. A. Roback and Thomas Kiernan.

Kraepelin, E. *One Hundred Years of Psychiatry.* 1917. Reprint, New York: Philosophical Library, 1962.

Roback, A. A., and T. Kiernan. *Pictorial History of Psychology and Psychiatry.* New York: Philosophical Press, 1969.

medical disorders that mimic psychotic disorders It has long been known that some physical illnesses can have serious effects on the mental health of an individual. Some of the more serious diseases can actually produce symptoms that, upon first presentation, may look like one of the psychotic disorders. A person may be disoriented and confused, act bizarrely and experience hallucinations and delusions, but then be found to be suffering only from a treatable physical ailment. The following medical disorders are those most likely to resemble a psychotic disorder, particularly schizophrenia:

Viral encephalitis This is literally a "viral infection of the brain." Such brain infections can resemble schizophrenia in their earliest stages of infection. The most commonly reported viruses implicated are cytomegalovirus, measles, coxsackie, herpes simplex, Epstein-Barr, and equine encephalitis. As we know from the history of the disorder that used to be called the GENERAL PARALYSIS OF THE INSANE, cerebral syphilis can resemble schizophrenia in its most advanced stages, though it is rarely encountered today. The suspected viral cause of the psychosis can be confirmed with a spinal tap (lumbar puncture). The human immunodeficiency virus (HIV) can cause mental deterioration (dementia), and individuals who are seropositive for HIV and manifest the AIDS DEMENTIA COMPLEX may be diagnosed with AIDS solely on the basis of this dementia.

Temporal lobe epilepsy This type of epilepsy has long been reported to include psychotic symptoms (delusions and hallucinations) in some people.

Thyroid disease Any disease process involving the hormones and their role in the nervous system of human beings (neuroendocrinopathy) can cause psychosis-mimicking symptoms. Primary hypothyroidism is perhaps the most commonly misdiagnosed medical disorder that mimics a psychiatric disorder, because it involves so many symptoms that resemble a severe depression (depressed mood, weight change, sleep disturbances, and, in its most extreme forms, delusions and hallucinations). Thyroid disease can be mistaken for the mood disorders and, in some cases, schizophrenia.

Huntington's disease A genetically transmitted disease that strikes in midlife, Huntington's disease in its earliest stages is perhaps more persistently misdiagnosed as schizophrenia than is any other medical disorder. When the characteristic abnormal movements begin later in the disease ("choreiform movements"), the actual diagnosis is usually made without difficulty.

Multiple sclerosis Multiple sclerosis has much in common with schizophrenia. Like schizophrenia, it often begins in people between the ages of 18 and 40. In its earliest stages, patients may report feeling "tired" or "weak" a lot of the time, may become depressed, and may undergo a certain amount of intellectual deterioration. Multiple sclerosis is commonly misdiagnosed in its early stages, but as the disease progresses the characteristic symptoms become obvious.

Brain tumors Brain tumors may cause psychotic symptoms that resemble schizophrenia. Although "psychosis secondary to brain tumor" is rare, it is easily misdiagnosed. Elderly persons are more likely to have psychotic symptoms from brain tumors. The most likely place for a brain tumor to cause schizophrenia-like symptoms is on the pituitary gland, although some temporal lobe tumors may also cause psychosis. The correct diagnosis is easily made with neuroimaging scans using magnetic resonance imaging or computed tomography.

Traumatic injury to the brain Psychotic syndromes occur more frequently in individuals who have had a traumatic brain injury than in the general population. Sometimes a chronic, schizophrenia-like syndrome can develop after a serious head injury. People diagnosed with schizophrenia have a higher frequency of traumatic brain injury than individuals diagnosed with other psychiatric disorders.

Parkinson's disease PD is a degenerative neurological disease caused by the arteriosclerotic changes in the part of the brain that controls smooth movement, the basal ganglia. It is often a crippling disease, characterized by muscular tremors, rigidity of movement, droopy posture, and masklike facial grimaces. In the latter stages of the disease, hallucinations and other psychotic symptoms develop in about 40 percent of all persons who have PD.

There are a number of other medical disorders that may produce symptoms resembling schizophrenia, though less commonly. These may include the following medical disorders: stroke (cerebral vascular accident, or CVA); metal poisoning (e.g., mercury, lead); insecticide poisoning (e.g., organo-phosphorous compounds); Wilson's disease; tropical infections; acute intermittent porphyria, metachromatic leukodystrophy; lupus erythematosus; normal pressure hydrocephalus; hepatic encephalopathy; pellagra; pernicious anemia; leptospirosis, and sarcoidosis.

Extein, I., and M. S. Gold. *Medical Mimics of Psychiatric Disorders.* Washington, D.C.: American Psychiatric Press, 1986.

Lisanby, S. H., et al. "Psychosis Secondary to Brain Tumor," *Seminars in Clinical Neuropathology* 3 (1998): 12–22.

McAllister, T. W. "Traumatic Brain Injury and Psychosis: What Is the Connection?" *Seminars in Clinical Neuropsychiatry* 3 (1998): 211–223.

Peyser, C. E., et al. "Psychoses in Parkinson's Disease," *Seminars in Clinical Neuropsychiatry* 3 (1998): 41–50.

medical model of mental disorders This is the prevailing philosophical position in our culture on the nature of mental disorders. Mental disorders are viewed as equivalent to physical "illnesses," which can be "diagnosed" and "treated." Critics of the medical model, such as American psychiatrist Thomas Szaz, believe the "myth of mental illness" has outlived its usefulness as a way to conceptualize the social and psychological phenomena we label "sick." Other models of mental disorder can be based on other premises. For example, in other

cultures (or subcultures within our own society), supernatural models may be more accepted, with mental disorders viewed as the result of spirits or demons that must be exorcised.

The psychotic disorders have been assumed to be brain diseases since the 19th century. However, due to the great influence in American psychiatry of psychoanalysis and FAMILY INTERACTION THEORIES throughout most of the 20th century, which emphasized the social and cultural causes of schizophrenia, the medical model did not really gain prominence again in schizophrenia research until the 1970s with the advent of new BRAIN IMAGING TECHNIQUES and other technological advances in the field of biochemistry genetics, and psychopharmacology.

Siegler, M., and H. Osmond. *Models of Madness, Models of Medicine*. New York: Macmillan, 1974.

medical restraint See CHEMICAL RESTRAINT.

médicine mentale Literally "mental medicine." This was one of the earliest terms used in France for the professional discipline of psychiatry. By the 1820s, the status of *médicine mentale* was debated in many circles. During this time J. E. D. ESQUIROL argued that former methods of studying human nature, particularly "metaphysical philosophy," completely ignored the "physical man." *Médicine mentale* was thus based on a physiological foundation, as evidenced by the methodology used by Esquirol and Philippe PINEL in their investigations of the causes of mental illness: namely, autopsies.

Meduna, Ladislaus von (1896–1964) The originator of chemically induced convulsive therapy for schizophrenia. Meduna was a neuropathologist in Budapest, Hungary, who also worked at a prominent asylum in that city. Meduna had observed that persons with schizophrenia rarely suffered from epilepsy. Using his microscopic skills as a neuropathologist, Meduna began to look for differences between the brain cells of epileptics and schizophrenics. To his eye, glial cells were quite different in the two disorders, thus verifying his clinical observation. From these two basic observations he created a theory that schizophrenia and epilepsy were somehow "in opposition" to one another. Therefore, he reasoned (somewhat poorly), if he could bring about an epilepsy-like seizure in schizophrenics it would cure them. He first used camphor to induce seizures, then switched to a cardiac stimulant, pentylenetetrazol, which was marketed in the United States as Metrazol and in Europe as Cardiazol. In his first series of 26 schizophrenics, 10 showed remarkable improvement after their chemically induced seizures. Meduna's published report of this study in the *Zeitschrift fuer die gesamte Neurologie und Psychiatrie* in 1935 attracted wide attention in central Europe but did not attract the attention of American psychiatrists until mid–1937. In that year Meduna published a book on his new therapy, *Die Konvulsionstherapie der Schizohrenie* (*The Convulsion Therapy of Schizophrenia*), and two years later he immigrated to the United States and took a position as professor of psychiatry at Loyola University in Chicago.

METRAZOL SHOCK THERAPY, as it was also called, did not have a long history in psychiatric therapeutics. ELECTROSHOCK THERAPY and INSULIN COMA THERAPY soon overshadowed it.

megavitamin therapy Megavitamin therapy for schizophrenia was first reported in a publication by psychiatrist Abram Hoffer and his colleagues in 1957. On the basis of the TRANSMETHYLATION HYPOTHESIS, a BIOCHEMICAL THEORY OF SCHIZOPHRENIA, they reasoned that a toxic substance was created when the NEUROTRANSMITTER epinephrine was metabolized in the brain. This toxic metabolite—adrenochrome—was thought to be responsible for producing the symptoms of schizophrenia. To block the production of adrenochrome, schizophrenic patients were administered high doses of niacin (vitamin B_{-3}). In later studies, the doses of niacin were raised even higher and combined with ECT and other somatic treatments. The literature on megavitamin therapy is voluminous, and highly controversial, with most knowledgeable assessments of this area of research tending to

discount the claims of lasting therapeutic success with megavitamin therapy.

In 1968 Linus Pauling, a Nobel laureate in chemistry, coined the term *orthomolecular psychiatry* to refer to the treatment of mental disorders through nutritional changes. Pauling argues in his first paper on the subject that mental illness is the result of chemical imbalances in the brain that could be corrected through a proper diet and nutritional supplements. Pauling speaks of creating an "orthomolecular environment of the mind" that eliminates the altered subjective experiences of PSYCHOSIS (which in orthomolecular psychiatry is called metabolic dysperception). Orthomolecular therapy grew in the 1970s among its adherents, and a wide variety of vitamins and minerals have been used in the treatment of SCHIZOPHRENIA and other disorders. These research reports have been reported in such publications as the *Journal of Orthomolecular Psychiatry.*

Although it is entirely possible—and even probable—that nutrition may affect the development and the course of schizophrenia and other psychotic disorders, due to its lack of conclusive evidence, orthomolecular treatment is considered at present to be outside the mainstream of psychiatry.

See also FOOD ALLERGIES AS A CAUSE OF PSYCHOSIS; TRANSMETHYLATION HYPOTHESIS.

Hawkins, D., and L. Pauling. *Orthomolecular Psychiatry: Treatment of Schizophrenia.* San Francisco: Freeman, 1973.

Hoffer, A., et al. "Treatment of Schizophrenia with Nicotinic Acid and Nicotinamide." *Journal of Clinical and Experimental Psychopathology* 18 (1957): 131–158.

Pauling, L. "Orthomolecular Psychiatry," *Science* 160 (1968): 265–271.

melancholia Along with MANIA, melancholia is one of the two great ancient categories of madness or insanity. In humoral medicine, melancholy was thought to be caused by an excess of "black bile" (which is the exact meaning of melancholy). From antiquity to the mid-1800s, mania and melancholia were prime organizing categories for all other insanities. Originally, melancholia had nothing to do with what we think of today as DEPRESSION. Instead the term was used as a general designation for the types of madness characterized by fixed DELUSIONS (such as found in PARANOIA). Mania was a broad category for any disorder that involved hallucinations. A second meaning for melancholia was any sort of lessening in intensity or weakness in mood, intellectual functioning, or "will." The multitude of various maladies and weakened states of mind that were grouped under this old term can be found in Robert Burton's (1577–1640) huge volume, *The Anatomy of Melancholy* (1621). Burton himself clearly suffered from both anxiety and depression (which we now know are often combined). The connection of melancholia with ancient humoral theories of health and illness was first severed by British physician William Cullen in his book *First Lines of the Practice of Physic* (1777).

Although some sort of mood disorder or anxiety disorder was always present in ancient descriptions of melancholy, melancholy was finally distilled down to something that resembles modern concepts of depression after 1850, and certainly by the last two decades of the 19th century. In 1980 *DSM-III* introduced the diagnosis of "major depression," and this concept has had a profound impact on psychiatric practice as well as on the public imagination, setting the state for the acceptance of ANTIDEPRESSANT DRUGS such as Prozac (1988) as the desired remedy for everyday psychic ills. The most comprehensive description of the millennia-old history of melancholia can be found in an excellent book on the subject by Yale University historian of psychiatry Stanley W. Jackson.

Jackson, S. W. *Melancholia and Depression: From Hippocratic Times to Modern Times.* New Haven, Conn.: Yale University Press, 1986.

Mellaril See ANTIPSYCHOTIC DRUGS.

Mendelian transmission The modern science of genetics is based upon the work of an Austrian biologist and Augustinian monk, Gregor Johann Mendel (1822–84). In his experiments with peas grown in the garden of the monastery at Brünn,

he discovered lawful patterns of heredity in the ways certain characteristics, or traits, were transmitted from generation to generation in the plants. Classical Mendelian transmission is monogenetic transmission—that is, a single gene with dominant and recessive ALLELES distributes certain traits (called Mendelian traits) in a typical fashion: Three offspring have the dominant characteristic for every individual with a recessive trait. It has long been known that the genetic predisposition to the psychotic disorders is passed on from generation to generation in a NON-MENDELIAN PATTERN OF TRANSMISSION that is, as yet, not well understood.

See also GENETIC TRANSMISSION.

mental alienation Mental illness. Although used in a different context for centuries, it was not until the 1800s that mental alienation (*aliénation mentale*) became a medical term. With legislative reforms in France in 1838, the term began to refer to the legal status of insanity (*folie*). At about this time it became popular with physicians who treated the mentally ill as a term for severe mental illness. The term "mental alienation" first began appearing in English medical texts about 1860, and it was at about this time that the term "ALIENIST" began to be popularly used to describe a physician who specialized in the treatment of the mentally ill. In English, "mental alienation" referred to mental disorders that were not diseases of the brain (as was delirium). Along with the concepts of "insanity" and "dementia," the old concept of mental alienation helped to form the concept of PSYCHOSIS in the latter half of the 19th century.

Berrios, G. E. "Historical Aspects of Psychoses: 19th-Century Issues," *British Medical Bulletin* 43 (1987): 484–498.

mental disorder This is now the officially accepted term for what has been called in the past mental illness, psychiatric disorder, or mental diseases. The word *disorder* is used to make the concept more neutral and specifically to downplay the causal assumptions of a medical model of madness that is communicated with the words *illness* or *disease*.

mental hospitals See ASYLUMS.

mental hygiene movement Since the reform era of the mid-1800s, in the United States and Europe there was a growing concern surrounding the treatment and possibly even the prevention of mental disorders. The term that came to be used for this concept—mental hygiene—was coined and first used in a book in 1843 by William C. Sweetwater, an American physician. It was later also used by Isaac RAY as the title of a book on this subject published in 1863. However, in this century the term *mental hygiene* has come to be associated with an American reformer, Clifford BEERS.

At the turn of the century, American businessman Clifford Beers suffered a mental disorder that led to his hospitalization in private and then in public institutions. The horrors of his treatment led him to seek reforms in the treatment of the mentally ill once he had recovered. The first step was the publication of his vivid autobiography, *A Mind That Found Itself*, in March 1908. On May 6, 1908, Clifford Beers met with 13 other interested men and women in New Haven and founded the Connecticut Society for Mental Hygiene. The objectives they agreed upon that day have influenced all other mental health organizations since that time and have remained a vital plan of action for community responses to mental illness in society:

> The chief purpose of the Society shall be to work for the conservation of mental health; to help prevent nervous and mental disorders and mental defects; to help raise the standards of care for those suffering from any of these disorders or defects; to secure and disseminate reliable information on these subjects; to cooperate with federal state, and local agencies or officials and with public and private agencies whose work in any way relates to that of a society for mental hygiene.

The public response to this new organization was impressive (helped, no doubt, by Beers's shocking book), and groups began to spring up in other areas of the country and, later, in other countries. By 1909 Beers formed the National Committee for Mental Hygiene and had the sup-

port of such prominent figures as psychologist and philosopher William James and psychiatrist Adolf MEYER. In 1930 the First International Congress on Mental Hygiene met in Washington, D.C. Later, this organization once again changed its name to the National Council for Mental Hygiene. It is now known as the National Mental Health Association.

Historical essays on the Mental Hygiene Movement and its influence can be found in the supplement included in later editions (starting in 1953) of Beers's book.

Beers, C. *A Mind That Found Itself: An Autobiography.* New York: Longman, Green, 1908.

mesoridazine See ANTIPSYCHOTIC DRUGS.

Messiah complex See AMENOMANIA; MONOMANIA.

metabolic disorder hypothesis In biological terms, the word *metabolism* refers to the chemical processes within the body in which new substances are synthesized (catabolism) or broken down (anabolism) in order to bring about growth, regulation (homeostasis), tissue repair, and energy supply. Although the notion of the physical basis of metabolism (conversion of organic matter from one form into another) dated from the time of the ancient Greeks, the rise in experimental biology in the mid-1830s led to a primary focus on the processes of metabolism. "Soluable ferments" (enzymes) were known and studied in the 19th century, but the importance of enzymes in metabolism was not recognized. It was not until 1926 that technological advances allowed for the identification and study of individual enzymes. However, by the 1890s it was certainly clear that "internal secretions" from glands with and without ducts were involved in metabolism, leading to the modern concept of the hormone (1905) and the rise of modern endocrinology. After 1930, the rise of MOLECULAR BIOLOGY deepened understanding of the hormones, enzymes, and other biological processes involved in metabolism. Since 1902 it had been hypothesized that hereditary transmission played a role in enzyme formation, leading to the "one-gene, one-enzyme" idea until the 1960s, when this notion was replaced with a "one-gene, one-polypeptide" hypothesis. Molecular biology research has focused on the genes linked to the formation of these chemicals involved in metabolism.

Mental disorders as metabolic disorders By the 1890s it was clear that some diseases—such as diabetes—were related to metabolism. As is the usual pattern in the history of medicine, the excitement caused by the discovery of a new mechanism for the cause of disease often leads to speculation that the new mechanism causes many, if not all, diseases. In the 21st century it is the assertion that genetics plays a role in the cause of most mental and physical disorders that has become popular. By the mid-1890s microbes (bacteria) and imbalances in the production of "internal secretions" by the glands, leading to "metabolic disorders," were two medical theories that were quickly extended as explanations of the cause of most physical and mental diseases. Together these were known under the general term *autointoxication.*

When Emil KRAEPELIN first introduced his concept of dementia praecox in 1896, he included it under a broad category of mental disorders that he believed were "metabolic disorders" (*Stoffwechselerkrankungen*) in the fifth edition of his famous textbook, *Psychiatrie.* In subsequent editions of *Psychiatrie,* he eventually dropped this broad assertion. However, for at least the first two decades after introducing dementia praecox as a diagnostic entity, Kraepelin held firm to the belief that this disease was caused by a poisoning of the brain arising from the "sex organs," since the disease most commonly appeared in the years directly following puberty. Heredity did, of course, play a role, but he claimed that it merely made one vulnerable to developing this abnormal functioning of the sex glands and did not directly cause dementia praecox. AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX (SCHIZOPHRENIA) was an influential hypothesis that led to many theories of etiology (and radical forms of treatment) until the 1930s. Following Kraepelin and advances in endocrinology, ENDOCRINE ALTERATIONS IN SCHIZOPHRENIA

were studied throughout the 20th century, but relatively few publications have appeared on this subject in the 21st century.

Metabolism and heredity The role of heredity (or genetics) in the development of metabolic diseases was documented convincingly by A. E. Garrod (1857–1936) in 1909 in his book *Inborn Errors of Metabolism.* Modern GENETICS STUDIES have found links between endocrine disorders and genes for some forms of diabetes and other disorders, but no such connection between genes and metabolic or endocrine disorders has been found for schizophrenia.

The return of metabolic studies in the 1950s Research on the "psychosis-causing" or psychotogenic effects of hallucinogenic drugs such as LSD-25 led to speculation that there may be a similar chemical process at work in the bodies of persons who suffer from schizophrenia. In 1952 Humphrey Osmond and J. R. Smythies proposed a new theory about the cause of schizophrenic symptoms based on this premise, the TRANSMETHYLATION HYPOTHESIS. The assumption was that if such a psychotogenic process was happening in the body, metabolic products of it should be detectable in the blood or urine. The search for such metabolites and the enzymes that led to their creation dominated psychiatric research from 1957 to 1967, an era that psychiatrist and historian David Healy characterized as "the flourishing of metabolic psychiatry." Ultimately no such endogenous psychotogenic substance was found in persons with schizophrenia, and by 1979 the transmethylation hypothesis no longer guided schizophrenia research. Findings were numerous, contradictory, and not directly applicable to the design of new antipsychotic drugs. Instead it was replaced by the DOPAMINE HYPOTHESIS and the search for neurotransmitters involved in the pathophysiology and possible etiology of schizophrenia. Basic research on neurotransmitters was directly relevant to the creation of new antipsychotic drugs and attracted significant funding by pharmaceutical companies. Despite a few promising leads, the pharmaceutical industry was far less interested in funding large scale research on the transmethylation hypothesis because drug development seemed less promising.

Problems in studying metabolism in schizophrenia Although endocrine and immune system alterations have been documented, though inconsistently, in schizophrenia, it is not possible to determine if these findings are due to the effect of ANTIPSYCHOTIC DRUGS or to the underlying disease process of schizophrenia. Antipsychotic drugs are known to affect both endocrine and immune functions. Another further problem lies in the difficulty in knowing if metabolic or immune disturbances cause schizophrenia, or if they are caused by schizophrenia. Although tighter links have been forged between AFFECTIVE DISORDERS and metabolic disorders, there is no convincing evidence that schizophrenia is a metabolic disorder.

See also ENDOCRINE ALTERATIONS IN SCHIZOPHRENIA; IMMUNE SYSTEM ALTERATIONS IN SCHIZOPHRENIA.

Healy, D. *The Creation of Psychopharmacology.* Cambridge, Mass.: Harvard University Press, 2002.

Yao, J. K., and R. D. Reddy. "Metabolic Investigations in Psychiatric Disorders," *Molecular Neurobiology* 31 (2005): 193–203.

Metrazol shock therapy One of the chemically induced forms of the CONVULSIVE THERAPIES of schizophrenia, invented by Hungarian psychiatrist Ladislas von MEDUNA (1896–1964) in the early 1930s. Believing that SCHIZOPHRENIA and epilepsy were physiologically incompatible, Meduna reasoned that the artificial induction of seizures in schizophrenic patients would alleviate their symptoms. First he used camphor. He then set out to do this through chemical means by administering an initial intravenous dose of 3 c.c. of pentylenetetrazol (Metrazol) with an increase of 1 c.c. if a convulsion was not induced in the patient. Achieving what he interpreted as a convincing success, he published his results in 1935. The treatment spread quickly, and by 1940 literally thousands of schizophrenic patients in Europe and the United States had been treated with Metrazol shock therapy, both in institutions and in private practice. Metrazol shock therapy was much easier to administer than the INSULIN COMA (OR SHOCK) THERAPY of Manfred Sakel (1900–57), which required a highly trained staff to administer and monitor the potentially life-threatening treatments.

Metrazol is a derivative of camphor, a substance used since the 18th century on institutionalized

mentally ill patients. In fact, the earliest use of a chemically induced convulsion therapy for mental illness was reported by British physician William Oliver in 1785. Oliver administered a high dose of camphor to a patient experiencing a manic episode in order to sedate him, but instead the patient experienced a convulsion. However, his manic symptoms seemed to miraculously disappear. But when the same patient was suffering from depression two years later, the same treatment had no effect. Oliver's report of convulsive treatment was cited occasionally in early psychiatric manuals, but it does not seem that it inspired others to apply the method as a formal treatment for mental disorders until Meduna's work in the 1930s.

In a 1938 article that reviewed the research on Metrazol shock therapy to date and gave a report on the treatment of 35 patients in a private practice setting, Philadelphia psychiatrist N. W. Winkleman of the University of Pennsylvania Medical School gives the following vivid description of what Metrazol shock therapy was like:

> The technic of the therapy as advised by von Meduna consists of two injections per week. Within a few seconds to minutes after the intravenous injection of 3 c.c. to 10 c.c. of metrazol, the patients usually give a short cough. This is followed in rapid succession by generalized body twitching, opening of the mouth, frequently with a cry, generalized convulsive seizures of the entire body, intense rigidity, gradual closing of the mouth with such vigor that frequently the patients have bitten through a wooden tongue depressor. Then cyanosis, dyspnea, apnea occur until finally after a few seconds of cessation of breathing the patient suddenly inspires and relaxes. The mouth gag is usually kept in the mouth rather tightly until the patient returns to full consciousness and frequently the patient makes sucking movements on the mouth gag. The patients are frequently in a confused state which lasts for a variable period after the convulsion is at an end. They may struggle to get out of bed or they may talk in an incoherent manner. Frequently they are confused for a period up to two hours and are then able to be up and around and are then given their food after three or four hours.

The convulsions (sometimes called "Metrazol storms") were often so severe that some patients experienced shoulder and jaw dislocations, with reports that sometimes teeth would actually break in the process. To prevent shoulder dislocations, Winkleman and A. M. Rechtman, a Philadelphia orthopedic surgeon, invented a leather "belt" or "restraining device" that fastened the wrists of a person to the hips so that the arms would be immobile during convulsions. A picture of this device, which resembles MECHANICAL RESTRAINTS used in the 18th and 19th centuries, can be found in Winkleman's article.

The primary drawback to Metrazol shock therapy was that the convulsion did not occur immediately after the injection of the drug, during which time the patient was conscious and experiencing feelings of intense fear and terror that were a side effect of the drug. Furthermore, sometimes convulsions could not be produced, and these patients would remain in an agitated state for days until another treatment could be applied. ELECTROSHOCK THERAPY replaced Metrazol shock therapy after 1940 because it induced immediate unconsciousness and convulsions and was therefore considered more humane.

See also MEDUNA, LADISLAS JOSEPH VON.

Oliver, W. "Account of the Effects of Camphor in a Case of Insanity," *London Medical Journal* 6 (1785): 120–130.

von Meduna, L. *Konvulsionstherapie der Schizophrenie.* Halle: Marhold, 1937.

———. "Versuche über die biologische Beeinflüssung des ablaufes der Schizophrenie. I. Campher- und Cardazolkampfe," *Zeitschrift für Neurologie und Psychiatrie* 152 (1935): 235–262.

Winkleman, N. W. "Metrazol Treatment in Schizophrenia: A Study of Thirty-five Cases in Private Practice, Complications and Their Prevention," *American Journal of Psychiatry* 95 (1938): 303–316.

Meyer, Adolf (1866–1950) A Swiss neurologist and psychiatrist who immigrated to the United States in 1892 after completing his medical studies, Adolf Meyer was perhaps the single most influential figure in American psychiatry from about 1895 to the 1920s. He established many links between

American and European psychiatrists, and he was instrumental in modernizing the medical school teaching of psychiatry. He became a professor of psychiatry at the Johns Hopkins Hospital in Baltimore, Maryland, in 1910 and director of the famous Henry Phipps Psychiatric Clinic in 1913.

He coined the term *psychobiology* to describe his approach to psychiatry, which emphasized that a person's mental state was influenced by biological and environmental factors. Meyer liked to emphasize the lifelong history of a person and his or her subjective experience of a disease. His influence can be seen in the first standard American diagnostic manual for mental disorders, *DSM-I* (1952), in which many of the disorders were labeled as various types of "reactions"—a reflection of Meyer's philosophy that all mental disorders were psychological responses (reactions) to the environment, past experience, or biological processes.

Meyer attempted to replace traditional terms for mental disorders and other psychiatric terms with his own idiosyncratic vocabulary (for example, *parergasia* for schizophrenia, *thymergasia reactions* for manic-depressive psychosis, *holergasic disorders* for the psychotic disorders, *ergasiology* for psychobiology, and *ergasiatry* for psychiatry). None of these terms, however, ever gained wide acceptance.

Meyer resisted the theories of Emil KRAEPELIN and those who believed in the strict biological causes of mental disorders. Meyer and his "Meyerians" (like the Freudians and psychoanalysts after them) refused to believe in heredity (genetics) as the primary cause of mental disorders. It is therefore not surprising that these "mind twist men" (the Meyerians and psychoanalysts) were hostile to the "brain spot men" (the Krapelinians).

Meyer's main contribution to the history of dementia praecox and schizophrenia was a monograph he coauthored in 1911. It reinterprets the causes and symptoms of dementia praecox as "reactions" to psychosocial stressors. Meyer was one of a long list of famous figures in early 20th-century psychiatry who treated the same psychotic patient, Stanley McCormick (1874–1947), of the prominent Chicago family. However, neither he nor any of the others could cure this patient.

Meyer has not fared well in histories of psychiatry. Meyer was seen as ruminative and vague even by his own contemporaries, and it is said he never met a theory or new treatment in psychiatry that he did not like. His vague and virtually useless concept of "psychobiology" seemingly welcomed biological research on dementia praecox and schizophrenia, psychoanalysis, psychological research, autointoxication and focal infection theories of the cause of insanity, dental and abdominal surgery as a treatment for psychosis, the convulsive therapies (Metrazol, insulin, and electroshock), and a whole host of other theories and techniques. Logical contradictions, inconsistencies, and potential dangers of treatments (for example, abdominal surgery as a treatment for schizophrenia) did not seem to bother him. Although it is true his notion of mental disorders as "reactions" was a corrective to those who believed in the influence of heredity, including Kraepelin, he also did not totally reject Kraepelin.

Meyer was the first psychiatrist in the United States to critique Kraepelin's concept of dementia praecox. In an 1896 book review of the fifth edition of *Psychiatrie,* he criticizes Kraepelin's view of dementia praecox as a "metabolic disorder" and criticizes Kraepelin's speculation that dementia praecox is caused by an autointoxication. However, by 1918, Meyer was willing to support Henry A. Cotton of the New Jersey State Hospital at Trenton when he began the first of thousands of surgical procedures to cut out infected tissues in the body that were causing autointoxications of the brain and producing mental illness.

Lidz, T. "Adolf Meyer and the Development of American Psychiatry," *American Journal of Psychiatry* 123 (1966): 320–332.

Meyer, A., S. E. Jelliffe, and A. Hoch. *Dementia Praecox: A Monograph.* Boston: R. G. Badger, 1911.

Noll, R. "Styles of Psychiatric Practice, 1906–1925: Clinical Evaluations of the Same Patient by James Jackson Putnam, Adolf Meyer, August Hoch, Emil Kraepelin and Smith Ely Jelliffe," *History of Psychiatry* 10 (1999): 145–189.

milieu therapy The idea behind milieu therapy is that by creating a specially designed "therapeutic environment" for patients with severe mental ill-

ness, the course of the disease can be affected in a positive way. This idea is as old as those of the earliest pioneers of reform in the MORAL TREATMENT of mental illness, namely Philippe PINEL in France, Vincenzo CHIARUGI in Italy, and especially William Tuke in England, whose YORK RETREAT may have been the first true attempt at such a therapeutic environment. Since the early 19th century there have always been small private institutions that have attempted to provide such environments, but it was not until the 1930s and 1940s that the concept of constructing special wards or buildings for the purpose of milieu therapy came about.

American psychiatrist Harry Stack Sullivan may be given credit for stimulating the use of milieu therapy with his 1931 publication describing his special unit for young males with acute schizophrenia. However, it was the work of T. F. Main with neurotics at the Cassel Hospital in England that popularized the notion of the "therapeutic community," a term coined by Main in a 1946 paper. This approach demanded a more active participation by the patients in the management of the environment and emphasized three elements: (1) a flattening of the hierarchical structure of authority, (2) the blurring of role differentiations between staff and patients, and (3) the cultivation of open communication in order to minimize differences between the social life within the institution and that of the world outside. Many such experimental wards and units for the treatment of schizophrenia were initiated using this approach.

The environments of many psychiatric institutions have undergone extensive transformations since the 1950s in order to make them more "therapeutic." However, as a specific mode of treatment for schizophrenia and the psychotic disorders, the measurable positive effects of such an environment have been small in research studies. Hence milieu therapy has been criticized by researchers Van Putten and May in a 1976 review of the research literature: "Milieu therapy has increasingly become an ideology rather than a defined method of treatment sustained to a large extent not by scientific evaluation but by a steady flow of rhetoric and by humanitarian and emotional justifications." Nonetheless, in conjunction with other forms of treatment, it seems incontrovertible that a more humane environment can only help those who are suffering from severe mental disorders.

Main, T. F. "The Hospital as a Therapeutic Institution," *Bulletin of the Menninger Clinic* 19 (1946): 66–70.

Sullivan, H. S. "Socio-Psychiatric Research: Its Implication for the Schizophrenia Problem and for Mental Hygiene," *American Journal of Psychiatry* 10 (1931): 977–991.

Van Putten, T., and P. R. A. May. "Milieu Therapy of the Schizophrenias." In *Treatment of Schizophrenia: Progress and Prospects,* edited by L. J. West and D. E. Flinn. New York: Grune & Stratton, 1976.

misidentification syndromes These are a group of syndromes characterized by delusions that persons or objects in the environment are something other than what their true nature is. Familiar persons can be regarded as impostors (as in CAPGRAS SYNDROME), strange persons can become known persons who are believed to be persecuting the delusional person (FREGOLI'S SYNDROME), or persons in the delusional individual's immediate environment can become other known individuals (such as in the INTERMETAMORPHOSIS SYNDROME, in which a doctor, for example, can be mistaken for a first grade teacher). All of the misidentification syndromes are generally part of one of the psychotic disorders and are not diagnostic categories themselves.

"The Delusional Misidentification Syndromes," *Biblioteca Psychiatrica* 164 (1986): 1–153.

mixed states When Emil KRAEPELIN introduced MANIC-DEPRESSIVE ILLNESS in 1899 as one of the two main categories of insanity (the other being DEMENTIA PRAECOX), he described a disorder in which mania, depression, and psychotic states that were a combination of the two alternated over the course of the life span of afflicted persons. The presence of these "mixed states" (*Mischzustande*) led Kraeplin to believe that mania and depression were indeed two aspects of the same pathological process. The primary study of these mixed states was conducted by an assistant physician working

under Kraepelin at the Psychiatric Clinic of Heidelberg University, Wilhelm Weygandt (1870–1939). In the same year that Kraepelin published his first description of manic-depressive illness, Weygandt also published his dissertation as a monograph describing these mixed states in detail, providing 16 case history examples of patients who were manifesting symptoms of both mania and depression at the same time. Such mixed states were not uncommon in manic-depression. In addition to pure mania and pure depression, Weygandt described six separate mixed states, many of which Kraepelin later included in subsequent editions of his textbook, *Psychiatrie.* Weygandt summarized his main conclusions thus:

> In summary, cases of circular or manic-depressive insanity, a mixture of the cardinal symptoms of each of the two typical phases commonly occurs. Those combinations are usually brief, although sometimes the mixed state marks the entire course of a single episode, or most of it. Later episodes with mixed features show a longer course than do pure depressive or manic episodes, yet the prognosis is favorable in any kind of episode. This clinical approach has achieved good results both diagnostically and prognostically in the Clinic of Heidelberg, where fewer than one-third of [manic-depressive] patients have shown no mixed states at all, and over 20 percent of patients have had one or more episodes in which mixed features predominate.

Since 1899, "mixed states" have been acknowledged by psychiatry but have been little understood. Following the pattern set by the reconceptualizing of manic-depression as BIPOLAR DISORDER in *DSM-III* in 1980, *DSM-IV-TR* (2000) merely defines a "mixed episode" as one in which "criteria are met for both a manic episode and for a Major Depressive Episode (except for duration) nearly every day during at least a 1-week period." Because these criteria have been so vague, in the 1990s researchers began to investigate the nature of "mixed states" and have attempted to develop better diagnostic criteria that could be included in future editions of the *DSM* series. In the early 21st century the trend is to view mixed states as primarily a form of mania, dysphoric mania, separate from the classical idea of mania as euphoric mania and a newly proposed form, psychotic mania.

Mixed mania (dysphoric mania) is found mostly in females. It is associated with a higher rate of suicidal thoughts than in those persons suffering other forms of mania. Dysphoric mania also does not respond well to treatment with LITHIUM but does seem to respond better to the ANTIPSYCHOTIC DRUG OLANZAPINE (Zyprexa). Persons with bipolar disorder who experience mixed states are much less stable between episodes and are more likely to be "rapid cyclers" (four or more episodes of mania or major depression in a 12-month period) or "continuous cyclers" (those for whom there is no clear break between episodes). Thus, the presence of multiple mixed episodes (dysphoric mania) is a feature of the most disabling and severe courses of bipolar disorder.

Marneros, A. "Origin and Development of Concepts of Bipolar Mixed States," *Journal of Affective Disorders* 67 (2001): 228–240.

Salvatore, P., et al. "Weygandt's *On the Mixed States of Manic-Depressive Insanity:* A Translation and Commentary on Its Significance in the Evolution of the Concept of Bipolar Disorder," *Harvard Review of Psychiatry* 10 (2002): 255–275.

Weygandt, W. *Uber die Mischzustande des manisch-depressive Irreseins.* Munich: Verlag von J. F. Lehmann, 1899.

M'Naughten Rules A legal interpretation named after Daniel M'Naughten (?–1865), the man whose celebrated trial legitimized the legal verdict "not guilty by reason of insanity," also referred to as the M'Naughten Rules. M'Naughten (also spelled McNaughton) was a British joiner who apparently led a solitary existence for most of his life. As an adult, he developed paranoid delusions that he had enemies who were trying to kill him. He also complained of violent headaches, which leaves open the possibility that he may have been suffering from one of the MEDICAL DISORDERS THAT MIMIC PSYCHOTIC DISORDERS. In any event, his paranoid delusions also began to take on a political nature. He became convinced that the members of the Tory party were the persecutors who were

out to get him, and to fight back he attempted to assassinate British prime minister Sir Robert Peel (1788–1850) but instead mistakenly shot Edward Drummond, the prime minister's secretary. In his subsequent trial in 1843 he was found not guilty by reason of insanity—a historic judicial decision that caused considerable public outrage. The House of Lords then required the judges in the M'Naughten trial to provide a written explanation of how they reached their controversial decision. Their criteria for judging a criminal not guilty by reason of insanity have been referred to as the M'Naughten Rules and have greatly influenced legislation in Great Britain and in the United States.

M'Naughten himself was involuntarily committed to the BETHLEM ROYAL HOSPITAL, where he was incarcerated for the remainder of his life. The attempted assassination of President Ronald Reagan in 1981 by John Hinckley Jr. caused a similar public outcry when he too was found not guilty by reason of insanity—based, in part, on the more than a century of legislation influenced by the M'Naughten Rules.

See also INSANITY DEFENSE.

Quen, J. M. "An Historical View of the M'Naughten Trial," *Bulletin of the History of Medicine* 42 (1968): 43–51.

West, D. J., and A. Walk, eds. *Daniel McNaughton: His Trial and the Aftermath.* Ashford, Kent: Headley Brothers for the British Journal of Psychiatry, 1977.

Moban See ANTIPSYCHOTIC DRUGS.

mode of inheritance In GENETICS STUDIES, the pattern of inheritance (e.g., dominant or recessive) of a particular ALLELE.

molecular biology Molecular biology is an interdisciplinary field of research that investigates the role of molecules in the form, function, and evolutionary descent of living things. The methods used are from organic chemistry, structural chemistry, and genetics. The term *molecular biology* was first used in 1938, but the field itself dates from about 1930. After the discovery of the structure of the DNA molecule in 1953 by Watson and Crick, molecular genetics became an important area of research.

Molecular biology has come to dominate research and treatment in psychiatry. Many psychiatrists openly admit they would like to see psychiatry disappear into molecular biology. In the last 30 years, many articles in the top psychiatric journals are about molecules rather than the mentally ill as individual persons. The rise in power of the pharmaceutical industry has fueled this revolution in the perspective of what constitutes a mentally ill person. New drugs are developed through basic molecular biological research. Molecular biology has strikingly redefined our culture's concept of what it means to be a human being, whether in health or illness.

molecular markers These are certain biochemical substances, identified by their molecules, that can be traced throughout a family to see if they are "markers" that are genetically transmitted along with the disease genes of a particular medical or mental disorder. If the disease and the marker are found to be inherited together in a family, it can be inferred that the disease gene lies very near (is linked to) the marker gene.

molindone See ANTIPSYCHOTIC DRUGS.

monasteries For many centuries in Europe, monasteries served as hospitals for the sick and the poor. Although the Roman Catholic church banned the practice of medicine by the clergy (particularly such treatments as BLEEDING) in the early 13th century, monks were still allowed to provide food and shelter to the needy. The mentally ill were among those cared for by the various religious institutions, and some of them later became asylums for the mentally ill (as was the case for the BETHLEM ROYAL HOSPITAL).

See also ALMSHOUSES; BASKET MEN.

monoamine oxidase (MAO) An enzyme that breaks down NEUROTRANSMITTERS such as norepinephrine and serotonin. The inhibition of this

enzyme in the functioning of the brain produces an antidepressant effect, and the MAO inhibitors were therefore the first drugs to be used in the treatment of depression.

monomania A term for a very popular psychiatric diagnosis in France in the 1830s and 1840s, monomania referred to a type of mental disorder in which a person would have fixed, and often grandiose, ideas that did not correspond to reality. Although the person maintained these delusions, no other sign of mental deterioration was present. Save for these pockets of delusions in their thought pattern, the persons affected were otherwise considered rational. After J. E. D. ESQUIROL introduced the term around 1810, "monomania" quickly caught on with intellectuals as a cultural metaphor for political, religious, and other social extremism. In his 1838 book, *Des Maladies Mentales,* Esquirol identified several subtypes of monomania, generally depending upon the content of the primary delusions, the cause of the disorder, or its behavioral consequences: for example, theomania (religious delusions), erotic monomania, or erotomania (erotic delusions), monomania resulting from drunkenness, incendiary monomania (pyromania) and homicidal monomania.

Although monomania was the most popular diagnosis given in French asylums in the 1830s and 1840s (rivaled only by the GENERAL PARALYSIS OF THE INSANE), the condition was criticized by many alienists for being too general and thus virtually disappeared by the end of the century. Perhaps the most specific modern equivalent to monomania is the delusional (paranoid) disorders listed in *DSM-IV,* particularly the "grandiose type." However, the category was so broad that it might have also included cases of what we may now term paranoid schizophrenia or bipolar disorder.

The best and only English-language history of this 19th-century psychotic disorder is the chapter entitled "Monomania" in a 1987 book by Jan Goldstein on the French psychiatric profession in the 19th century.

Goldstein, J. *Console and Classify: The French Psychiatric Profession in the Nineteenth Century.* Cambridge: Cambridge University Press, 1987.

monosymptomatic hypochondriacal psychosis A proposed psychotic disorder, especially in Europe, in which a person maintains a psychotic hypochondriacal delusional system that is distinct from the rest of the personality. The single delusion usually contains one of the three following themes: FORMICATION (a tactile hallucination in which the person feels that bugs are crawling under his or her skin); dysmorphophobia (the delusional belief that one is misshapen and unattractive); or the "olfactory reference syndrome" (the delusion that one emits a foul body odor).

Munro, A., and J. Chamara. "Monosymptomatic Hypochondriacal Psychosis: A Diagnostic Check List Based on 50 Cases of the Disorder," *Canadian Journal of Psychiatry* 27 (1982): 374–376.

monozygotic twins "Identical twins." Monozygotic twins share all of their genes in common, whereas "fraternal twins" share only half of their genetic heritage. Therefore, the CONCORDANCE RATE for genetically transmitted disorders is much higher in monozygotic twins than in fraternal, or dizygotic, twins.

The study of monozygotic and dizygotic twins has provided some of the strongest evidence of the significant role that genes play in the predisposition to developing schizophrenia. The median monozygotic (MZ) concordance rate for schizophrenia is 46 percent. This is three times the corresponding concordance rate for dizygotic (DZ) twins, which is 14 percent. Two conclusions can be drawn from this: (1) The MZ:DZ ratio of more than 3:1 strongly indicates that genes play a role in the development of schizophrenia, and (2) since the MZ concordance rate is significantly less than 100 percent, this means that schizophrenia is not caused 100 percent by genetic factors. Therefore, nongenetic factors of unknown origin also play a significant role in schizophrenia.

Prescott, C. A., and I. I. Gottesman. "Genetically Mediated Vulnerability to Schizophrenia," *Psychiatric Clinics of North America,* 16 (1993): 245–267.

mood This term refers to a pervasive and long-lasting emotion that seems to color a person's

perception of the world and of the self. The most commonly experienced moods are anxiety, elation (elevated mood), depression (dysphoric mood), anger (irritable mood), and euphoria (euphoric mood). In an expansive mood, a person may just blurt out whatever emotions he or she may be feeling at the time, and this often includes grandiose overevaluations of self-importance. When a person is not experiencing an elevated or a depressed mood, the term for this is euthymic mood, that is, mood in the "normal" range of experience.

mood disorders An umbrella term introduced in *DSM-III-R* in 1987 to apply to the group of disorders previously termed the AFFECTIVE DISORDERS. These include the BIPOLAR DISORDERS (cyclothymia, and the three types of bipolar disorders: mixed, manic, and depressed) and the depressive disorders (formerly called unipolar depression). The mood disorders have been found to have seasonal patterns in which the mood disorder returns during a particular 60-day period every year.

Moon, influence of on madness Since classical times it was thought that the Moon caused madness or made it worse, and the idea of "lunacy" in the ancient sense of the word did not really die out until the 1800s. Although many of the 18th-century authors of the earliest psychiatric texts (such as John HASLAM) expressed their skepticism of this theory of the cause of mental illness, American physician Benjamin RUSH did not dismiss it outright. Instead, he concocted a pseudoscientific theory that mental illness gives some people a "sixth sense" that renders them more sensitive to moonlight and to the changes in the temperature and density of the air when the moon was full. In his 1812 book on the diseases of the mind, Rush writes:

> The moon, when full, increases the rarity of the air and the quantity of light, each of which I believe acts upon sick people in various diseases, and, among others, in madness … The inference from these facts is, that the cases are few in which mad people feel the influence of the moon, and that when they do, it is derived chiefly from an increase of its light … It is possible, further, that in the few cases in which the light of the moon, or the rarity of the air, is felt by deranged persons in a hospital, that their noise, by keeping a number of patients in neighboring cells awake, and in a state of inquietude from the want of sleep, may have contributed to establish that general belief in the influence of the moon upon madness, which has so long obtained among physicians.

Oliver, J. F. "Moonlight and Nervous Disorders: A Historical Study," *American Journal of Psychiatry* 99 (1943): 579–584.

Rush, B. *Medical Inquiries and Observations upon the Diseases of the Mind.* Philadelphia: Kimber & Richardson, 1812.

moral insanity A term introduced in English by psychiatrist and anthropologist James Cowles Prichard in 1835 to refer to a type of mental illness in which a person would exhibit severe disturbances in emotions or engage in highly pathological or self-destructive behaviors but would not have any intellectual impairment (i.e., no FORMAL THOUGHT DISORDER). Thus, a person had the ability to reason yet would engage in irrational behaviors. Unlike another popular diagnosis in Europe at that time, MONOMANIA, there were no delusions in a particular subject area or any hallucinations relating to those specific delusions.

In his book *A Treatise on Insanity and Other Disorders Affecting the Mind,* Prichard defines "moral insanity" in the following way:

> . . . a morbid perversion of the natural feelings, affections, inclinations, temper, habits, moral dispositions, and natural impulses, without any remarkable disorder or defect of the intellect or knowing and reasoning faculties, and particularly without any insane illusion or hallucination . . . The individual is found to be incapable, not of talking or reasoning upon any subject proposed to him, for this he will often do with great shrewdness and volubility, but of conducting himself with decency and propriety in the business of life.

Although Prichard based his idea of a moral insanity on many similar ideas proposed perhaps

as early as the 17th century, his concept that there was no intellectual impairment came under attack by other medical authorities. However, by 1850 the debate had shifted from the intellectual versus emotional issue to the irrational behavior of such persons, specifically on how "moral insanity" was related to immoral and criminal actions. Thus, by the 20th century, the original meaning of Prichard's "moral insanity" as essentially a synonym for an "emotional illness" was eliminated from the psychiatric vocabulary and was reduced to our modern notions of sociopathic personalities, psychopathic personalities, and, as they are now called, antisocial personalities—that is, persons who repeatedly engage in acts destructive to themselves or others (e.g., criminal activities) without any realization of the consequences of their actions or any seeming ability to feel empathy for those persons who become the "victims" of their antisocial behaviors.

The term *moral insanity* was first used in German (*moralische Insanie*) in 1819 by J. C. A. Grohmann (1769–1847) to describe a particular symptom.

Carlson, E. T., and N. Dain. "The Meaning of Moral Insanity," *Bulletin of the History of Medicine,* 1962, pp. 130–140.

Prichard, J. C. *A Treatise on Insanity and Other Disorders Affecting the Mind.* London: Sherwood, Gilbert & Piper, 1835.

moral treatment The treatment of mental illness through means other than physical ones (e.g., bleeding, bathing and purging). Perhaps the best modern translation of the meaning of "moral treatment" is a broad interpretation of our word *psychotherapy* but also may refer to modern ideas of MILIEU THERAPY. *Traitement moral* is the name for the revolutionary philosophy for the treatment of the mentally ill proposed by the great French reformer and physician Philippe PINEL in his 1801 book, *Traite médicophilosophique sur l'aliénation mentale, ou la manie* (English translation of 1806 entitled *A Treatise on Insanity*).

Moral treatment, as prescribed by Pinel, did not solely mean an ethical approach to treating the mentally ill, nor did it mean a method of treatment that instructed patients in ethics. Since the early 1800s the French word *moral* had several meanings, especially referring to that which was psychological in nature and not physical. Thus, Pinel could talk of the "passions" (emotions) as a "moral cause" of mental illness.

In his book, Pinel advocates an understanding of the character of the patient and his or her humane treatment. Coercion and mechanical restraints were to be banned except in extreme circumstances. Pinel also thought that by improving the physical environment of asylums that patients would improve, and so he advocated the supervised daily cleaning of the patients' cells. Certain physical activities were recommended as beneficial to patients, such as exercise, work, experiencing beautiful scenery and listening to soft, melodious music. Although these ideas seem quaint and rather obvious today, in Pinel's time the mentally ill were thought to have brain lesions that rendered them to a bestial level, and were therefore incurable. Hence, treatment to improve or rehabilitate the mentally ill in any permanent sense was not considered a rational idea.

Thus, the trend toward "moral medicine," as it was sometimes called, began with Pinel and finally culminated in a general interest throughout Europe in rehabilitating treatments about the year 1820. The NONRESTRAINT MOVEMENT that began in the 1830s in England was directly inspired by Pinel in France (and at about the same time by Chiarugi in Italy and Tuke in England). Our continuing efforts today to improve the daily life of the mentally ill person and to discover new methods of treatment and rehabilitation are a continuation of the *traitement moral* of Pinel.

Bockoven, J. S. *Moral Treatment in American Psychiatry.* New York: Springer, 1963.

Carlson, E. T., and N. Dain. "The Psychotherapy That Was Moral Treatment," *American Journal of Psychiatry* 117 (1960): 519–524.

Riese, W. "An Outline of a History of Ideas in Psychotherapy," *Bulletin of the History of Medicine* 25 (1951): 442–456.

morbid jealousy See OTHELLO SYNDROME.

Moreau de Tours, Jacques-Joseph (1804–1884) A French alienist who was part of the "Esquirol Cir-

cle." He wrote his 1830 doctoral thesis on MONOMANIA under the supervision of J. E. D. ESQUIROL. He is best remembered for his self-experimentation with hashish and cannabis to produce ALTERED STATES OF CONSCIOUSNESS that helped him gain insight into mental illness. In his 1845 book on these experiments, he introduced the concept of DISSOCIATION for the first time. Moreau de Tours is considered the first medical researcher to use drugs to produce an "artificial psychosis," although reports of the creation of an "artificial insanity" through the use of chemical substances date from at least the experiments of the Paracelsian iatrochemist Jan Baptista van Helmont (1577–1644).

See also PSYCHOTOMIMETIC.

Moreau de Tours, J.-J. *Du hachisch et de l'aliénation mentale: Etudes psychologiques.* Paris: Fortin, Masson, & Cie, 1845.

Morel, Bénédict-Augustin (1809–1873) AFrench psychiatrist who worked under Jules FALRET at the SALPÊTRIÈRE hospital in Paris. He wrote several important psychiatric texts during his career, but he is best remembered for his 1857 theory that many mental diseases were the result of physical, intellectual, and moral (emotional) DEGENERATION. Morel coined the term *démence précoce* in 1852 to refer to rapid degeneration, and this concept was later borrowed by Emil KRAEPELIN when describing DEMENTIA PRAECOX in 1896.

Morel, B. A. *Etudes cliniques: Traité théorique et pratique des maladies mentales.* Nancy: Grimblot: Paris: J.-B. Baillière, 1852.

mortality in schizophrenia Since the first mortality studies of people with schizophrenia were published in 1934, it has been known that schizophrenia is a life-shortening disease. In fact, in a major review of the mortality research on schizophrenia that was published in 1989, researcher Peter Allebeck of Huddinge, Sweden, concludes that the overall death rate is about twice that of the general population. In the studies of institutionalized schizophrenic patients prior to the invention of ANTIPSYCHOTIC DRUGS, tuberculosis was the major cause of death. However, starting in the 1950s, most patients were treated with antipsychotic medication and were returned to the community through DEINSTITUTIONALIZATION. As these patients are no longer monitored on a daily basis by medical staff, and often cast into the community with little or no social support, it is not surprising that suicide has become the leading cause of death for persons with schizophrenia. In fact, some estimates are so high that it is estimated that perhaps 10 percent to 13 percent of schizophrenics commit suicide. A second major cause of death is accidents. Young white schizophrenic men with high levels of premorbid functioning and high expectations are particularly at risk.

Other studies have been conducted to see if the high mortality rates in schizophrenics are due solely to suicides and accidental deaths. It has been found that the death rate due to "natural" cardiovascular disorders is also higher in schizophrenics than in the general population. Other studies have shown that institutionalized psychiatric patients (regardless of diagnosis) have a higher mortality as a whole than the general population.

Currently it is estimated that persons with schizophrenia live, on average, 10 to 15 years less than persons in the general population.

Allebeck, P. "Schizophrenia: A Life-Shortening Disease," *Schizophrenia Bulletin* 15 (1989): 81–89.

Caldwell, C. B., and I. I. Gottesman. "Schizophrenics Kill Themselves Too: A Review of Risk Factors for Suicide." *Schizophrenia Bulletin* 4 (1990): 571–589.

Malzberg, B. *Mortality among Patients with Mental Disease.* New York: State Hospital Press, 1934.

mosaicism A term used in GENETICS STUDIES that refers to the condition of having a mixture of normal and abnormal chromosomes. A person who has mosaicism has various amounts of normal cells and trisomies (cells with three chromosomes), resulting in varying degrees of illness.

motion pictures, depictions of psychosis in Persons with psychotic disorders have been portrayed

in Greek classical tragedy, Elizabethan and Jacobean plays, stage melodramas, and Gothic novels of the 18th and 19th centuries and 20th-century feature films. Perhaps the first extensive portrayal of the interior world of psychosis in motion pictures is the famous German expressionist film of 1919 *The Cabinet of Dr. Caligari.* In the surprise ending to this dreamlike film the audience learns that the entire story was merely the delusion of an institutionalized psychotic patient.

In a book on the portrayal of insanity in the feature film, authors Michael Fleming and Roger Manvell identify several major "themes of madness" that have often reflected prevailing societal attitudes toward mental illness and the psychiatric profession. These are

(1) the family and madness (*A Woman under the Influence,* 1974)
(2) institutionalization of the mad (*The Snake Pit,* 1948; *One Flew over the Cuckoo's Nest,* 1975)
(3) possession as madness (*The Exorcist,* 1973; *Three Faces of Eve,* 1957)
(4) the struggle between love and aggression (*Bad Timing: A Sensual Obsession,* 1980)
(5) the love of aggression (*M,* 1931; *Straw Dogs,* 1971)
(6) violence against women (*Psycho,* 1960)
(7) murder and madness (*White Heat,* 1949; *Badlands,* 1974)
(8) war and madness (*The Deer Hunter,* 1978)
(9) drugs and madness (*The Lost Weekend,* 1945)
(10) paranoia and madness (*The Caine Mutiny,* 1954; *Repulsion,* 1965)
(11) sanity as madness, madness as sanity (*Harvey,* 1950; *The King of Hearts,* 1966)
(12) madness and the psychiatrist (*Dressed to Kill,* 1980)

Fleming and Manvell's book also provides a synopsis of 150 films dealing in one way or another with the problems of mental illness.

Prior to *The Cabinet of Dr. Caligari,* many shorter films appeared that depicted psychiatric patients, asylums, and psychiatrists. Perhaps the earliest American film to depict a psychotic individual is the 1904 one-reeler *The Escaped Lunatic.* The Biograph publicity bulletin for this film reveals that it is about the escapades of an insane man who imagines himself to be Napoleon I. He escapes from the asylum by a miraculous jump from a third story window, and is pursued across the country by the keepers through a series of ludicrous adventures, until finally disgusted at the chase, he jumps back into the window of the asylum, and is very comfortably reading a newspaper when the tired and mud-spattered keepers enter.

A subsequent one-reel film made in 1906, *Dr. Dippy's Sanitarium,* is the first American film to depict a mental health professional other than an attendant (a "keeper"). The first motion picture image of a psychiatrist is the one we still often see depicted in comedies and cartoons today: bearded (often with a goatee), wearing pince-nez glasses, and somewhat portly with a distinctive formal continental European bearing. As in *The Escaped Lunatic,* there is a psychotic individual who grandiosely believes he is Napoleon, but there is also a depiction of a woman with HYSTERIA who resembles a somnambulist, gliding about in a flowing white gown with her extended arm holding a candle in its holder. Whereas *Dr. Dippy's Sanitarium* appears to be the first film portrayal of a psychiatrist, the first literary appearances of the figure of the alienist can be found at least as early as 1861 in the novels of Oliver Wendell Holmes.

As with the mentally ill, psychiatrists have been depicted in films in a number of different ways. In their book *Psychiatry and the Cinema,* Krin Gabbard and Glen O. Gabbard propose that psychiatrists have been portrayed in three primary ways: as the "alienist," the "quack," or the "oracle."

Recent trends in motion pictures and television have unjustly overemphasized the "homicidal maniac" stereotype of people suffering from psychotic disorders—particularly in films in the horror genre. Many advocacy groups for the mentally ill have formally objected to these unrealistic portrayals and have attempted to counter these negative stereotypes with factual information about mental illness for the general public.

Fleming, M., and R. Manvell. *Images of Madness: The Portrayal of Insanity in the Feature Film.* Cranbury, N.J.: Associated University Presses, 1985.

Gabbard, K., and G. O. Gabbard. *Psychiatry and the Cinema.* Chicago: University of Chicago Press, 1987.

moxa See CAUTERY TREATMENT.

MRI See MAGNETIC RESONANCE IMAGING.

muffs A form of MECHANICAL RESTRAINT in which a patient's hands were bound together at the wrists in a thick, tubular canvas casing. In his autobiography, Clifford BEERS describes his experience of being forced to wear muffs every night during his first few weeks in a "sanitarium" while the attendant who watched over him slept:

> . . . I was subjected to a detestable form of restraint that amounted to torture. To guard me at night while the remaining attendant slept, my hands were imprisoned in what is known as a "muff." A muff, innocent enough to the eyes of those who have never worn one, is in reality a relic of the Inquisition. It is an instrument of restraint which has been in use for centuries and even in many of our public and private institutions is still in use. The muff I wore was made of canvas, and differed in construction from a muff designed for the hands of fashion only in the inner partition, also of canvas, which separated my hands, but allowed them to overlap. At either end was a strap which buckled tightly around the wrist and was locked.

Beers, C. *A Mind That Found Itself: An Autobiography.* New York: Longman, Greens, 1908.

multifactorial threshold model of genetic transmission This is the hypothetical model of the genetic transmission of schizophrenia first proposed in detail by I. I. Gottesman and J. Shields in 1967. Essentially, the multifactorial threshold model suggests that schizophrenia is caused primarily by the additive effect of a large numberof genes of small effect, in addition to certain environmental (but somewhat less powerful) influences. This is a type of polygenetic model of transmission and is sometimes called complex development (as opposed to another type of polygenetic model, GENETIC HETEROGENEITY). Genetic influences are assumed to account for 80 percent of the development of schizophrenia, and environmental factors 20 percent. This is a more complex revision of older DIATHESIS-STRESS THEORIES of the cause (etiology) of schizophrenia. In the multifactorial model, it is assumed that schizophrenia only becomes fully developed in those persons in whom a critical threshold of liability is exceeded (i.e., in those persons in whom enough of the disease-causing genes have added together, plus enough of the right environmental causes have been introduced—thus pushing the person's nervous system "over the edge," as it were, to provoke the onset of the illness).

In this model, the chance of developing this disorder is normally distributed throughout the population. On the average, relatives of schizophrenics are at greater risk than the general population, and therefore a greater proportion of these people have a liability that exceeds the threshold. This model predicts that those schizophrenic persons who have the most severe manifestations of the disorder (i.e., those with the highest liability) will have the greatest proportions of relatives who will be affected. This is a feature of the model that corresponds to the findings of twin studies and consanguinity studies of schizophrenia. This model also makes the prediction that a person is at greater risk for developing schizophrenia if two or more persons in the family are affected.

There have been several criticisms of this model. One is that the specific environmental causes of schizophrenia are hard to pin down. Second, all of the genes that combine their effects may not be of equal importance, for there may be a single major gene that has a far greater effect upon the risk for schizophrenia than the other "polygenes." This second idea is the basis for a "mixed model" of genetic transmission, first proposed as a possible mode of GENETIC TRANSMISSION for schizophrenia by Paul Meehl in 1972.

Gottesman, I. I., and J. A. Shields. "A Polygenic Theory of Schizophrenia," *Proceedings of the National Academy of Sciences of the United States of America* 58 (1967): 199–205.

McGue, M., et al. "The Transmission of Schizophrenia under a Multifactorial Threshold Model," *American Journal of Human Genetics* 35 (1983): 1,161–1,178.

Meehl, P. E. "A Critical Afterward." In I. I. Gottesman and J. A. Shields, *Schizophrenia and Genetics: A Twin Study Vantage Point.* New York: Academic Press, 1972.

multiple insanity See FOLIE À DEUX.

multiple personality and schizophrenia Many people often confuse schizophrenia with having "split personalities." Although schizophrenia literally means "split-mind," schizophrenia is a very distinct disorder from multiple personality disorder. An expanded definition of multiple personality disorder (MPD) made its first appearance in *DSM-III* in 1980 as one of the new category of mental disorders known as the DISSOCIATIVE DISORDERS. Prior to 1980, multiple personality was considered to be rare, with only about 200 cases reported in the psychiatric literature. However, since that time it is estimated that more than 6,000 cases have been diagnosed. In *DSM-IV* (1994) MPD was renamed "dissociative identity disorder."

Multiple personality was far more commonly recognized prior to 1910, and reports of this disorder virtually disappeared between 1910 and 1975. It has been suggested that this was due to the fact that most people with MPD were misdiagnosed with schizophrenia, the then-new diagnosis that Bleuler was popularizing at that time as a much more inclusive disorder than Emil Kraepelin's DEMENTIA PRAECOX. In 1988 a major study by Canadian psychiatrist Colin Ross found that in a sample of 236 persons diagnosed with MPD, almost 41 percent had once previously been diagnosed with schizophrenia. It was found that many FIRST-RANK SYMPTOMS that are thought to characterize schizophrenia also characterize MPD. People with multiple personality disorder experience delusions, experiences of being influenced, feeling that their thoughts were being broadcast from their heads, feeling that their thoughts were being withdrawn from their heads, and they also report auditory hallucinations (which are thought to be the "alternate personalities" talking to one another inside the person's body). All these are also commonly reported in schizophrenia.

Rosenbaum, M. "The Role of the Term Schizophrenia in the Decline of the Diagnosis of Multiple Personality," *Archives of General Psychiatry* 37 (1980): 1,383–1,385.

Ross, C., and G. R. Norton. "Multiple Personality Disorder Patients with a Prior Diagnosis of Schizophrenia," *Dissociation* 1 (1988): 39–42.

multiple sclerosis and schizophrenia Multiple sclerosis (MS) is a neurological disease primarily of body musculature and movement but with certain psychological effects as well. Although it is quite distinct from schizophrenia in its total picture, there are nonetheless many similarities between the two disorders that may point to a common type of cause for them. For example, the age of onset in both MS and schizophrenia is at its peak in the early to mid-20s, with a range between ages 15 and 45. The course of the two diseases is very similar, with periods in which the symptoms are very active (exacerbations) often interspersed, at least in the earlier stages, with partial or total disappearance of the symptoms for short periods (remissions). The highest pockets of the disease seem to be distributed in the Northern Hemisphere, particularly in Europe and North America. All these points of correspondence were discussed in a 1988 paper on this topic by psychiatrist J. R. Stevens that was published in *Schizophrenia Bulletin*. Her interpretation of the similarities between MS and schizophrenia is that they both may be neurological disorders that are caused by viruses.

See also VIRAL THEORIES OF SCHIZOPHRENIA.

Stevens, J. R. "Schizophrenia and Multiple Sclerosis," *Schizophrenia Bulletin* 14 (1988): 231–241.

Munchausen's syndrome This is a type of mental disorder in which the person fakes a serious physical illness, constructs an elaborate system of lies to account for it, and then must wander until finally a physician "catches on" to the pathological lying of the patient, who then repeatedly enacts the same scenario for other physicians. In *DSM-III-R*

(1987) this is known as a factitious ("not genuine") disorder with physical symptoms. Other proposed names for this syndrome have been hospital addicts and hospital hoboes. In 1951 R. Asher published the first description of this disorder and named it after an 18th-century German baron, Hieronymus Carl Friedrich von Münchausen (1720–97), who became famous for telling tall tales of exotic adventures to his friends. There have been cases on record of such persons even faking psychotic disorders such as schizophrenia just to be admitted to a psychiatric hospital. Although these persons are not found to be out of touch with reality, no one theory has been put forth that adequately explains their behavior.

Asher, R. "Munchausen's Syndrome," *Lancet* 1 (1951): 339.

museums, psychiatric In the United States there are several small museums that contain items relating to the treatment of institutionalized people with psychotic disorders. The better collections can be found in the Midwest. The museum at the Menninger Institute in Topeka, Kansas, maintains a collection of restraining devices, including straitjackets and photographs from old asylums from around the world. The Medical History Museum in Indianapolis, Indiana, is notable for the exquisite architectural detailing from psychiatric wards. The St. Joseph's State Hospital Museum in Kirksville, Missouri, has a collection of restraining devices and other items, which chronicle the history of psychiatric treatment from the 15th century to the present. This museum also contains a unique exhibit featuring 1,446 objects that were surgically removed from a psychiatric patient's gastrointestinal tract, including nuts, bolts, spoon handles, nails, stones, pins, pieces of glass, and a thimble.

Lipp, M. *Medical Landmarks USA*. New York: McGraw-Hill, 1990.

music therapy The act of listening to or playing music as a treatment for mental illness. In 1727 the first book devoted to music therapy appeared in print, *Medicina Musica* (the shortened title of the expanded 1729 edition), written by an English apothecary named Richard Browne. He recommended its use in calming "maniacal" patients. Philippe Pinel in France recommended it as a form of his MORAL TREATMENT of mental illness, and this suggestion was repeated by many other authors of psychiatric books. Music therapy remains a part of most psychiatric institutions today and helps to make them more humane places to live.

mustard pack A form of treatment developed in the late 1800s that involved adding "crude mustard" to wet sheets in which agitated patients were packed. It is said that the technique of packing agitated mentally ill people in wet sheets was invented in 1840 by a Silesian peasant named Priessnitz who gained a reputation for favorably treating disease by packing people in cold, wet sheets. It was apparently first used to treat mental illness in 1860 by an English physician, Lockhart Robinson, at the Sussex County Asylum in England.

In the traditional wet pack, a cold, wet sheet is wrapped around the naked body of a patient, who is then rolled up in two or three blankets. In the mustard pack (apparently first used on the mentally ill by another English physician, S. Newington), two handfuls of crude mustard are tied in a cloth, put in hot water and then squeezed, then wrapped around the abdomen or legs, with a blanket then wrapped around this. Because the mustard acted as an irritant to the skin, this was quite an unpleasant procedure to experience. Packing in wet sheets was a technique that continued to be used until well into the 20th century and probably did not disappear until the advent of ANTIPSYCHOTIC DRUGS in the 1950s.

Williams, D. "Baths." In *A Dictionary of Psychological Medicine,* edited by D. H. Tuke. London: J. & A. Churchill, 1892.

mystic paranoia See FOLIE À DEUX.

myth of mental illness In 1960 American psychiatrist Thomas Szaz published a paper in which

he argues that the concept of mental illness is, in reality, a myth. Szaz insists that the term is used to stigmatize anyone who deviates from certain psychological, ethical, or legal norms. "We call people physically ill when their body-functioning violates certain anatomical and physiological norms; similarly, we call people mentally ill when their personal conduct violates certain ethical, political and social norms." Furthermore, since (at that time) there was very little evidence for the physiological basis of the various mental disorders, they are not medical disorders that should be treated with medical procedures. Hence, there is no such thing in reality as a purely "mental illness."

Szaz gained notoriety for his notion of the "myth of mental illness," and his many publications that question the standard operating procedure of psychiatrists and the mental health system created much animosity toward him. Nonetheless, the value in his writing is that he dared to "question authority," and his works stimulated a good deal of discussion about psychiatric procedures, patients' right to refuse treatment, and other significant issues with medical and legal implications.

Szaz, T. "The Myth of Mental Illness," *American Psychologist* 15 (1960): 113–118.

N

National Institute of Mental Health The primary research and information organization in the United States devoted to the study of mental disorders. It was established by the National Mental Health Act passed by the U.S. Congress in 1946 but did not formally begin operation until 1949. NIMH distributes federally mandated grant money to states and institutions for research on mental disorders. Since 1954, NIMH has devoted a major effort to schizophrenia research with the establishment of the NIMH Laboratory of Psychology and Psychopathology at the NIMH campus in Bethesda, Maryland. From 1955 to 1966 the laboratory carried out a program of research on the nature of the behavioral deficits in schizophrenia, initiated by David Shakow, who was then Chief of the Laboratory. David Rosenthal (who succeeded Shakow as chief in 1977) and Seymour Kety conducted other studies on the genetics of schizophrenia, the most famous of which is the case of the GENAIN QUADRUPLETS. Rosenthal's work on the genetic factors in the development of schizophrenia helped to define the nature of the transmission of schizophrenia. In 1989, NIMH launched a program to find the genes involved in schizophrenia, bipolar disorder, and Alzheimer's disease. Interestingly, all three of these disorders were first described by Emil KRAEPELIN and his research group in Heidelberg, Germany, in the late 1890s, but their search for the patterns of hereditary transmission was unsuccessful. The NIMH Genetics Initiative has taken up Kraepelin's unfinished task. The goal is to create a national resource of demographic, clinical, and diagnostic data that would be available to the world scientific community. DNA extracted from immortalized cell lines is also available to researchers for genetics work.

Mirsky, A. F. "Research on Schizophrenia in the NIMH Laboratory of Psychology and Psychopathology, 1954–1987," *Schizophrenia Bulletin* 14 (1988): 151–156.

Navane See ANTIPSYCHOTIC DRUGS.

negative symptoms The symptoms of schizophrenia that are best conceptualized as "defects"—that is, as something "taken away" from the personality of the afflicted person. The negative symptoms seem to most resemble those types of symptoms found in people with brain damage due to other causes, and as such, negative symptoms have been correlated to structural BRAIN ABNORMALITIES IN SCHIZOPHRENIA. Prominent negative symptoms are: (1) poverty of speech (alogia), (2) restricted affect and diminished emotional range, (3) diminished interest in the environment and a reduction in curiosity, (4) diminished sense of purpose, and (5) a diminished interest in social interaction with others. POSITIVE SYMPTOMS, on the other hand, are those symptoms that seem to be "added to" the personality, such as hallucinations and delusions.

The distinction between negative and positive symptoms has its origins in 19th-century neurology. Perhaps the first use of these terms was by the British neurologist J. R. Reynolds in 1858. They became popularized, although not in a sense directly appropriate to schizophrenia, by the famous British neurologist John Hughlins Jackson, who discussed them in 1894 as part of the FACTORS OF INSANITIES. The explicit application of these concepts to schizophrenia can be credited to a paper published in 1974 by J. S. Strauss, W. T. Carpenter, and J. J. Bartko.

Negative symptoms characterize the most chronic forms of schizophrenia, and their early signs indicate a poor prognosis. ANTIPSYCHOTIC DRUGS have a minimal effect in diminishing or reversing negative symptoms. At present, there is no fully effective treatment for these symptoms.

See also CROW'S HYPOTHESIS; DEFICIT SYMPTOMS/SYNDROME.

Berrios, G. E. "Positive and Negative Symptoms and Jackson: A Conceptual History," *Archives of General Psychiatry* 42 (1985): 95–97.

Reynolds, J. R. "On the Pathology of Convulsions, with Special Reference to Those of Children," *Liverpool Medico-Chirurgical Journal* 2 (1858): 1–14.

Strauss, J. S., W. T. Carpenter, and J. J. Bartko. "The Diagnosis and Understanding of Schizophrenia: III. Speculations on the Processes That Underlie Schizophrenic Symptoms and Signs," *Schizophrenia Bulletin* 1, Experimental Issue 11 (1974): 61–69.

negativism, schizophrenic A concept put forth in 1910 by Eugen BLEULER to account for the baffling and often frustrating "contrary" or "oppositional" behavior of people with schizophrenia. Such reactions often infuriate those responsible for the care of people with schizophrenia, who may frequently forget that such actions are expressions of the disease itself. The best example of this is the primary schizophrenic symptom of AMBIVALENCE, in which an impulse is balanced by contrary ones, thus paralyzing the willful activity of the schizophrenic. In his 1911 book, Bleuler notes that in "negativism," "the patients cannot or will not do what is expected of them (passive negativism); or they do just the very opposite or, at least, something else than what is expected (active or contrary negativism)." Bleuler largely attributed this negativism to the nature of the disease rather than to the intentions of the patient. Bleuler's concept of negativism was criticized in 1911 by his former assistant, C. G. JUNG, who was then a disciple of Sigmund FREUD's and who thus interpreted such "negativism" according to the psychoanalytic concept of an unconscious (but meaningful) resistance. Negativism is no longer discussed in the modern literature of schizophrenia.

Bleuler, E. *Dementia Praecox, Or the Group of Schizophrenias,* tr. J. Zinkin. 1911. Reprint, New York: International Universities Press, 1950.

———. "Zur Theorie des schizophrenen Negativismus," *Psychiatrisch-neurologische Wochenschrift* (Halle) 12 (1910–11): 171–195.

Jung, C. G. "A Criticism of Bleuler's Theory of Schizophrenic Negativism." In *The Collected Works of C. G. Jung.* Vol. 3. Princeton, N.J.: Princeton, University Press, 1960.

negligent release In the United States, there have been many legal suits brought against institutions and responsible psychiatrists for releasing patients who then go on to do harm to themselves or others. In such "negligent release" suits, the charge is that psychiatric authorities released individuals to the community who were still dangerous and in need of commitment.

neologisms The expression of neologisms (literally meaning "new words") by people with psychotic disorders (particularly schizophrenia) is a clear sign of FORMAL THOUGHT DISORDER. A person may create entirely new words, distort actual words, or give new and unusual meanings to words that already have an accepted meaning.

neural circuits in schizophrenia Neural circuits are the information superhighways of the brain. It has long been known that information is processed by the human brain in "cell assemblies" or "neural networks" that cut across the lobes of the cortex, as well as involved subcortical structures of the brain (such as the thalamus, a major relay center, and the hippocampus, a major center for turning short-term memories into long-term memories). These pathways of nervous tissue use electrical impulses and chemicals (NEUROTRANSMITTERS) to excite or inhibit neighboring clusters of neurons as messages are sent and received. Information from the external senses (sight, hearing, touch, taste, scent) and from internal sources (the autonomic nervous system, for example) is processed along certain discrete pathways or neural networks that crisscross several major "functional centers" of the brain.

For years there have been computer models of neural networks in cognitive neuroscience research that have been used to understand the functioning of the normal human brain. With advances in computing power and software innovations, the trend in the schizophrenia research of the 1990s was to develop complex, interactive models of the neural circuits that seem to dysfunction in the brains of people who suffer from schizophrenia (and those of close biological relatives, who often have some of the same dysfunctions).

In recent years, inferences about the location and function of such neural circuits in schizophrenia have come from (1) postmortem neuropathological studies, (2) neuropsychological test data, (3) structural neuroimaging studies, particularly those employing positron magnetic resonance spectroscopy, and (4) functional neuroimaging studies (rCBF, PET, fMRI), which actually allow us to see the pathways in the brain "light up" as the brain of a person with schizophrenia performs a particular task.

There is much that still needs to be resolved in the definition of the neural circuits involved in schizophrenia, but some of the most promising neural circuits are (1) the temporolimbic cortex, (2) the prefrontal cortex, and (3) the thalamus. Imbalances in the functioning between these regions or neural circuits is the basis of DISCONNECTION THEORIES OF SCHIZOPHRENIA.

Bogerts, B. "The Temporolimbic System Theory of Positive Schizophrenic Symptoms," *Schizophrenia Bulletin* 23 (1997): 423–435.

Jones, E. G. "Cortical Development and Thalamic Pathology in Schizophrenia," *Schizophrenia Bulletin* 23 (1997): 483–501.

McCarley, R. W., et al. "Neural Circuits in Schizophrenia," *Archives of General Psychiatry* 51 (1994): 515.

neurasthenia A word coined by New York neurologist George Miller Beard in 1869 for a type of "nervousness" disorder that could be treated by HYDROTHERAPY, weak electrical currents, and rest. It was considered a uniquely American neurotic disorder, for "nervous exhaustion" was brought about by the "wear and tear" on the nervous system induced by overwork. In the upper classes, MASTURBATION was also thought by Beard to be a significant cause of neurasthenia, although among members of the lower classes, as Beard points out in his 1884 book *Sexual Neurasthenia,* this was not the case because, for example, "Strong, phlegmatic Irish servant-girls may begin early the habit of abusing themselves and keep it up for years, but with little apparent harm." Whereas Beard thought many of the vague and mild symptoms were part of an actual nervous disease, many of his contemporaries rejected them as mild and easily reversible symptoms of tiredness or out-and-out signs of malingering and attention seeking. Special private sanitariums, retreats, spas, and hydropathic institutions were set up in the late 1800s to treat individuals, largely female and from the upper classes of society, who suffered from "nervousness" or neurasthenia.

Neurasthenia is still included as a diagnostic category in the World Health Organization's *ICD-10* (1992). It is defined as "a neurotic disorder characterized by fatigue, irritability, headaches, depression, insomnia, difficulty in concentration, and a lack of capacity for enjoyment (anhedonia). It may follow or accompany an infection or exhaustion, or arise from continued emotional stress."

Beard, G. M. *American Nervousness.* New York: Putnam's, 1881.

———. *Sexual Neurasthenia: Its Hygiene, Causes, Symptoms, and Treatment.* Edited by A. D. Rockwell. New York: Treat, 1884.

Drinka, G. F. *The Birth of Neurosis: Myth, Malady, and the Victorians.* New York: Simon & Schuster, 1984.

neurochemistry of schizophrenia See BIOCHEMICAL THEORIES OF SCHIZOPHRENIA.

neurodevelopmental model of schizophrenia At the beginning of the 21st century, this is the dominant explanatory paradigm in schizophrenia research. Rather than assuming that the causes of schizophrenia are to be found around the time the first symptoms usually appear in late adolescence or early adulthood, the neurodevelopmental model assumes that the underlying disease process

must begin during fetal development along with the development of the nervous system.

Proposals for a similar model of certain psychotic disorders had been made by Thomas Clouston in 1873 for a syndrome he called ADOLESCENT INSANITY, Emil KRAEPELIN in 1896 for DEMENTIA PRAECOX, and Eugen BLEULER in 1908 for SCHIZOPHRENIA. The neurodevelopmental model of schizophrenia was first articulated in its modern form in the work of R. M. Murray in 1985 and Daniel R. Weinberger in 1986. It became influential as a paradigm almost immediately. The neurodevelopmental model has proven to be a useful organizational concept for a wide range of studies in neuropathology, neuroimaging, genetics, neuropsychology, epidemiology, and developmental biology. One criticism of the neurodevelopmental model of schizophrenia is that it may concern only one subtype or syndrome of schizophrenia and may ignore others with a later onset.

The primary argument in favor of a neurodevelopmental model is the evidence that has accumulated that schizophrenia is probably not a neurodegenerative disease. Circumstantial evidence pointing to causes that happen during fetal neural development, during gestation, or around the time of birth all lend support to a neurodevelopmental model. However, strong evidence in favor of the neurodevelopmental model is lacking. Some aspects of the model as proposed by Daniel Weinberger of the National Institute of Mental Health in Bethesda, Maryland, are based on speculative models of the role of dopamine and on connections between the frontal lobe and subcortical structures. However, the neurodevelopmental model has directed basic research into new areas and will probably be a very difficult model to reject or falsify conclusively.

See also BRAIN ABNORMALITIES; CHILDHOOD-ONSET SCHIZOPHRENIA; FETAL NEURAL DEVELOPMENT.

Murray, R. M. "Neurodevelopmental Schizophrenia: The Rediscovery of Dementia Praecox," *British Journal of Psychiatry* 165 (1994): 6–12.

Weinberger, D. R. "The Pathogenesis of Schizophrenia: A Neurodevelopmental Theory." In *The Neurology of Schizophrenia,* edited by H. A. Nasrallah and D. R. Weinberger, 397–406. Amsterdam: Elsiever, 1986.

neurohistological studies of schizophrenia See BRAIN ABNORMALITIES IN SCHIZOPHRENIA.

neuroimaging studies of schizophrenia See BRAIN IMAGING STUDIES OF SCHIZOPHRENIA.

neuroleptic This is another word for any drug that changes the mental state of anyone who ingests it. It is often used synonymously with the term *psychotropic.* The term *neuroleptics* is sometimes used as an alternative name for ANTIPSYCHOTIC DRUGS as well, although technically it can refer to antianxiety or antidepressant drugs.

neuroleptic malignant syndrome This is a rare but serious disorder that may be a side effect from the use of ANTIPSYCHOTIC DRUGS. The symptoms of this disorder are fever, muscular rigidity, stupor, autonomic dysfunction (increased pulse, sweating, and respiration), and, occasionally, death. NLMS, as it is sometimes abbreviated, develops suddenly over a 24- to 72-hour period anywhere from hours to months after the initiation of therapy with antipsychotic drugs. At present, it is difficult to predict who will or will not develop NLMS, because a person who had previously undergone a period of treatment without developing the syndrome may suddenly develop it during other treatment periods. Neuroleptic malignant syndrome is often associated with the use of high-potency antipsychotic drugs. It is more common in young adult males with psychotic disorders and in persons with organic mental disorders. The use of antipsychotic drugs must be discontinued immediately if NLMS occurs, for about 15 percent to 20 percent of the patients who develop this disorder die. The exact cause of the disorder is unknown.

Caroff, S. N. "The Neuroleptic Malignant Syndrome," *Journal of Clinical Psychiatry* 41 (1980): 79–83.

Levinson, J. L. "Neuroleptic Malignant Syndrome," *American Journal of Psychiatry* 142 (1985): 1,137–1,145.

neuropathology of schizophrenia See BRAIN ABNORMALITIES IN SCHIZOPHRENIA.

neuropsychological studies of schizophrenia In the 1970s, special batteries of psychological tests were devised to assess brain functioning in persons suspected of having an organic brain dysfunction. These "neuropsychological tests" targeted such processes as memory, perception, concept formation, visual-spatial ability, attention span and intelligence to see if they were disrupted in ways that were characteristic of brain-damaged individuals who took such tests. Perhaps the two most famous of these batteries are the Halstead-Reitan battery and the Luria-Nebraska battery. Major reviews of the more than 100 studies of the performance of persons with schizophrenia on neuropsychological tests have confirmed that "chronic" and "nonparanoid" schizophrenics are indistinguishable from persons who have known brain damage that is diffuse rather than focal (i.e., spread throughout the brain rather than localized damage in one place).

In the 1980s and 1990s, neurological studies of schizophrenia were often correlated with neuropathological findings and with neuroimaging findings to develop new models of how the schizophrenia disease process works in the brain. The studies of C. D. Frith of the cognitive neuropsychology of schizophrenia have been highly influential.

In schizophrenia the following cognitive functions have been consistently found to be impaired: attention, working memory (a form of short-term memory associated with the functioning of the frontal lobe of the brain), episodic or autobiographical memory, and executive functioning (the overall organization of various goal-oriented cognitive functions). Additionally, as we now know from long-term follow-up studies of children of schizophrenic parents who later went on to develop schizophrenia, all these cognitive deficits have been found to be present in the prodromal phase of schizophrenia, years before the first psychotic episode. Furthermore, most of the cognitive impairment in schizophrenia happens early in the disease process. Very little decline in cognitive functioning is found after the first episode of psychosis. This contradicts the view of schizophrenia as a progressive neurodegenerative disease. Antipsychotic drugs do not improve cognitive functioning in schizophrenia.

It has long been known that many of the problems people with schizophrenia face every day stem from these severe problems in cognition. To address the treatment implications of this issue, including the development of new drugs that may enhance cognitive performance in schizophrenia, the NATIONAL INSTITUTE OF MENTAL HEALTH began a new research initiative in April 2003, the NIMH-Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS). There are two goals: one, to develop a standard "consensus battery" of neuropsychological tests that can measure cognition in schizophrenia in a valid and reliable way; and two, to develop a consensus among experts in the field as to which molecules should be targeted for the development of new drugs that can improve the cognitive performance of people with schizophrenia as measured in drug trials by this new test battery. Seven cognitive deficits in schizophrenia are being targeted:

(1) speed of information processing
(2) attention or vigilance
(3) working memory
(4) verbal learning and memory
(5) reasoning and problem solving
(6) verbal comprehension
(7) social cognition

David, A. S., and J. C. Cutting. *The Neuropsychology of Schizophrenia.* East Sussex, England: Lawrence Erlbaum Associates, 1994.

Frith, C. D. *The Cognitive Neuropsychology of Schizophrenia.* Hove, England: Lawrence Erlbaum, 1992.

neurosis In contemporary usage, the term *neurosis* refers to a wide variety of mental disorders that do not involve a break with reality (as in PSYCHOSIS) and do not have an apparent organic basis. However, this term has changed its meaning over the past two centuries, and even now there is some controversy about the actual meaning of the word.

The word *neurosis* was first used by English physician William Cullen in 1776 in his book *Synopsis Nosologiae Methodical.* Following Cullen, throughout most of the 19th century neuroses referred

to a large class of diseases that included present-day neurotic and psychotic disorders, neurological disorders, and many other medical disorders. The defining characteristics of the neuroses were a disorder of the "general" functions of the central nervous system and the lack of fever in an individual. Thus, throughout the 19th century, a neurosis was a disease of the brain and nervous system, whereas a psychosis (particularly in Germany) originally referred to the psychological aspects of a mental state.

However, by the year 1900, the term *neurosis* began to take on more of the meaning of a "psychological disorder" without reference to its organic nature, and thus the types and number of neuroses were greatly reduced. *Psychosis* began to be used instead to refer to the growing number of mental disorders that were organic in nature (e.g., dementia praecox). At about this time Sigmund FREUD began to redefine the neuroses (which he also termed *psychoneuroses*) according to psychoanalytic theory—specifically, that the neuroses were mental disorders that were caused by an unconscious conflict. This latter meaning of neuroses became the standard during much of the 20th century, and the "neurotic disorders" were a common part of most diagnostic manuals. However, in 1980, the AMERICAN PSYCHIATRIC ASSOCIATION'S *DSM-III* eliminated the term *neurosis* because of its theoretical assumptions based on psychoanalysis and instead introduced a largely atheoretical and neutral descriptive terminology, using various classifications of "mental disorders" to account for the more traditional neuroses.

The WORLD HEALTH ORGANIZATION'S *ICD-9* (1978), however, used the category termed "neurotic disorders" and defined them in the following way:

> The distinction between neurosis and psychosis is difficult and remains subject to debate. However, it has been retained in view of its wide use.
>
> Neurotic disorders are mental disorders without any demonstrable organic basis in which the patient may have considerable insight and has unimpaired reality testing, in that he usually does not confuse his morbid subjective experiences and fantasies with external reality. Behavior may be greatly affected although usually remaining within socially acceptable limits, but personality is not disorganized. The principal manifestations include excessive anxiety, hysterical symptoms, phobias, obsessional and compulsive symptoms, and depression.

López Piñero, J. M. *Historical Origins of the Concept of Neuroses,* trans. G. Berrios. Cambridge: Cambridge University Press, 1983.

neurotransmitter Any specific chemical agent released by one brain cell or neuron (the pre-synaptic cell) when it is stimulated that crosses the gap between neurons (the synapse) to stimulate or inhibit a neighboring brain cell (the post-synaptic cell). More than 100 such neurotransmitters are currently known.

The rise of endocrinology as a new medical science in the early 20th century provided a direct and important analogical bridge that led to the discovery of neurotransmitters in the brain. Following the 1921 discovery by Otto Loewi (1873–1961) of a substance in the brain later identified as acetylcholine, neurotransmitters were referred to as neurohormones or neurohumors. Indeed, the term *neurotransmitter* did not come into use until the 1960s. It is important to remember that neurotransmitters have been conclusively demonstrated to be part of the pathophysiology of mental disorders and have been related to certain symptoms (such as dopamine for hallucinations and delusions in some persons with schizophrenia). Neurotransmitters have never been found to cause any mental disorder, whether it is schizophrenia or depression.

See also ANTIDEPRESSANT DRUGS; ANTIPSYCHOTIC DRUGS; DOPAMINE HYPOTHESIS .

neurotransmitter disorder as a cause of schizophrenia The first theory of the cause of schizophrenia that is based on the hypothesis of a neurotransmitter disorder was put forth by biochemists D. W. Wooley and E. Shaw in 1954. They proposed that a decrease in the (then) newly discovered transmitter serotonin (5HT) may be related to the development of schizophrenia. Part

of the reason for this was that LSD was thought to be a powerful serotonin agonist, and at that time the "psychedelic model" of psychosis was in vogue, which suggested that schizophrenic experience was related to the experiences of those who ingested hallucinogenic substances. This hypothesis was not seriously considered for very long and was largely replaced by the DOPAMINE HYPOTHESIS in 1976. Other neurotransmitters that have been implicated as possible causes of schizophrenia are norepinephrine, GABA, the endorphins, and glutamate.

Wooley, D. W., and E. Shaw. "A Biochemical and Pharmacological Suggestion about Certain Mental Disorders," *Proceedings of the National Academy of Sciences of the United States of America* 40 (1954): 228–231.

———. "A Biochemical and Pharmacological Suggestion about Certain Mental Disorders," *Science* 119 (1957): 587–588.

night attendant service Until 1829, it was customary for patients in almost all asylums throughout Europe and the United States to be locked in their cells or strapped or chained to their beds for the night without supervision. The death of such a restrained patient in that year at the Lincoln Asylum in England led to the eventual adoption of "night attendants" who would keep watch over such mechanically restrained patients. However, this policy was not adopted in every British asylum nor throughout Europe on a large scale for many years. Even in the 20th century, reports of unsupervised patients in restraints continue to surface from time to time. However, the general policy in psychiatric institutions today is that physically restrained patients must be continually supervised by at least one staff member.

NIMH See NATIONAL INSTITUTE OF MENTAL HEALTH.

nitrogen inhalation therapy This is one of the forms of COMA THERAPY that were developed in the 1930s as a type of treatment for schizophrenia. Introduced by Franz A. Alexander and colleagues in 1939, this form of treatment involved having schizophrenic patients breathe in pure nitrogen to reduce the amount of oxygen in the brain (cerebral hypoxia) in order to induce a comatose state. It never became popular, for ELECTROSHOCK THERAPY and INSULIN COMA (OR SHOCK) THERAPY, introduced just prior to the invention of nitrogen inhalation therapy, had already taken root and were considered much more successful in the treatment of schizophrenia.

Alexander, F. A. D., and H. E. Himwich. "Nitrogen Inhalation Therapy for Schizophrenia," *American Journal of Psychiatry* 94 (1939): 643–655.

nitrogen metabolism disorder hypothesis This is the hypothesis put forth by the Norwegian psychiatric researcher Rolf Gjessing (1889–1959) in 1938 that the catatonic subtype of schizophrenia is caused by a primary disturbance of nitrogen metabolism that causes a shift back and forth from positive to negative balances of nitrogen in the body of a catatonic. Gjessing discovered that by administering the drug thyroxin, these metabolic shifts could be prevented with therapeutic results. Unfortunately, the nitrogen metabolism disorder hypothesis as a cause of schizophrenia was found to apply only to the very small group of persons suffering from periodic catatonia, and thus Gjessing's findings were not generalizable to the other subtypes of schizophrenia.

Gjessing, R. "Disturbances of Somatic Functions in Catatonia with a Periodic Course and Their Compensation," *Journal of Mental Science* 84 (1938): 608–621.

nonallelic genetic heterogeneity Because many mental disorders—in particular, schizophrenia and bipolar disorder—seem to constitute a spectrum of disorders rather than a single disease entity, it has been thought that there are different genetic causes of these disorders that nevertheless manifest similar symptoms when they are evident in a person. This has been called ETIOLOGIC HETEROGENEITY. One reason for etiologic heterogeneity may be nonallelic genetic heterogeneity, which refers to

the fact that although two or more persons may manifest the same symptoms of a particular disease, and therefore may have the same diagnosis, nonetheless different genes may be affected in different individuals to cause the disorder. In other words, the differences are not caused by alternate forms of the same gene (alleles). Nonallelic genetic transmission has been hypothesized for the psychotic disorders.

noninjurious torture This is the self-explanatory term used by German physician Johann Christian Reil (1759–1813) to refer to his philosophy of the treatment of institutionalized patients with mental disorders. Although Reil was more of a philosopher than a clinician and had no extensive experience in treating the mentally ill, he nonetheless wrote a 500-page volume in 1803 outlining his suggestions for the psychological treatment of such patients. He advocated the use of fear and intimidation to shock patients back into rationality, as well as the BATH OF SURPRISE, sudden loud noises, FLOGGING with a whip, the use of the straitjacket, and a whole host of other "treatments."

Reil, J. C. *Rhapsodien über die Anwendung der psychischen Curmethode auf Geisteszerruttungen.* Leipzig: 1803.

non-Mendelian patterns of transmission This term is used as an umbrella for a wide variety of theories of genetic transmission that do not fit strict "single gene" patterns that are known to characterize classical MENDELIAN TRANSMISSION. The psychotic disorders follow non-Mendelian patterns of genetic transmission. All theories that resort to the hypothesis that more than one gene is implicated in the transmission and development of a particular disorder (i.e., polygenetic theories) can be referred to as non-Mendelian.

nonparanoid schizophrenia In 1911 schizophrenia was divided into a paranoid subtype and three nonparanoid subtypes, which are currently known as the disorganized type, the catatonic type and simple schizophrenia. It has long been observed that those schizophrenics with nonparanoid diagnoses tended to be more disorganized and have more FORMAL THOUGHT DISORDER than the paranoid subtype; they were believed to have an earlier onset and a poorer prognosis than the paranoid subtype; and they tended to exhibit a more diffuse set of symptoms than the paranoid subtype. Starting in the 1970s and 1980s, research psychologists conducted numerous studies that found significant differences between paranoid and nonparanoid schizophrenics in many areas. On cognitive, perceptual, and problem-solving tests, paranoids and nonparanoids have shown consistent differences. Nonparanoids tend to exhibit a more conservative response style than paranoids, who often "jump to conclusions" without having enough of the relevant information to make a logical decision on tasks presented on various tests.

Many of these differences between nonparanoid and paranoid schizophrenics that have been found in COGNITIVE STUDIES OF SCHIZOPHRENIA support the notion that schizophrenia is not a unitary disorder but may instead be several different disorders.

A major issue of *Schizophrenia Bulletin* devoted to reviewing the research on the differences between nonparanoid and paranoid cognition was published in 1981 (vol. 7, no. 4).

Kendler, K. S., and K. L. Davis. "The Genetics and Biochemistry of Paranoid Schizophrenia and Other Paranoid Psychoses," *Schizophrenia Bulletin* 7 (1981): 698–709.

Magaro, P. A. "The Paranoid and the Schizophrenic: The Case for Distinct Cognitive Style," *Schizophrenia Bulletin* 7 (1981): 632–661.

nonrestraint movement This term was used by English physician John CONOLLY to describe the great shift in the philosophy and treatment of the institutionalized mentally ill in the 19th century that advocated the absolute minimum use of MECHANICAL RESTRAINTS. Although the philosophy of MORAL TREATMENT and moral medicine had been given lip service since the time of Philippe PINEL around 1801, a truly humane approach to

the institutionalized mentally ill was not adopted by the vast majority of European asylums that still restrained most patients whether they were violent or not. First-person descriptions of conditions in asylums in the early 1800s attest to these terrible abuses. Considered incurable by most, and no better than animals, the mentally ill were feared by many. Although some institutions began experimenting with nonrestraint policies, it was not until John Conolly successfully adopted such policies at the Hanwell Asylum in England between 1839 and 1843 that the issue was discussed in earnest around the world. His ideas caught the imagination of the public, due largely to strong support from publications such as the *Lancet* and the *Times* of London.

When Conolly first arrived at the Hanwell Asylum, he found the following items and immediately abolished them: 51 leather straps, 10 leather muffs, two screw-gags, two extra-strong chain leg-locks, 353 handcuffs and leg-locks, 49 restraint-chairs (similar to the American physician Benjamin RUSH'S TRANQUILLIZER), and 78 leather-and-ticking restraint-sleeves. Despite loud cries of criticism, Conolly implemented his experimental program with great success. His methods were copied by most English asylums and then by European and American institutions in the years that followed. Our modern policies of nonrestraint except in the most extreme circumstances is directly due to the influence of John Conolly and his nonrestraint movement.

Marx, O. M. "Descriptions of Psychiatric Care in Some Hospitals during the First Half of the 19th Century," *Bulletin of the History of Medicine,* 1967, pp. 208–214.

Zilboorg, G. *A History of Medical Psychology.* New York: W. W. Norton, 1941.

nonsense syndrome See GANSER'S SYNDROME.

norepinephrine and schizophrenia The neurotransmitter norepinephrine (or "noradrenaline"), a CATECHOLAMINE (like DOPAMINE), has been studied for a possible link to schizophrenia. Some studies have found increased levels of norepinephrine (NE) in the brain, blood and cerebro-spinal fluid of schizophrenics. Some studies have even connected these increased blood plasma levels of NE with POSITIVE SYMPTOMS and the paranoid subtype of schizophrenia. However, further studies that replicate these findings need to be done before any firm conclusions can be reached.

Hornykiewicz, O. "Brain Catecholamines in Schizophrenia—A Good Case for Noradrenaline," *Nature* 299 (1982): 484–486.

Norway See SCANDINAVIA.

nosology The science of the classification of diseases. Nosology involves, more specifically, the underlying theory behind the grouping of diseases. In psychiatry there are no "diseases" in the sense that they can be found in the rest of the medical sciences, because no distinctive cellular pathology (disease at the level of cells), nor distinct biological etiologies (causes), nor, therefore, any objective diagnostic tests (such as a blood test) exist that enable us to identify any mental disorder as a disease. Instead, mental disorders are syndromes (distinctive clusters of symptoms and signs linked to particular courses and outcomes). The nosological approach in psychiatry starts with the premise of an underlying disease process (e.g., in the brain) that exists before the production of symptoms. The disease determines the symptoms.

A contrasting approach, also influential in psychiatry, is that of psychopathology. The assumption since at least Karl Ludwig Kahlbaum's 1874 book on catatonia is that the objective identification and classification of symptoms of mental illness led to their grouping into syndromes. Concepts of disease were constructed from symptoms identified in this way. The symptoms determine the disease.

Classification systems reflect the cognitive categories of the cultural and scientific beliefs of their historical eras. As a result, in psychiatry there are fundamental differences in certain diagnostic categories that are due to national traditions and histories. Differences between North American,

German, and French classifications for certain mental disorders persist to this day. However, most of our current diagnostic concepts for mental disorders found in *DSM-IV-TR* (2000) and *ICD-10* (1992) were first established by German and French psychiatrists between 1860 and 1920. However, the original classification systems differed widely in their nosologies.

obsession A persistent, intrusive, generally undesirable idea, mental image, or impulse that cannot be wilfully eliminated through logical or rational thought. Although obsessions are the hallmark of obsessive-compulsive disorder, which is not one of the psychotic disorders, obsessions may nonetheless be found in psychotic disorders such as schizophrenia. The term was first used in its modern psychiatric sense by the French alienist Benedict Augustin MOREL in 1860.

obstetric complications and schizophrenia See PERINATAL FACTORS AND SCHIZOPHRENIA.

occupational therapy Perhaps the earliest form of therapy for the mentally ill. Since the days of ancient Egypt, afflicted persons have traditionally been given physical activities or manual labor to perform. This "occupational therapy" has probably derived from the observation that persons with debilitating mental illnesses just seem to get worse if they are left alone to vegetate without becoming involved in meaningful activities. With the rise of the philosophy of "moral treatment" in the early 1800s, many institutions for the insane developed work programs involving their residents. In his 1801 *A Treatise on Insanity,* Philippe PINEL noted that his patients at the BICÊTRE in Paris "were supplied by the tradesmen of Paris with employments which fixed their attention." By the 20th century, the term *occupational therapy* came into vogue and developed a professional status, with occupational therapists now part of practically every inpatient psychiatric unit or hospital. The current focus has shifted to more of a rehabilitation model, so that activities are designed to (ideally) teach skills that enable the patient to find employment when he or she is discharged and returned to the community. For the most chronic forms of mental illness (such as schizophrenia), this goal is not so realistic; nonetheless, anyone who has ever been employed in a psychiatric inpatient facility would no doubt agree with the observation made by C. G. JUNG in 1939 that "the results of occupational therapy in mental hospitals have clearly shown that the status of the hopeless cases can be enormously improved."

See also FARMING AS TREATMENT.

Jung, C. G. "On the Psychogenesis of Schizophrenia," *Journal of Mental Science* 85 (1939): 999–1011.

odor of the insane For centuries it was believed that mentally ill people may have a particular odor that distinguishes them from others. This idea was given a certain shortlived credibility in a book by English physician George Man Burrows (1771–1846), who ran his own private asylum known as the Clapham Retreat. In his 1828 *Commentaries on Causes, Forms, Symptoms and Treatment of Insanity* he asserted that "mania" could be diagnosed by a particular odor, that of fermenting henbane. Needless to say, there is no scientific validation of this idea. However, in modern times, persons under treatment for a psychotic disorder are often characterized by the strong odor of "THORAZINE breath" that is part of the olfactory environment of many psychiatric inpatient units.

olanzapine See ANTIPSYCHOTIC DRUGS.

olfactory hallucinations These are hallucinations of smell. Olfactory hallucinations are not

commonly reported among people with psychotic disorders, but they can occur. More commonly they occur along with such neurological disorders as convulsive disorders, especially those due to temporal lobe lesions (temporal lobe epilepsy) or uncinate gyrus fits. They have also been reported in person's suffering from migraines or Parkinson's disease.

Asaad, G., and B. Shapiro. "Hallucinations: Theoretical and Clinical Overview," *American Journal of Psychiatry* 143 (1986): 1,088–1,097.

olfactory reference syndrome This is the delusion in which a person is convinced (falsely) that he or she is emitting a strong, foul body odor, such as a fecal or rotting-flesh stench. It is a delusion and not an OLFACTORY HALLUCINATION. It can be a part of a psychotic disorder, or it can be a part of a less serious disorder known as the monosymptomatic hypochondriacal syndrome.

oligophrenia See PROPFSCHIZOPHRENIA.

oligosymptomatic types A term coined by psychiatrist Silvano ARIETI in 1959 to describe "very mild" cases of schizophrenia. Arieti distinguishes the oligosymptomatic forms of the four subtypes of schizophrenia from BORDERLINE CASES by noting that the latter are not psychotic, whereas the mild cases of schizophrenia are psychotic. Arieti's term never gained prominence in psychiatric terminology.

Arieti, S. *Interpretation of Schizophrenia.* 2nd ed. New York: Basic Books, 1974.

onset of psychosis See AGE AT ONSET.

opium Opiates were commonly used in the 18th and 19th centuries as a form of CHEMICAL RESTRAINT to quell the agitation of certain persons confined to asylums. In the 20th century, the search for other somatic treatments eventually led to the discovery of ANTIPSYCHOTIC DRUGS, thus finally eliminating the use of opiates for persons with psychotic disorders.

Orap See ANTIPSYCHOTIC DRUGS.

organicity in schizophrenia See BRAIN ABNORMALITIES IN SCHIZOPHRENIA.

organic mental disorders This is the generic name for a group of mental disorders that have a known or presumed organic cause. For example, such disorders as alcohol withdrawal delirium or multi-infarct dementia would be classified as organic mental disorders.

organic mental syndromes This term refers to a cluster of psychological or behavioral signs and symptoms whose cause is unknown. These signs and symptoms are those that have long been identified by physicians as due to the dysfunctioning of the brain. For example, an individual who enters a hospital may exhibit the signs and symptoms of delirium or dementia, but the exact cause may be unknown. Such behavior may be due to the influence of a stroke, substance abuse, or other toxicity, or perhaps even a brain tumor or other neurological disease. In this case, a tentative diagnosis of an organic mental syndrome is given until the source of brain dysfunction is known, at which time it is rediagnosed as an organic mental disorder.

organic psychosis See FUNCTIONAL PSYCHOSIS.

orthomolecular psychiatry See MEGAVITAMIN THERAPY.

Othello syndrome This is a delusional syndrome in which the dominant delusion is that one's spouse or sexual partner is secretly unfaithful.

When this delusion of infidelity occurs in its purest form, it is often called the Othello syndrome after the Shakespearean character whose jealousy was the central delusion that led to his madness. Other names that have been given to this delusional syndrome are sexual jealousy, the erotic jealousy syndrome, morbid jealousy, and psychotic jealousy. In all these cases the jealous person maintains a psychotic delusion that accompanies a significant break from reality. However, there are persons who are generally not suffering from a psychotic disorder who may be jealously obsessed with the past sexual activity of their mates, but there is no delusion about any current infidelity. In this case the syndrome is called retrospective ruminative jealousy. In *DSM-IV* (1994), the Othello syndrome was included under the label "delusional disorder, jealous type."

Enoch, M. D., and W. H. Trethowan. *Uncommon Psychiatric Syndromes.* 2nd ed. Bristol, England: John Wright & Sons, 1979.

oubliettes A term popular in the 19th and early 20th centuries for the primitive seclusion cells that were used to contain agitated or violent patients in mental hospitals. They were usually cylindrical pits large enough for only one person that were dug into the basement floor and covered with a heavy metal grate. Such oubliettes once existed in the basement of the Center Building of St. Elizabeth's Hospital in Washington, D.C. The word is derived from the French verb *oublier,* meaning "to forget." Such inhumane forms of seclusion were also more commonly called "strong rooms."

outpatient care The concept that mentally ill persons could still live in the community and yet come to a clinic or hospital for outpatient treatment was first put into practice by the Pennsylvania Hospital in Philadelphia (at its Pine Street location) in November 1885. Although "nerve clinics" offering primarily HYDROTHERAPY and various tonics were established almost two decades earlier in Philadelphia (1867) and Boston (1873) for what would later be called NEURASTHENIA, Pennsylvania Hospital was the first mental hospital to offer an outpatient department. The clinic was operated by the medical staff of the Department for the Insane of the Philadelphia Hospital. The concept that such a clinic could be used for preventing the development of more serious mental illness was quite revolutionary for its time. Historian of the Pennsylvania Hospital Thomas G. Morton writes in 1897 that

> . . . the service was regarded at that time as experimental. . . . It was undertaken under a conviction that in a city of one million inhabitants, a large number were suffering from premonitory symptoms of insanity as nervous prostration and depression, who might receive timely advice and treatment, and that a further development of mental disorder might thus be arrested.

In England the first outpatient departments were opened at Saint Thomas' Hospital in London, and at the Wakefield Asylum, in 1890.

Morton, T. G. *History of the Pennsylvania Hospital.* Philadelphia: 1897.

outpatient commitment This is a legal procedure allowed in about two-thirds of the United States in which a person is committed to treatment in an outpatient program rather than a psychiatric hospital. This differs from "conditional release," in which a person who is already committed and residing in a psychiatric hospital is released to the community on the condition that he or she follows through with an outpatient treatment program. Outpatient commitment has been used infrequently due to the extra responsibility it places on psychiatrists, who must first initiate a legal proceeding and go to court to testify. Psychiatrist E. Fuller Torrey is an advocate of outpatient commitment.

Torrey, E. F. *Surviving Schizophrenia.* 2nd ed. New York: Harper & Row, 1988.

ovariotomy The surgical removal of the ovaries in a woman was thought to be a cure for severe

mental disorders. French surgeon Jules-Émile Péan (1830–98) performed the first ovariotomy in France in 1864 and performed what may have been the first such operation for the treatment of hysteria in 1882. In the late 19th century, it was performed on women suffering from HYSTERIA following the theory of Jean Martin Charcot that the disorder had a sexual basis. Hysterectomies and ovariotomies were also considered a cure for schizophrenia according to the focal theory of infection of American psychiatrist Henry Cotton, who performed such operations on patients with schizophrenia at the Trenton State Hospital in New Jersey around 1920.

See also FOCAL INFECTION AS CAUSE OF PSYCHOTIC DISORDERS.

P

P300 event-related potential One of the proposed BIOLOGICAL MARKERS OF SCHIZOPHRENIA found in EEG STUDIES.

pacifick medicines The 18th-century term for drugs given to the mentally ill to "calm" or perhaps "subdue" them. They were commonly derivatives of OPIUM. The modern term for such drugs might be "tranquilizers."

See also ANTIPSYCHOTIC DRUGS.

Packard, Elizabeth Parsons Ware See COMMITMENT.

packing (as treatment) Until well into the 20th century, a common method for treating agitated persons with mental disorders. It involved packing the patients in wet sheets, usually cold, and then wrapping them further in several blankets. Sometimes these sheets were saturated with mustard, which acted as an irritant and thus caused such agony in patients that they eventually succumbed to exhaustion. This practice is said to have been invented in 1840 by a Silesian peasant named Priessnitz, who gained a reputation for treating physical illness by applying cold-water wet packs. This technique was first used on the mentally ill in 1860 in the Sussex County Asylum in England by Dr. Lockhart Robinson. It was finally judged an inhumane form of treatment and abandoned in the 20th century.

Williams, D. "Baths." In *A Dictionary of Psychological Medicine.* Vol. 1., edited by D. H. Tuke. London: J. & A. Churchill, 1892.

padded room A single-person room lined with rubber and cork in which agitated mental patients were incarcerated. The first padded room was invented by Ferdinand AUTENREITH (1772–1835) for use in German asylums. Throughout the 19th century and into the 20th, practically every large institution for the care of the mentally ill possessed such a room for the seclusion of violent or agitated patients.

paleologic thought A term coined by Silvano ARIETI for the type of primitive logic that underlies the thought processes of all schizophrenics. It is the particular laws of this type of logic that Arieti proposes lead to delusions. Arieti also argues that the thought processes of very young children and people in primitive societies also manifest this type of logic. Paleologic thought was believed to be a developmentally earlier type of thinking than Aristotelian logic, which Arieti says is the "usual logic of the normal human being."

Arieti, S. *Interpretation of Schizophrenia.* 2nd ed. New York: Basic Books, 1974.

Papua New Guinea In 1929 physician and anthropologist C. G. Seligman reported that he found no cases of psychotic disorders in Papua New Guinea native villages living a traditional life-style but found several cases among those "natives" who were in close contact with Europeans. A major study conducted by E. Fuller Torrey, B. G. Burton-Bradley, and colleagues in the early 1970s found that the prevalence rates for schizophrenia differed greatly across the country. However, Torrey concludes: "Papua New Guinea provides another case

study in which schizophrenia appears to be more common in areas with longer contact with Western civilization and rare in areas with little such contact."

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

paralytic insanity See GENERAL PARALYSIS OF THE INSANE.

paranoia A psychotic disorder described since antiquity in which a person has a fixed false belief about reality. This has been the traditional meaning of the word *DELUSIONS* in English, the word *délire* in French, and *Wahn* in German since at least the 16th century. Insanity has often been defined by the presence of delusion, and so these two terms were used interchangeably. These false beliefs are the result of faulty logical reasoning, and although they may dominate the person's mental life, usually their intellectual ability and general global level of functioning remain intact. This has traditionally distinguished paranoia from either DEMENTIA PRAECOX (SCHIZOPHRENIA) or manic depressive illness. Paranoia thus has been regarding as a third class of psychotic disorders that fall in-between these two major insanities identified by Emil KRAEPELIN in the sixth edition of his textbook, *Psychiatrie,* in 1899.

Throughout most of the 19th century psychiatrists did not use the word *paranoia* for these delusional disorders. Delusion, insanity, *délire,* and *Verrücktheit* (in German) were most often the terms used for paranoia. Starting in the 1850s, French psychiatrists began to identify and classify specific delusions (such as "delusions of persecution," identified by Ernest-Charles Lasegue in 1852, the later the identification and classification of "systematized" delusions in the work of Valentin Magnan and his colleagues starting in the 1880s). Likewise, in German psychiatry there was a growing acknowledgement that some persons could have fixed delusions and not undergo intellectual impairment or further deterioration in functioning. In 1863 Karl KAHLBAUM called delusions "diastrephia" and distinguished them from the major forms of psychosis, the *"Vesania typica,"* which were chronic and deteriorating. In 1893, in the fourth edition of *Psychiatrie,* Emil Kraepelin introduced the concept of "*Verrückheit* (Paranoia)" which was a "durable delusional system in the presence of an intact personality." In this edition of his textbook, in which he introduced the term *dementia praecox* for the first time, he identified a chronic degenerative psychotic disorder which he calls "dementia paranoides." In the sixth edition of *Psychiatrie* (1899), dementia paranoides would become the paranoid subtype of dementia praecox. In this edition he distinguishes between dementia praecox and paranoia:

> The delusions in dementia praecox are extremely fantastic, changing beyond all reason, with an absence of system and a failure to harmonize them with events of their past life; while in paranoia the delusions are largely confined to morbid interpretations of real events, are woven together into a coherent whole, gradually becoming extended to include even events of recent date, and contradictions and objections are apprehended and explained.

By the end of the 1800s, paranoia referred to a whole class of fixed delusions that dominated a person who did not deteriorate further into dementia praecox or MANIC-DEPRESSIVE ILLNESS, as in the CHRONIC DELUSIONAL STATES IN FRENCH PSYCHIATRY. These could be delusions of persecution, jealousy, grandiosity, erotomania, hypochondria, litiginous, and so on. Today, such a broad class of delusions is seen as "types" of a larger "delusional disorder" in *DSM-IV-TR* (2000) or "persistent delusional disorders" in *ICD-10* (1992). Paranoia is no longer viewed as an independent class of psychotic disorders in its own right, and *paranoid* now referring to delusions of persecution specifically. In the early 1980s, literature reviews by noted schizophrenia researcher Kenneth Kendler concluded that the available evidence indicates that paranoia is not a subtype of manic-depressive illness and that "paranoia and schizophrenia are distinct syndromes."

Since the 1913 volume of the eighth edition of Kraepelin's *Psychiatrie,* there has been a continuum

of paranoid disorders from paranoia to PARAPHRENIA (a deteriorating form of paranoia resembling dementia praecox, in that hallucinations may be present, but the delusions remain systematic and there is no intellectual deterioration), then finally the dementia paranoides subtype of dementia praecox. In *DSM-IV-TR* this continuum is reflected in the increasing severity of paranoid personality disorder to delusional disorder (paranoid type) to schizophrenia (paranoid type).

Kendler, K. S. "Nosology of Paranoid Schizophrenia and Other Paranoid Psychoses," *Schizophrenia Bulletin* 7 (1981): 594–610.

paranoia erotica A now-defunct term for EROTOMANIA, it was coined and first described by psychiatrist L. Bianchi in 1906. He felt that this type of delusional syndrome could sometimes occur alone without any other evidence of a psychotic disorder and that it "occurred often in individuals of defective sexual life, not much inclined to copulation, sometimes in old maids who have never had an opportunity of marrying."

Bianchi, L. *A Textbook of Psychiatry,* trans. J. H. MacDonald. London: Baillière, Tindall & Cox, 1906.

paranoid cognitive style A concept derived from COGNITIVE STUDIES OF SCHIZOPHRENIA, it refers to the fact that people diagnosed with paranoid schizophrenia have a unique way of responding to perceptual, cognitive, and behavioral tasks in experiments. Paranoid cognitive style is characterized by a "jump to conclusions" strategy—that is, such persons give a response to an ambiguous stimulus (for example) without really having enough information in the first place to make a reasonable correct response. Paranoid cognitive style is also marked by a certain rigidity of thought processes and a reliance on verbal information processing.

Magaro, P. A. "The Paranoid and the Schizophrenic: The Case for Distinct Cognitive Style," *Schizophrenia Bulletin* 7 (1981): 632–661.

paranoid-nonparanoid distinction, the It has become clear after decades of research that there are some fundamental differences between the paranoid subtype of schizophrenia and the three nonparanoid subtypes. Persons with the nonparanoid forms of this disorder tend to be more disorganized and to have more formal thought disorder, more overall cognitive deterioration, an earlier age of onset, and a poorer prognosis than those persons diagnosed with the paranoid subtype. In cognitive, perceptual and behavioral studies of schizophrenia, many differences have been demonstrated to exist between these two major divisions of schizophrenia. Much of this research has been summarized in the special 1981 issue of *Schizophrenia Bulletin* (vol. 7, no. 4) devoted to paranoia.

paranoid personality disorder This is nonpsychotic disorder in which a person maintains a pervasive and unwarranted tendency, beginning before early adulthood, to interpret the words and actions of people as deliberately demeaning or threatening. These sorts of persons often expect to be hurt or exploited in some ways by others, read "hidden meanings" into the harmless remarks or actions of others, and are generally hypersensitive and easy to anger. They usually bear grudges forever, are generally somewhat humorless and are often interested in mechanical devices or electronics. Such persons are often sensitive to rank and often are jealous of those in positions of power and disdain those persons of lower rank. It is not exactly known how this personality disorder is related to schizophrenia, paranoid type, or to the delusional (paranoid) disorders.

paranoid schizophrenia, or paranoid type One of the classic forms of DEMENTIA PRAECOX and SCHIZOPHRENIA. In *DSM-IV-TR* (2000) the "paranoid type" is defined as "preoccupation with one or more delusions or frequent auditory hallucinations" and the absence of "disorganized speech, disorganized or catatonic behavior, or flat or inappropriate affect." The classic AUDITORY HALLUCINATIONS are of voices. The delusions are "bizarre" and do not seem to be based on a faulty logical premise, as is the case

in DELUSIONAL DISORDER. Delusions of persecution ("The pope is turning my family against me and stealing my money") and grandiosity ("I am Christ") are common.

The current paranoid type of schizophrenia is a descendant of the syndrome named and described by Emil KRAEPELIN in the 1893 fourth edition of his textbook, *Psychiatrie*. In that edition, Kraepelin introduced DEMENTIA PRAECOX for the first time (which was essentially the same syndrome as HEBEPHRENIA, identified in 1871 by Ewald Hecker), and placed it alongside CATAONIA and DEMENTIA PARANOIDES as forms of "psychic degenerative processes." Dementia paranoides differed from an earlier description of PARANOIA by Karl KAHLBAUM in terms of its sudden onset and its deteriorating course, resulting in "feeble-minded confusion." In 1899 dementia praecox became a comprehensive category of degenerative psychoses, and the "paranoid form" was subsumed under it along with catatonic and hebephrenia. In 1911 Eugen BLEULER kept the paranoid type as one of his forms of schizophrenia. This subtype has remained relatively unchanged up to the current time. However, although subtypes of schizophrenia have been a part of clinical lore, at present there is no hard scientific evidence from biological, genetic, or longitudinal studies that the various subtypes of schizophrenia are independent disorders. In the course of the life of a person with schizophrenia it is not unusual for them to have symptoms from one or more of the classic subtypes, thus blurring the vision we have of the variants of this tragic disorder.

Kendler, K. S., and M. T. Tsuang. "Nosology of Paranoid Schizophrenia and Other Paranoid Psychoses," *Schizophrenia Bulletin* 7 (1981): 594–610.

paraphrenia The term, no longer in use, for a type of paranoid MENTAL DISORDER that was introduced by Emil KRAEPELIN in the 8th edition of his *Psychiatrie*, which was published in four volumes between 1909 and 1913. Paraphrenia is a paranoid psychotic disorder in which people may present fantastic or bizarre delusions that are somewhat organized and accompanied by hallucinations; but, unlike the paranoid form of DEMENTIA PRAECOX, FORMAL THOUGHT DISORDER is usually absent, and there is little or no deterioration of the rest of the personality. Like dementia praecox, Kraepelin thought that paraphrenia was a chronic disorder, but that unlike dementia praecox it did not lead to dementia. Kraepelin identified four subtypes of paraphrenia: systematica (the most common type), expansive, confabulans, and phantastica. In terms of the severity of the paranoid psychotic disorders described by Kraepelin, paraphrenia occupies a midpoint between paranoid dementia praecox (the most severe disorder) and paranoia (the least severe of the three).

Kendler, K. S., and M. T. Tsuang. "Nosology of Paranoid Schizophrenia and Other Paranoid Psychoses," *Schizophrenia Bulletin* 7 (1981): 594–610.

parataxic distortion A term used by American psychiatrist and psychoanalyst Harry Stack Sullivan (1892–1949) to identify one of the three developmental modes of experience through which all humans pass: the prototaxic, the parataxic, and the syntaxic. Experiences in the parataxic mode are often fragmented, momentary states of being that have no logical connections or relationship between them. Sullivan thought that this mode of experience, usually found only in very young children, characterized many schizophrenic adults, leading to distorted interpretations of interpersonal situations. This happens by incorrectly inferring casual relationships between events that are actually independent. If parataxic distortions are not corrected, Sullivan felt that the schizophrenic would then receive less and less "consensual validation" and that this lack of respect and validation for the thoughts and feeling of the afflicted person would only serve to increase problems in his or her day-to-day interpersonal relationships.

Sullivan, H. S. In *The Interpersonal Theory of Psychiatry,* edited by H. S. Perry and M. L. Gawel. New York: W. W. Norton, 1953.

parergasia A term coined by Adolf MEYER for schizophrenia. Meyer attempted to rename all the

major mental disorders based on concepts from his own theory of "psychobiology." None of his proposed terms—including this one—were ever adopted by mainstream psychiatry.

paresis See GENERAL PARALYSIS OF THE INSANE.

Parkinsonism The cluster of Parkinsonian symptoms that is induced as a side effect of treatment with ANTIPSYCHOTIC DRUGS. The signs and symptoms are very much like those found in Parkinson's disease, which was first described by British physician and surgeon James Parkinson (1755–1824) in 1817 in his treatise *Essay on the Shaking Palsy.* However, Parkinson's disease is caused by an unknown pathological process of the nervous system, whereas Parkinson's syndrome is a drug-induced disorder.

Parkinson's syndrome is characterized by a triad of signs: tremor, rigidity, and AKINESIA (also called BRADYKINESIA). The tremor is worse when the person's afflicted body part is at rest, and it is usually found in the hands, often with the thumb rubbing against the pad of the index finger to produce a "pill-rolling" movement. However, the wrists, elbows, head, or almost any other body part can experience tremor. Rigidity is the increase in the normal resting tone of a body part and is usually only detectable upon physical examination. Akinesia (an absence of motion) or bradykinesia (a slowness of motion) are more commonly found earlier in Parkinson's syndrome than in Parkinson's disease. The bradykinetic person may have a masklike face, with diminished expressiveness and less frequent eye blinking. The body is turned "en bloc," as if the person were a solid mass without joints. The slowed movements may make the person seem apathetic or "zombie-like," and drooling can often occur.

Parkinson's syndrome can develop in persons who are taking antipsychotic drugs within weeks to months after the beginning of therapy. Women and elderly persons are the most commonly affected. Treatment for this syndrome may include lowering the dosage of antipsychotic drugs, switching to a less potent drug and/or introducing an antiparkinsonian agent such as AMANTADINE (trade name Symmetrel), BENZTROPINE (Cogentin), biperiden (Akineton), DIPHENHYDRAMINE (Benadryl), or trihexyphenidyl (Artane).

Gelenberg, A. J. "Psychoses." In *The Practitioner's Guide to Psychoactive Drugs.* 2nd ed., edited by E. L. Bassuk, S. C. Schoonover, and A. J. Gelenberg. New York: Plenum, 1983.

Parkinson's disease and psychosis See MEDICAL DISORDERS THAT MIMIC PSYCHIATRIC DISORDERS.

pathogen Something that causes a disease process.

pathognomonic Certain signs and symptoms are said to be pathognomonic of a particular disease if they alone can identify the presence of that particular disease. Although this may be true for many medical disorders whose physiological basis is quite well known and can be diagnosed through physical measurements, such is not the case for mental disorders. For example, because DELUSIONS and HALLUCINATIONS can occur in many disorders (and sometimes in normal persons), they would not be considered pathognomonic of SCHIZOPHRENIA. No single symptom alone is pathognomonic of schizophrenia.

See also FIRST-RANK SYMPTOMS.

pathognomy A 19th-century pseudoscience that, like phrenology and PHYSIOGNOMY, influenced the development of psychiatry as a science. Pathognomy (also called "movable physiognomy") was the study of the various expressions of the human face as they reflect different emotions and underlying musculature, and particularly as they reflect the inner emotional states of the mentally ill. The internationally acclaimed Scottish anatomist, physiologist, and neurologist Sir Charles Bell (1774–1842) of Edinburgh was one of the earliest to take a scientific interest in the expressions of mentally ill persons, and in his 1806 book, *Essays on the Anatomy of Expressions in Painting,* he compares the expres-

sions of "madness" with those found in "lower animals" and attributed them to fear and terror. Bell was a gifted illustrator and included a sketch of a typical "outrageous maniac" that he observed on a visit to the ROYAL BETHLEM HOSPITAL ("Bedlam") in July 1805. In his book he gives advice to painters on "what ought to be represented as the prevailing character and physiognomy of a madman," and in doing so, Bell sets the following scene:

> You see him lying in his cell regardless of every thing, with a death-like fixed gloom upon his countenance. When I say it is a death-like gloom, I mean a heaviness of the features without knitting of the brows or actions of the muscles.
>
> If you watch him in his paroxysm you may see the blood working to his head; his face acquires a darker red; he becomes restless; then rising from his couch he paces his cell and tugs his chains. Now his inflamed eye is fixed upon you, and his features lighten up into an inexpressible wildness and ferocity.

The famous Scottish physician Alexander Morison (1779–1866), who in 1822 delivered the first formal lectures in psychiatry in Great Britain, published a textbook in several editions that discussed the pathognomy of mental illness and included a series of relevant illustrations of patients who represented various diagnostic categories. In his *Outlines of Lectures on Mental Diseases* (1826), Morison writes: "The appearance of the face, it is well known, is intimately connected with, and dependent upon, the state of mind." He continued his research on the pathognomy of mental disorders and in 1840 published a textbook with 108 original drawings of the facial expressions of the mentally ill, *The Physiognomy of Mental Diseases*. Many of the expressions depicted would be similar to those seen on the faces of persons with psychotic disorders in the psychiatric hospitals and wards of today.

Gilman, S. L. *Seeing the Insane*. New York: Wiley, 1982.

pauper lunatics A term especially popular in the 19th century for the destitute mentally ill. An analogous term today might be the "homeless mentally ill."

Pavlov's theory of schizophrenia The famous Russian physiologist Ivan Pavlov (1849–1936), who influenced the field of learning by establishing the importance of the autonomic nervous system in the phenomenon known as "conditioned reflexes" (the discovery of which led to a Nobel Prize in 1904), became interested in SCHIZOPHRENIA after several visits to a Russian psychiatric hospital in 1918. Pavlov was particularly interested in catatonic patients and in his writings compared them to animals that had been experimentally conditioned. In early articles (1919), he interpreted the behavior of catatonic schizophrenics as resulting from an inhibition of the cerebral cortex of the brain, specifically a motor inhibition (inhibition of voluntary movement). Later (1930) Pavlov theorized that schizophrenia was a chronic state of hypnosis caused by hereditary and learned weakness of the cells of the cerebral cortex. Pavlov felt that the disease might begin as a learned response but later becomes organic in nature.

Pavlov, I. P. "Last Communications on the Physiology and Pathology of the Superior Nervous Activity," *Journal of Mental Science* 80 (1934): 187–197.

peas therapy Yet another of the bizarre somatic treatments for psychotic disorders and other MENTAL DISORDERS in the 18th and 19th centuries, peas therapy involved the creation of a head wound into which strings of dried peas would be inserted. It was thought that this would work as a counter-irritant to the irritation of the brain within the skull that was causing the insanity. It was reportedly used by the famous Scottish physician James Cowles Prichard (1786–1848), who in his day was one of the most eminent alienists in Britain.

pedigree A diagrammed ancestral line of descent (a "family tree") that is used in GENETICS STUDIES to analyze the inheritance of psychiatric disorders

or other associated characteristics. It is often more difficult to determine correct pedigree information for genetics studies of psychiatric disorders than for studies of other types of illnesses. Often family members may be inaccessible or uncooperative, or, as in the case of people with schizophrenia, who tend to produce fewer children than normals, the families may simply be too small to do a thorough study. Researchers often try to minimize the limitations to pedigree studies by locating and studying "geographical isolates," that is, communities that have been in one place for many generations and have not interbred very much with groups from other areas. The geographical isolation itself, as well as consanguineous marriages (marriages within the same bloodlines), helps to minimize the probability that the illness that is being studied for its possible genetic transmission is due to more than one genetic variant.

Pardes, H., et al. "Genetics and Psychiatry: Past Discoveries, Current Dilemmas, and Future Directions," *American Journal of Psychiatry,* 146 (1989): 435–443.

pediluvia One of the inhumane somatic treatments for mental illness used in the 19th century in which the legs of patients were plunged into vast amounts of water containing an irritating substance.

pellagrous insanity Pellagra is a disease caused by a deficiency of niacin. The term is derived from two Italian words meaning "skin" and "rough." Pellagra was first described in the 1730s in Spain, and its symptoms include diarrhea, dermatitis, and in its latter stages, mental disorders such as DEPRESSION and DEMENTIA. Thus, many persons who survived into the final stages of this disorder needed institutional care, usually in psychiatric hospitals. Although cases of pellagra are relatively uncommon today, it was estimated that in 1917 there were 125,000 cases of pellagra in the United States, primarily in the southeastern states. However, it was estimated that only 4 percent to 10 percent of persons with pellagra ("pellagrins") went on to develop the psychotic disorder known as "pellagrous insanity."

Copper, T. C. "Pellagrous Insanity," *American Journal of Insanity*, 1928, pp. 945–952.

penetrance In GENETICS STUDIES, the proportion of persons with a given GENOTYPE that actually manifest a particular PHENOTYPE.

peptides and schizophrenia A peptide is an intermediate level of biochemical synthesis between amino acids and proteins. A protein is composed of one or more peptides. Some of these protein particles have been demonstrated to have significant effects on behavior. Neuropeptides have been demonstrated to act as NEUROTRANSMITTERS, and therefore it has been suggested that a neuropeptide abnormality in the brain might be a possible contributing cause of SCHIZOPHRENIA. However, an informed review of the existing studies thus far by Herbert Meltzer in 1987 concludes, "It should be clear from this brief review that there is as yet no clear evidence for a neuropeptidergic mechanism in schizophrenia." Nonetheless, he recommends the exploration of the relationship between neuropeptides and schizophrenia as a possibly fruitful area of research for the future.

Meltzer, H. Y. "Biological Studies in Schizophrenia," *Schizophrenia Bulletin* 13 (1987): 77–111.

perceptual anomalies in schizophrenia It has long been known that persons who are undergoing a brief psychotic episode or who have a chronic psychotic disorder have quite a different sensory experience of the world than those who are not psychotic. Although many attempts have been made by clinical observers (as well as by writers in fictional treatments of madness) to understand and describe this "other worldliness" of psychosis, it was not until the 1960s that the first scientific studies attempted to find a measure that could quantify the phenomenology of the ALTERED STATES OF CONSCIOUSNESS found in psychosis, and specifically in SCHIZOPHRENIA. The perceptual anomalies caused by the ingestion of hallucinogenic substances such as peyote or LSD led to their early label as "psychotomimetic"

or "psychosis-mimicking" drugs. Disorders of attention in schizophrenia have often suggested that a "filtering" mechanism that separates out meaningful from peripheral information is dysfunctional in persons with schizophrenia, and so along these lines some theorists have suggested that "perceptual dyscontrol" may be a useful way of attempting to describe and understand the mysterious symptoms of this psychotic disorder.

In a 1976 paper published in *Schizophrenia Bulletin,* psychiatrist Lionel Corbett lists the following perceptual anomalies found in people with schizophrenia:

1. Changes in stimulus intensity control:
   - Enhancement; increased vividness of sounds, colors, appetite, even to the point of pain.
   - Diminution; sensations become muted; awareness is deadened.
2. Shifts in quality: Objects change size, faces swell, printed words rearrange themselves and zigzag; sudden changes in gestalts occur.
3. Abnormal concomitant perceptions: Each true stimulus is accompanied by a second sensation; for example, every word heard is associated with a pain in the head.
4. Abnormal perceptual alienation: Things and people look strangely different; voices sound unreal; the world looks fresh, exciting, and overpoweringly beautiful or uncanny and menacing. Sometimes perceptions lose their meaning, so that sounds, faces, and speech do not make any sense.
5. Splitting of perceptions: For example, a bird is heard chirping, but the bird and its song seem separated as though they do not belong together.
6. Loss of perceptual constancy: Depth perception and perspective are lost, so that everything looks two-dimensional and flat. Buildings seem to be crumbling, the steepness of stairs cannot be judged, the edges of rooms curve.
7. Failure of gating: The perceptual world is flooded with uncontrolled images, originating both internally and externally.
8. Abnormal time perception: Time speeds, slows, stands still, or the moment expands into eternity. Events become discontinuous, or time sensation becomes erratic.
9. Abnormal space perception: For example, micropsia, dysmegalopsia; space expands.
10. Distortion of bodily perception: The limbs feel light or heavy, or as though they are coming apart. The nose, hands, face, feet, or hips seem to have changed size. The skin texture or body odor seems different, the head feels odd or numb.
11. Hallucinations, including hallucinatory memory.
12. Changes in the perception of emotion: The experience of having lost all feelings; changes in the feeling tone of perceptions—for example, the touch of normal objects becomes charged with unpleasant affect. Sometimes percepts become unduly imbued with ecstatic, wonderful feelings.

See also ATTENTION, DISORDERS IN; PSYCHEDELIC EXPERIENCES IN SCHIZOPHRENIA; SUBJECTIVE EXPERIENCES IN SCHIZOPHRENIA.

Corbett, L. "Perceptual Dyscontrol: A Possible Organizing Principle for Schizophrenia Research," *Schizophrenia Bulletin* 2 (1976), 249–265.

perceptual delusions See DELUSIONAL PERCEPTION.

perinatal factors hypothesis Because genetics cannot account for 100 percent of the causes of SCHIZOPHRENIA, many theorists have postulated that there may be environmental causes of this brain disease. One possibility that has attracted attention is that certain factors surrounding the birth of the person who later develops schizophrenia may contribute to or actually cause the disease itself. Among the first to investigate these perinatal factors was researcher W. Pollin and colleagues in the mid-1960s. Many other investigators have followed suit and have examined a variety of possible factors in the development of schizophrenia. For example, in examining birth weight as a perinatal factor, it has been found that in those pairs of MONOZYGOTIC TWINS ("identical twins") discordant for schizophrenia (that is, one has it and the other doesn't),

the "normal" twin is usually the one who weighed more at birth and is usually born first. Other studies (conducted in the 1970s by Sweden's Thomas F. McNeil and colleagues) indicate that birth complications are more likely to have occurred in the ill twin of monozygotic twins discordant for schizophrenia, thus suggesting that given identical genes, environmentally induced injuries may influence the later expression of the illness.

Perhaps the most important study of the role of pregnancy complications and the risk of schizophrenia was conducted by Christiana Dalman and colleagues in Sweden and published in 1999. In this longitudinal cohort study, Sweden's National Birth Register was linked to the National Inpatient Register. The researchers followed up on the lives of 507,516 children born between 1973 and 1977 with regard to a diagnosis of schizophrenia between 1987 and 1995. They found 238 cases that matched. Using Sweden's detailed central medical databases, they also had access to data on physical and psychiatric illnesses in the mothers. Risk factors that increased the risk of schizophrenia in a newborn were (1) preeclampsia (hypertension in the mother that is also an indicator of fetal malnutrition), which was the only statistically significant risk factor, (2) vacuum extraction from the womb during birth, and (3) minor physical abnormalities in the fetus. These problems are caused by (1) malnutrition during fetal development, (2) extreme prematurity, and (3) hypoxia or ischemia around the time of birth.

Other perinatal factors that have been investigated in schizophrenia research are the mother's nutritional status at the time of the birth of the child, complications arising during the delivery of the child, possible hypoxia due to postnatal apnea in the newborn, intracranial hemorrhages, the immediate postnatal living environment of the newborn, and possible exposure to infectious diseases. Currently, new research on perinatal factors is being conducted in the area of fetal neural development.

See also FETAL NEURAL DEVELOPMENT AND SCHIZOPHRENIA; RISK FACTORS.

Dalman, C., et al. "Obstetric Complications and the Risk of Schizophrenia," *Archives of General Psychiatry* 56 (1999): 234–240.

McNeil, T. F. "Perinatal Factors in the Development of Schizophrenia." In *Biological Perspectives of Schizophrenia,* edited by H. Helmschen and F. Henn. Chichester, England: John Wiley & Sons, 1987.

Pollin W., et al. "Life History Differences in Identical Twins Discordant for Schizophrenia," *American Journal of Orthopsychiatry* 36 (1966): 492–509.

perphenazine See ANTIPSYCHOTIC DRUGS.

persecutory delirium See DELUSIONS, PERSECUTORY.

persecutory type According to *DSM-IV* (1994), the variant of delusional disorder in which the predominant theme of the person's delusion is that the afflicted person (or someone that he or she is close to) is being deliberately mistreated or threatened in some way. Persons with this disorder may continually complain to landlords, the police, or the FBI, for example, about being mistreated. Persons with this disorder are often resentful and angry and may become violent toward those they believe are persecuting them. This is the most common subtype of delusional disorder.

See also PARANOIA.

perseveration The tendency to continue to repeat particular behavior long after it is necessary to perform it. Persons with brain damage often perseverate, since it seems that the ability to inhibit an impulse to perform an action once it has started is impaired, thus causing the organically impaired person to repeat ritually the same activity over and over again. Due to the evidence for the underlying organic basis of schizophrenia, it is not surprising to at times find such behaviors in people with this disorder.

persistent delusional disorders See DELUSIONAL DISORDERS.

pervasive developmental disorders See CHILDHOOD SCHIZOPHRENIA.

PET scan A type of BRAIN IMAGING TECHNIQUE or neuroimaging technique that measures regional brain metabolism. The acronym stands for positron emission tomography, and the first published report of its use was in a paper by L. Sokoloff in 1977. PET scans examine functional changes in the brain, specifically: (a) biochemical changes such as oxygen metabolism, glucose metabolism, and changes in neurotransmitter receptor numbers, and (b) changes in physiological parameters, such as regional blood flow and blood volume.

PET uses computer-generated images, displayed as if they were slices of the brain. These images serve to map and quantify metabolic changes throughout the brain. Through either intravenous or inhaled means, the subject is administered "tracer agents" that have been tagged with a short-lived (usually two to four hours) positron-emitting isotope. A variety of brain functions can be studied with PET since hundreds of different tracer agents can be tagged with positron-emitting isotopes. The PET scanner follows the course of the positron emissions and translates these signals into pictures.

The first published report of the use of PET in schizophrenia research was a preliminary report on a single chronic schizophrenic subject by T. Farkas and colleagues in 1980. The first published controlled study of PET using schizophrenics and normal control subjects was produced by M. S. Buchsbaum and colleagues in 1982.

Farkas, T., et al. "The Application of [18F] 2-deoxy-2-fluoro-D-glucose and Positron Emission Tomography in a Study of Psychiatric Conditions." In *Cerebral Metabolism and Neural Function,* edited by J. V. Passonneau et al. Baltimore: Williams & Wilkins, 1980.

pharmacologic challenge A method employed in GENETICS STUDIES to search for markers of vulnerability by administering drugs in subclinical doses for a limited period of time. A selected drug is given both to persons who are thought to be genetically vulnerable to the later development of a disease and to normals. If the two groups respond differently, then the difference in response is attributed to genetic differences. At that point, response differences to a particular drug can be used as a useful marker of vulnerability. No such marker has yet been discovered for schizophrenia using a pharmacologic challenge.

pharmacotherapy of the psychotic disorders See ANTIPSYCHOTIC DRUGS.

phenocopy An individual who exhibits a trait that is due to nongenetic factors.

phenomenology of schizophrenic experience See ALTERED STATE OF CONSCIOUSNESS; PERCEPTUAL ANOMALIES IN SCHIZOPHRENIA; SUBJECTIVE EXPERIENCES OF SCHIZOPHRENIA.

phenothiazine Technically, the parent chemical compound for the synthesis of a large number of ANTIPSYCHOTIC DRUGS, including promethazine and CHLORPROMAZINE. By the late 1940s, researchers had discovered all the major chemical groups that are currently used in psychopharmacology. At about this time it was discovered that promethazine, a phenothiazine derivative, effectively potentiated the sedative properties of barbiturates (the type of drugs primarily used for mental illness for the first half of the 20th century) when used together but was useless when used alone. Therefore, researchers sought to develop other phenothiazines that might have a stronger effect. This was achieved in 1949 when Charpentier synthesized chlorpromazine (trade name: THORAZINE). By 1952 the antipsychotic effect of this drug had been documented in published reports, and it was approved for use with persons with psychotic disorders in the United States in 1954.

phenotype An observable trait in a person, physical or behavioral, surmised to be due genetics.

Philadelphia Association, the See LAING, RONALD DAVID.

photophilia in schizophrenia It has been reported by many observers of people with psychotic disorders that they sometimes exhibit photophilic (sun-loving) or photophobic (sun-avoiding) tendencies. Schizophrenics in particular have been observed in sun-gazing activities, sometimes resulting in damage to the retina. Psychiatrist Hector Gerbaldo suspects that people with schizophrenia have a decreased sensitivity to light, and that this may be important later in understanding the relationship between SCHIZOPHRENIA and photosensitive neuroendocrine processes (neural and hormonal processes that are stimulated by sunlight). It has been hypothesized that psychotic symptoms may be tied in with natural biological rhythms, and therefore the study of photophilia in schizophrenia may shed light on chronobiological studies of the psychotic disorders.

Gerbaldo, H., B. Thaker, and S. Cassady. "Sun Gazing and Photophilia in Schizophrenia," *American Journal of Psychiatry* 148 (1991): 693.

physical abnormalities in schizophrenia Many investigators looking for "biological markers" of schizophrenia have found minor physical abnormalities in schizophrenia, confirming, somewhat, the approach of the study of PHYSIOGNOMY. Minor physical anomalies (PAs) are often defined in research studies as slight defects of the head, hands, mouth, hair, eyes, ears, and feet. Generally, most researchers believe that these anomalies are due to perinatal factors and are associated with injury or unusual development during the first trimester of pregnancy, since this is the most critical period for the development of the epidermis, hair, ears, nose, and eyes. Between 1967 and 1989 the only five studies of PAs in schizophrenics that have ever been conducted have all found positive results. In a 1989 study by M. F. Green and colleagues at the UCLA Research Center in Camarillo, California, schizophrenic patients had significantly more physical anomalies than the normal control group subjects. They also found that the most common anomalies in schizophrenics were anomalies of the mouth and unusual head circumference, especially in women. In addition, the more prevalent physical anomalies were found in those persons, especially males, who had an earlier age of onset for schizophrenia. None of these anomalies, particularly the head circumference anomalies, were found to be related to cognitive performance, confirming a conclusion that Philippe PINEL made in 1801: "I have also taken, by means of a caliber compass, the dimensions of the heads of different persons of both sexes, who had been, or who were at the time in a state of insanity. I generally observed that the two most striking varieties, the elongated and the spheroidal skulls are found indifferently and bearing, at least, no evident relation to the extent of the intellectual faculties."

See also PERINATAL FACTORS HYPOTHESIS.

Green, M. F. "Minor Physical Anomalies in Schizophrenia," *Schizophrenia Bulletin* 15 (1989): 91–99.

Pinel, P. *A Treatise on Insanity,* trans. D. D. Davis Shefield. 1801. Reprint, England: W. Todd, 1806.

physical disease and schizophrenia The belief in the existence of a relationship between physical and mental illness has a long history. Indeed, throughout the centuries it has been reported that severe physical illnesses can sometimes alleviate the symptoms of mental illness, as was the basis for the rationale for FEVER THERAPY. Many studies have examined the risk factors for specific physical illnesses to which persons with SCHIZOPHRENIA may or may not be susceptible. A 1988 review of this vast area of research by psychologist Anne Harris of Arizona State University has concluded that: (a) persons with schizophrenia may be at increased risk for breast cancer and possibly for cardiovascular disease, (b) persons with schizophrenia seem to have a decreased risk for developing rheumatoid arthritis or lung cancer (even in light of the fact that so many of them are heavy smokers), and (c) the overall risk for cancer is, however, greater in persons with PARANOID SCHIZOPHRENIA than in those diagnosed with the other subtypes. The problem with these studies, however, is that the risk factors for particular disease may one day be found to have nothing to do with the schizophrenic disease process per se in individuals but instead may be determined by the effects of antipsychotic medication or other as yet unknown confounding factors.

Harris, A. H. "Physical Disease and Schizophrenia," *Schizophrenia Bulletin* 14 (1988): 85–96.

physiognomy The attempt to gain insight into a person's character or personality based on his or her physical characteristics (particularly facial expressions) dates from at least Aristotle, who, in the *Physiognomica* (a book attributed to him), suggested that people have the temperament of animals they may resemble. In 1775 J. K. Lavater published his *Physiognomische Fragmente,* which attempted to construct a classification system of character based on facial expressions. In a later work published in Paris, *L'Art de connaitre les hommes par la physionomie* (1806), Lavater explains that "physiognomy is the science or knowledge of the correspondence between the internal and external man, the visible superficies and the invisible contents." Franz Joseph Gall's (1758–1828) influential pseudoscience of phrenology (which dominated psychiatric thought between the 1820s and 1840s) likewise drew attention to the relationship between physiology and mental faculties, with the structure of the skull allegedly related to structural characteristics of the brain that were correlated with specific mental functions. Phrenology had a profound effect on the history of psychiatry, since it conclusively introduced the (then) controversial notion that the mind had a primarily physiological basis in the brain.

It has long been proposed that specific psychotic disorders could be diagnosed in part through the physical characteristics of a particular individual. This early protoscientific attempt to understand the "biological markers" of mental illness involved the study and classification of the physiognomy of the "insane." Philippe PINEL devoted considerable effort to measuring the size and shapes of the heads of many of his institutionalized patients as well as "a great number of skulls in different museums," finding only a relationship between skull size and shape and mental retardation. He devotes a whole section to the topic—"Of Malconformation of the Skulls of Maniacs and Idiots"—in his 1801 *A Treatise on Insanity.* Pinel's pupil, J. E. D. ESQUIROL (1772–1840) maintained a large collection of plaster casts of the faces of institutionalized patients at the Salpêtrière in Paris. During the early 1820s, another member of the "Esquirol Circle," Etienne-Jean Georget (1795–1828), commissioned the painter Géricault to paint 10 studies of "lunatics," all of which were "monomaniacs." Later in the 19th century, Cesare Lombroso (1836–1909) studied criminal behavior and believed that certain physical characteristics in a person were "stigmata of degeneracy" that could identify the "criminal type."

In the 20th century, German psychiatrist Ernst Kretschmer (1888–1964) correlated body type and constitution with specific mental disorders in his famous book *Körperbau und charakter* (1921). The ASTHENIC TYPE was thought to characterize schizophrenics. In the United States, American psychologist William H. Sheldon (1899–1977) correlated various psychotic disorders with body types and proposed that certain very thin individuals called ectomorphs would be more likely to develop schizophrenia than endomorphs, who were heavier and more likely to develop manic-depressive psychosis. Similarly, American psychiatrist Alexander Lowen, a disciple of Wilhelm Reich's "bioenergetics analysis," combined physiognomy and psychoanalytic thought by identifying the "schizophrenic character" and the "schizoid character" in his writings of the 1950s.

Cooter, R. "Phrenology and the British Alienists, ca. 1825–1845." In *Madhouses, Mad-Doctors, and Madmen: The Social History of Psychiatry in the Victorian Era,* edited by A. Scull. London: Athlone Press, 1981.

Goldstein, J. *Console and Classify: The French Psychiatric Profession in the Nineteenth Century.* Chicago: Chicago University Press, 1987.

Lowen, A. *Physical Dynamics of Character Structure: Bodily Form and Movement in Analytic Therapy.* New York: Grune & Stratton, 1958.

Sheldon, W. H. *The Varieties of Human Physique.* New York: Harper Brothers, 1940.

pica The eating of nonfood substances (e.g., dirt, paint chips, hair, cloth). Pica can sometimes be the result of a person's psychotic disorder, particularly in severe cases of chronic schizophrenia.

pimozide See ANTIPSYCHOTIC DRUGS.

Pinel, Philippe (1745–1826) A French ALIENIST and one of the most important figures in the development of modern psychiatry. In 1793, following the French Revolution, Pinel was appointed chief physician at the BICÊTRE asylum in Paris, where he became famous for freeing more than 50 male patients from their chains. (Although the action was initiated by Jean-Baptiste Pussin, not Pinel.) In 1795 he became the head of the other major asylum in Paris at that time, the Salpêtrière, where he was also known for his humane philosophy of treatment, which he later called the MORAL TREATMENT. His 1801 textbook, *Traité médico-philosophique sur l'alienation mental ou la maine,* is one of the long-standing classics of psychiatry and had a profound effect on the classification and treatment of the mentally ill worldwide. He is credited (along with John HASLAM of England) with providing the first complete description of a case of schizophrenia in 1809.

Goldstein, J. *Console and Classify: The French Psychiatric Profession in the Nineteenth Century.* Chicago: Chicago University Press, 1987.

Riese, W. *The Legacy of Philippe Pinel: An Inquiry into Thought on Mental Alienation.* New York: Springer, 1969.

Pinel-Haslam syndrome, the The proposed name for the type of schizophrenia that according to CROW'S HYPOTHESIS is called "Type II" schizophrenia—the type that is characterized by NEGATIVE SYMPTOMS, is more organically based, and has an earlier onset and a more chronic course. This term was first proposed by M. Altschule in 1967 as a replacement for the term *schizophrenia.*

See also HISTORICAL EVIDENCE OF SCHIZOPHRENIA.

Altschule, M. D. "Whichophrenia, or the Confused Past, Ambiguous Present, and Dubious Future of the Schizophrenia Concept," *Journal of Schizophrenia* 1 (1967): 8–17.

placebo A harmless, impotent substance that can be given to a patient and affects that person through suggestion. Placebos are important in testing the efficacy of new drugs, since control groups given the placebo should not show any difference in affect, behavior, or other areas, whereas those persons in the experimental group who are given an actual drug should indeed show such differences. The word is derived from a liturgical hymn from the Roman Catholic church, specifically, the first antiphon of the vespers for the dead: "Placebo Domino in regione vivorum" ("I shall be pleasing to the Lord in the land of the living").

platelet MAO activity hypothesis See ENZYME DISORDER HYPOTHESIS.

Poland Although no conclusive studies have been conducted in Poland, the prevalence rate for schizophrenia is estimated to be higher than in most countries. This is based on data from Australia, England, and the United States, which concludes that Polish immigrants (as well as Russian and, in some studies, Swedish immigrants) have very high rates of first admission to psychiatric hospitals when compared with other ethnic groups.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

polydipsia This is a medical term for frequent drinking because of excessive thirst. Polydipsia is a commonly observed behavior in people with psychotic disorders. Although studies have indicated that 6 percent to 17 percent of all chronically ill psychiatric patients manifest this behavior, 69 percent to 83 percent of people diagnosed with SCHIZOPHRENIA do so. Both relatives and institutional caretakers of people with schizophrenia can acknowledge that this is a very common activity, but the reason for it still remains a matter of conjecture. Irrational or psychotic thoughts that encourage drinking, the mouth dryness caused by ANTIPSYCHOTIC DRUGS, and the hyperactivity of the thirst centers in the hypothalamus in the brain have all been posited as contributing to this behavior. However, polydipsia can be dangerous, as it can lead to abnormally low concentrations of

sodium ions in the circulating blood, which is a condition known as hyponatremia. The constant drinking of water can lead to water intoxication, with such symptoms as confusion, lethargy, the worsening of psychotic symptoms, and even death. Perhaps the earliest case report of a person with schizophrenia engaging in dangerous polydipsia was reported in 1938 by Barahal, who described an example "in which a female dementia praecox patient drank excessive quantities of tap water resulting in edema, coma, convulsions, with subsequent recovery." Other terms for this syndrome have been *compulsive water drinking, self-induced water intoxication and psychosis, psychogenic polydipsia, primary polydipsia,* and *psychosis-intermittent hyponatremia-polydipsia (PIP) syndrome.* The primary treatment remains fluid restriction and the removal of exacerbating factors.

Barahal, H. S. "Water Intoxication in a Mental Case," *Psychiatric Quarterly* 12 (1938): 767–771.

Illowsky, B. P., and D. G. Kirch. "Polydipsia and Hyponatremia in Psychiatric Patients," *American Journal of Psychiatry* 145 (1988): 675–683.

polygenetic theory See DIATHESIS-STRESS THEORIES.

polymorphic psychotic symptoms A term used in *ICD-10* (1992) to distinguish a syndrome of psychotic symptoms found in ACUTE AND TRANSIENT PSYCHOTIC DISORDERS that are not characteristic of the longer-term symptoms found in SCHIZOPHRENIA. Polymorphic symptoms are rapidly changing and variable, changing from hour to hour or day to day. These symptoms include HALLUCINATIONS, DELUSIONS, perceptual disturbances, and emotional turmoil (irritability and anxiety, although sometimes alternating with feeling of ecstasy and happiness).

polypharmacy The mixing of several drugs in one prescription. Psychiatrists are often cautious about the possible dangers of such a practice, since care must be taken when prescribing, for example, an antipsychotic, an antidepressant, and an ANTIPARKINSONIAN DRUG all at the same time.

poor houses See ALMSHOUSES.

portmanteau word This is a word that has two separate meanings "packed" into it in a forced fit. Persons with psychotic disorders, particularly schizophrenia, can sometimes create such NEOLOGISMS that are usually quite meaningless. For example, the "pillfill" might be a word for the little plastic cup in which a nurse hands a patient his or her medication. Author Lewis Carroll coined the term in his novel *Through the Looking Glass* (1872).

positive symptoms Specifically, DELUSIONS and HALLUCINATIONS. Positive symptoms have been postulated to be the characteristic symptoms of "Type I" schizophrenia by British researcher Timothy Crow and are thought to be related to increased dopamine receptors in the brain. However, CROW'S HYPOTHESIS has been challenged by prominent schizophrenia researcher Herbert Meltzer of Case Western Reserve University, who argues that the connection between increased DOPAMINE activity and positive symptoms is not clear-cut, and indeed dopamine activity may be related to NEGATIVE SYMPTOMS as well.

See also FACTORS OF INSANITIES, THE; NEGATIVE SYMPTOMS.

Berrios, G. E. "Positive and Negative Symptoms and Jackson: A Conceptual History," *Archives of General Psychiatry* 42 (1985): 95–97.

Meltzer, H. Y. "Dopamine and Negative Symptoms in Schizophrenia: A Critique of the Type I-II Hypothesis." In *Controversies in Schizophrenia,* edited by M. Apert. New York: Guilford Press, 1985.

possession syndrome Since antiquity there have been numerous reports of persons who claim to be "possessed" by evil spirits. French ALIENIST J. E. D. ESQUIROL referred to this syndrome in the 19th century as CACODEMONOMANIA. Case histories of such persons continue to appear from time to time in modern psychiatric literature. More than likely, such persons are experiencing a DISSOCIATIVE DISORDER in which a person's consciousness, memory, and

identity are split into two or more separate personality states or personalities. Many persons who were thought to be "possessed" over the centuries may have instead been afflicted with multiple personality disorder, with the switching of alternate personalities leading to a supernatural explanation. However, in persons with schizoprenia, it is not uncommon to encounter reports that the person feels "possessed" or has delusions about being possessed by evil spirits, malevolent family members, and so on.

The belief in possession is so widespread that an exhaustive study of 488 randomly selected societies in 1968 by cultural anthropologist Erika Bourguignon of Ohio State University found that 74 percent of them had some sort of belief in possession, and many had ritualized forms of "possession trance" that were accepted among religious practitioners. Due to the influx of many immigrants into the United States and Canada from South America and the Carribean, where there are many cultures that promote such beliefs and religious practices, clinicians are encountering more and more examples of such cases.

Bourguignon, E. *Possession.* San Francisco: Chandler & Sharp, 1976.

Goodman, F. D. *How about Demons? Possession and Exorcism in the Modern World.* Bloomington: Indiana University Press, 1988.

McAll, R. K. "Demonosis or the Possession Syndrome," *International Journal of Social Psychiatry* 17 (1971): 150–158.

Noll, R. *Vampires, Werewolves and Demons: Twentieth Century Case Reports in the Psychiatric Literature.* New York: Brunner/Mazel, 1991.

postpartum psychosis The phenomenon that still occurs from time to time in which a psychotic episode (usually a psychotic depression) or more serious psychotic disorder (such as schizophrenia or bipolar disorder) seems to be induced by the stress of childbirth. It was first described by the French physician Charles Lepois (1563–1633), who thought it was due to an excess (*plethora*) of dark humors (see HUMORAL THEORY OF MENTAL ILLNESS). Well into the 1800s some physicians believed that the severe mental disorders suffered by women shortly preceding and especially directly following childbirth were related to the production (or lack of production) of milk (see LACTATION PSYCHOSES). In 1838 French alienist J. E. D. ESQUIROL observed that fully one-twelfth of the women admitted to the SALPÊTRIÈRE in Paris became psychotic after giving birth.

Research into the types of psychotic disorders that are brought on by childbirth has resulted in conflicting conclusions over the years. In a major study published in 1969 by Protheroe in England, almost twice as many cases of manic-depressive psychosis were reported as cases of schizophrenia. In some previous studies, more cases of schizophrenia were reported as postpartum or puerperal insanity. One of the best sources of information on postpartum psychotic disorders is the chapter titled "Postpartum Schizophrenic Psychoses" in Silvano ARIETI's book *Interpretation of Schizophrenia* (1974). Today, with the use of synthetic hormones, ANTIPSYCHOTIC DRUGS and psychotherapy, such psychotic episodes in women rarely become chronic illnesses.

Arieti, S. *Interpretation of Schizophrenia.* 2nd ed. New York: Basic Books, 1974.

Protheroe, C. "Puerperal Psychoses: A Long-Term Study, 1927–1961," *British Journal of Psychiatry* 115 (1969): 9–30.

postpsychotic depression See DEPRESSION.

poverty of content of speech Also known as Alogia, one of the NEGATIVE SYMPTOMS of schizophrenia. According to *DSM-III-R* (1987), this is "speech that is adequate in amount but conveys little information because of vagueness, empty repetitions, or use of stereotyped or obscure phrases."

poverty of speech One of the NEGATIVE SYMPTOMS of schizophrenia, it is reduction in the amount and frequency of speech.

predisposing factors Any fact of a person's life, whether genetic or environmental, that may increase the likelihood that that person will

develop a specific disease. For example, in both schizophrenia and bipolar disorder, a family history that includes several afflicted persons with the same psychotic disorder is a strong predisposing factor to the possible development of the disease.

See also HIGH-RISK STUDIES; RISK FACTORS.

prefrontal lobotomy See LOBOTOMY.

pregnancy complications and schizophrenia See PERINATAL FACTORS HYPOTHESIS.

pregnancy delusions A commonly encountered type of delusion found in both women and men with severe psychotic disorders, usually schizophrenia. A man may claim, for example, that he has been pregnant for nine years.

In persons who may not have psychotic disorders, there have been many cases on record of women who have developed a psychosomatic syndrome in which they may fully believe they are pregnant and at times mysteriously manifest many of the symptoms of pregnancy but may not actually be so. With this mysterious syndrome—called pseudocyesis (a term coined by John Mason Good in his *Physiological System of Nosology* in 1823)—women may report morning sickness or feeling fetal movements, and, incredibly, the abdomen may enlarge and the breasts may enlarge and actually begin to produce milk. This psychosomatic disorder has been reported since 300 B.C. when Hippocrates, the father of medicine, wrote about women "who imagined they were pregnant, seeing the menses suppressed and the matrices swollen," treating 12 such cases himself. Although modern technology has allowed the early detection of pregnancy and has eliminated most cases of pseudocyesis, the continued rare occurrence of such cases has led to a new scientific name for the syndrome: the galactorrhea-amenorrhea hyperprolactinemia syndrome, or GAHS. A related syndrome in men is *couvade*, from the French for to "brood" or "hatch," and it essentially refers to what is conventionally known as "sympathetic labor pains."

Enoch, M. D., and W. H. Trethowan. *Uncommon Psychiatric Syndromes.* 2nd ed. Bristol, England: John Wright & Sons, 1979. (The chapter on the *couvade* syndrome is an exemplary resource.)

Small, G. W. "Pseudocyesis: An Overview," *Canadian Journal of Psychiatry* 31 (1986): 452–457.

premorbid functioning The physical, psychological and interpersonal level of functioning of a person before the first clear signs of a mental disease process are apparent. Another, older term for this is "premorbid personality." In schizophrenia it has generally been found that persons with the paranoid subtype have a higher level of premorbid functioning than those with the nonparanoid subtypes. Premorbid functioning is a factor in the PROCESS-REACTIVE DISTINCTION IN SCHIZOPHRENIA, with "process" schizophrenics being characterized by poor premorbid history and "reactive" schizophrenics having a much better premorbid level of functioning.

See also AGE AT ONSET; COURSE AND OUTCOME OF SCHIZOPHRENIA.

prenatal factors See FETAL NEURAL DEVELOPMENT AND SCHIZOPHRENIA; PERINATAL FACTORS HYPOTHESIS; RISK FACTORS.

prepsychotic panic A commonly reported phenomenon by people who later develop a full psychotic episode or disorder. It is the crucial point in the person's life when he or she realizes that his or her experiences of the world are aberrant, and this engenders a sense of isolation and loneliness. Fear, terror and sheer panic are experienced by the individual who experiences the world as splitting or crumbling. It may very well be the point at which the person realizes he or she is losing control and will soon no longer be able to function in a healthy way. Many people enter treatment at this point and can be helped with pharmacotherapy and psychotherapy, although many still go on to develop a psychosis. American psychiatrist Harry Stack Sullivan described just such a "schizophrenic panic," which he thought was the

result of an extreme injury to self-esteem or sense of self. Silvano ARIETI describes this initial stage of "prepsychotic panic" in the development of a full case of schizophrenia as follows: "when the patient starts to perceive things in a different way, is frightened on account of it, appears confused, and does not know how to explain 'the strange things that are happening.'"

Arieti, S. *Interpretation of Schizophrenia.* 2nd ed. New York: Basic Books, 1974.

Sullivan, H. S. *Conceptions of Modern Psychiatry.* New York: Norton, 1953.

prepsychotic personality See LATENT SCHIZOPHRENIA.

pressured speech This is one of the hallmarks of a MANIC EPISODE. It occurs when a person is rapidly talking in great bursts and is difficult, if not impossible, to interrupt. Often the person is speaking very loudly and emphatically and without any prompting from anyone else. Indeed, such persons may continue to speak even though no one is listening. Beside manic episodes, pressured speech may occur in persons who are diagnosed with schizophrenia, an organic mental disorder, major depression with psychomotor agitation, other psychotic disorder, or in short-term reactions to stress.

prevalence of schizophrenia See EPIDEMIOLOGY.

primary process According to Sigmund FREUD, this is the type of psychological process that is characteristic of the unconscious. From the point of view of psychoanalysis, primary process is the most primitive and infantile form of psychological activity, and it is most evident in dreams, fantasies, and hallucinations. A psychotic episode or psychotic disorder would then be considered the eruption or intrusion of this primitive and infantile mode of experience into consciousness. Primary process is to be distinguished from secondary process, which is the more logical, sequential, and rational form of thought that typifies normal waking consciousness. The principal drive behind primary process, according to Freud, is the pleasure principle, whereas the primary motivation behind secondary process is the reality principle. Freud developed the distinction between primary and secondary process as early as 1895 in his "Project for a Scientific Psychology" but developed these ideas in more detail in his book, *The Interpretation of Dreams*.

Laplanche, J., and J. B. Pontalis. *The Language of Psycho-Analysis,* trans. D. Nicholson-Smith. New York: W. W. Norton, 1973.

primary symptoms of schizophrenia See FUNDAMENTAL SYMPTOMS OF SCHIZOPHRENIA.

primitive thinking See MAGICAL THINKING.

prison psychosis See GANSER'S SYNDROME.

private madhouses Common in France, Germany, and especially Britain in the 18th and 19th centuries, these were privately owned "madhouses" for mentally ill people with money. Those without money—the "pauper lunatics"—sometimes had their costs paid by local church parishes. The earliest of the private madhouses were developed in England in 1615 (the Kingsdown house at Box, closed finally in 1940), but they did not become a popular practice until the next century. Most were owned by businessmen, not medical professionals, and many were run by women—usually the wives, widows, and daughters of the owners. Some of these private madhouses were passed on for many generations within the same family.

Private madhouses were a profit-making enterprise, and scandals and abuses were frequent. In 1706 British author Daniel Defoe wrote an essay calling for the abolition of private madhouses because of the inhumane treatment prevalent in so many of them. It was finally a novel, *Hard Cash,*

by British author Charles Reade (1814–84), that ignited the movement for reform in the 1860s. *Hard Cash* (first published in England in 1863, and then in the United States in 1864 under the title *Very Hard Cash*) is the story of a sane young man who is diabolically committed to a private asylum by his business associates who covet the young hero's wealth. Reade based the novel on an actual incident in his own life in which he was instrumental in gaining the release of a young man who was wrongfully committed to a private madhouse. Prior to being released as a novel, Reade's *Hard Cash* was first serialized in a periodical edited by Charles Dickens, *All the Year Round,* and both of these men were attacked by the *British Medical Journal* for being irresponsible in making "diabolical charges upon the character of all medical men connected with the management of lunatics."

Ackerknecht, E. H. "Private Institutions in the Genesis of Psychiatry," *Bulletin of the History of Medicine* 60 (1986): 387–399.

Parry-Jones, W. L. *The Trade in Lunacy: A Study of Private Madhouses in England in the Eighteenth and Nineteenth Centuries.* London: Routledge & Kegan Paul, 1972.

proband In GENETICS STUDIES, the proband is the person in a given PEDIGREE diagnosed with the disease. Relationships between that person and others in the family are then studied to determine possible patterns of genetic transmission. Another name for proband is INDEX CASE or "propositus" (plural: probands or propositi).

process-reactive distinction in schizophrenia, the This distinction is one attempt to further differentiate the possible subtypes of schizophrenia. The process-reactive distinction divides persons with schizophrenia into two groups based on differences in premorbid personality, the course of the disease, and its PROGNOSIS. The idea is that the premorbid history of a person who develops schizophrenia and the rapidity with which the first symptoms appear are related to how well or ill the person eventually becomes in the course of his or her lifetime. Therefore, it is also sometimes referred to as the "poor premorbid/good premorbid" distinction, or, by some, the "poor prognosis/good prognosis" distinction (see PREMORBID FUNCTIONING).

Eugen BLEULER first discussed the differences between psychotic disorders that were based on a "morbid reaction to an affective experience" (such as an emotional shock or stressor), which he called reactive psychoses or situation psychoses, and those psychoses based on a "morbid process in the brain," which he termed process psychoses or progressive psychoses. However, as Bleuler notes in the fourth edition (1923) of his *Textbook of Psychiatry,* "no (diagnostic) division can be based on these classes because the two symptomatologies intermingle."

However, based on Bleuler's observation about psychotic disorders in general, the idea was further developed by others that some persons with schizophrenia could have a variety of the disease caused by an organic disease of the brain and another variety that seemed to be induced as a reaction to stress or other environmental factors. Revising some proposals for studying the problem of prognosis in schizophrenia first put forth in a 1937 article, in 1956 Gabriel Langfeldt (1895–1983) of Norway proposed that schizophrenics who had a poor premorbid history (that is, a long-term history of poor social, occupational, and psychological functioning perhaps dating from childhood) be called process schizophrenics. Furthermore, Langfeldt also argued that these persons generally had a poor prognosis and a lifelong history of long-term institutionalization. Langfeldt noticed that there was another type of schizophrenia characterized by persons who may have had a generally good premorbid history and who develop an acute onset of symptoms rather than the slow, insidious development of symptoms found in process schizophrenics. Furthermore, these persons had a better chance of recovery than those with process schizophrenia. Langfeldt called this reactive disorder schizophreniform psychosis.

Throughout the years, the process-reactive distinction has been given many other names as well. These clinical dichotomies have been termed true

schizophrenia/schizophreniform, demential praecox/schizophrenia, typical schizophrenia/atypical schizophrenia, chronic schizophrenia/episodic schizophrenia, and degenerative schizophrenia/psychogenic schizophrenia.

Decades of research that has divided schizophrenia into these two forms has proven useful, for significant differences have been found between the two types of persons with schizophrenia. Process schizophrenics tend to perform more poorly on cognitive, perceptual, and behavioral tasks in experiments. Reactives perform closer to normals on these tasks. Process schizophrenics are also more likely to have NEGATIVE SYMPTOMS, which is to be expected if this is a form of the disorder that seems to be the most organic and genetically based. Reactive schizophrenics tend to demonstrate a fuller range of affect and have shorter hospitalizations and fewer admissions than process schizophrenics. The paranoid subtype of schizophrenia tends to be more common among those in the reactive category, whereas the nonparanoid subtypes tend to be found among those considered process schizophrenics.

The process-reactive distinction has been important for understanding schizophrenia. One of the most consistent research findings is that the premorbid level of social functioning is an important factor in determining the prognosis of cases of schizophrenia, although it is not 100 percent predictive and must be considered with other factors. This vast literature is reviewed by J. Higgins in a 1969 article, and in 1977 an entire issue of *Schizophrenia Bulletin* (vol. 3, no. 2) was devoted to the issue of the premorbid adjustment aspect of the process-reactive distinction.

Bleuler, E. *Lehrbuch der Psychiatrie.* 4th ed. Berlin: Springer, 1923. (English translation, 1924.)

Higgins, J. "Process-Reactive Schizophrenia," *Journal of Nervous and Mental Disease* 149 (1969): 450–465.

Langfeldt, G. "The Prognosis in Schizophrenia and the Factors Influencing the Course of the Disease," *Acta Psychiatrica et Neurologica Scandinavica Supplementum* no. 13 (1937).

———. "The Prognosis in Schizophrenia," *Acta Psychiatrica et Neurologica Scandinavica Supplementum* no. 110 (1956).

prochlorperazine See ANTIPSYCHOTIC DRUGS.

prodromal phase The prodromal phase is the period prior to the full expression of psychotic symptoms (DELUSIONS, HALLUCINATIONS, etc.) in which there is a clear deterioration in a person's previous level of functioning. Often during this period the person will tend to withdraw from social situations, perhaps begin to exhibit poor grooming and hygiene or express odd or bizarre ideas. Often the person's affect will become rather blunted, or he or she may express it inappropriately (e.g., laughing to him- or herself in the middle of a serious discussion). Sometimes he or she will have perceptual abnormalities and may seem to have lost a zest for life by developing a lack of initiative or energy. Insensitive family members or friends may accuse the person of being "lazy" when in fact this is not really the case. Often those who know the person who is undergoing the prodromal phase of schizophrenia will comment on that fact that he or she "is no longer the same person." The length of the prodromal phase is extremely variable, perhaps weeks in some cases to many years in others. The poor premorbid adjustment of "process schizophrenics" (see the PROCESS-REACTIVE DISTINCTION IN SCHIZOPHRENIA) may be due to the presence of the prodromal phase of the illness.

See also AGE AT ONSET.

prognosis The foretelling of the probable course and outcome of a disease. Even after more than a century of scientific research on schizophrenia, it is impossible to predict with any certainty the course and outcome of any individual case of schizophrenia.

Much attention has been paid to the prognosis of schizophrenia. Indeed, Emil KRAEPELIN's classification of the psychotic disorders was based on prognosis, with dementia praecox representing the types of psychosis that follow a chronic degenerating course, and MANIC-DEPRESSIVE PSYCHOSIS being the type of psychotic disorder that has a better outcome. Within the field of schizophrenia research specifically, the concept of "poor prognosis/good prognosis" types of schizophrenia has been examined in depth.

In *Surviving Schizophrenia: A Family Manual,* psychiatrist E. Fuller Torrey lists the following factors, which, when considered together in an individual's unique history, help to determine whether that person fits in the good prognosis or the poor prognosis group:

1. *History of adjustment prior to onset of illness.* This has often been regarded as perhaps the most important factor. If the person seemed relatively normal prior to the obvious onset of schizophrenia, then the chances for a better outcome are greater than for those who may have seemed "odd," withdrawn, or delinquent since childhood.
2. *Gender.* Women have a much better prognosis for schizophrenia than men. Women have a later AGE AT ONSET than men, shorter hospital stays, and fewer relapses.
3. *Family history.* A family history of schizophrenia often indicates a poor prognosis, especially if the blood relationship is close between the INDEX CASE and the affected relatives. A good outcome is suggested by no family history of schizophrenia or psychiatric disorders, or, as it turns out, if there is a history of depression or bipolar illness in the family.
4. *Age of onset.* The earlier schizophrenia develops and is diagnosed in a person, the worse the potential outcome will be. Alternatively, those persons who develop schizophrenia relatively late (especially after age 30) have a much better prognosis.
5. *Suddenness of onset.* If the first symptoms come on rapidly, then the prognosis is much better than if the symptoms developed over a period of months or years.
6. *Precipitating events.* If there is a definite stressful situation or event that is pointed to as the starting point for the onset of the schizophrenic symptoms, the prognosis is good. This corresponds to the "reactive schizophrenia" notion of a subtype that may be more environmentally induced and less genetically and organically based.
7. *CT scan findings.* If a person who is diagnosed with schizophrenia is given a CT scan and the ventricles of the brain are found to be enlarged, this is an indication of poor prognosis. If the CT scan results are normal, then the prognosis is much better.
8. *Response to medication.* One of the strongest indicators of prognosis is response to ANTIPSYCHOTIC DRUGS. If the initial response to antipsychotic medication is weak, then the prognosis is far worse, especially since these drugs are the first line of defense against the debilitating effects of schizophrenia.
9. *Clinical symptoms.* Torrey lists a number of symptoms that may appear during the first schizophrenic episode that he states "can be used as predictive factors." Initial symptoms that indicate a good outcome are the presence of (a) paranoid symptoms, (b) catatonic symptoms, (c) depression or other emotions, (d) a previous diagnosis of schizoaffective disorder, (e) symptoms that are not typical of schizophrenia, and (f) confusion ("I don't understand what is happening to me!" is an example Torrey gives). Initial symptoms that indicate a poor outcome are the presence of (a) NEGATIVE SYMPTOMS such as flat or blunted affect, apathy, extreme social withdrawal, poverty of speech, blocking, etc., and (b) obsessive and compulsive symptoms.

See also COURSE AND OUTCOME OF SCHIZOPHRENIA; GENDER DIFFERENCES IN SCHIZOPHRENIA; HIGH-RISK STUDIES; LONGITUDINAL STUDIES; PROCESS-REACTIVE DISTINCTION IN SCHIZOPHRENIA, THE.

Stephens, J. H. "Long Term Prognosis and Follow-up in Schizophrenia," *Schizophrenia Bulletin* 4 (1978): 25–47.

Torrey, E. F. *Surviving Schizophrenia: A Family Manual.* 2nd ed. New York: Harper & Row, 1988.

projection In Sigmund FREUD's psychoanalysis, projection is a defense mechanism in which feelings, qualities, or wishes that the person refuses to recognize or are rejected in him- or herself are expelled ("projected") from the self and located in another person, group, or thing. Projection is one of the most primitive of the defense mechanisms and is prevalent in the psychotic disorders,

particularly those involving PARANOIA or paranoid delusions. In fact, Freud first became aware of the phenomenon of projection in 1895–96 when studying the mental processes involved in paranoia.

projective tests Psychological tests that attempt to infer qualities of an individual's personality by analyzing the free responses he or she gives to selected stimuli. The idea is based on FREUD's concept of PROJECTION. The answers given on a projective test are thought to contain information about the unconscious wishes, fears, and desires within a person, as well as give an idea of how, at a more conscious level, the person constructs reality and how approaches are taken to problem solving. Projective tests give a good idea of how strong a person's defense mechanisms are, thereby indicating how strong the ego is and how well the person can deal with the demands of life and of reality. Projective tests can use structured stimuli (such as words for the Word Association Test, or charcoal drawings for the Thematic Apperception Test) or unstructured stimuli (such as the various inkblot tests, especially the Rorschach). What is interesting about the history of projective tests is that they were first developed by clinicians using institutionalized people with dementia praecox (schizophrenia) and other serious mental disorders.

C. G. JUNG (1875–1961), the Swiss psychiatrist and psychoanalyst, was the first to use a projective test for diagnostic purposes with people with mental disorders. Even though the Word Association Test had been used by others in previous studies to study the way the "normal," rational, conscious mind works, Jung used the association test to discover the unconscious feelings, wishes, fears, and desires that revealed something about the deeper aspects of the human personality. He experimentally demonstrated the phenomenon of COMPLEXES using these tests, and his published research (which appeared in journals between 1904 and 1910) made him world famous.

Swiss psychiatrist Hermann Rorschach (1884–1922) initially invented an inkblot test to examine the fantasy capacity of successful art students versus less talented ones. Although Rorschach conducted his initial experiments with the inkblots in 1911, over the years he experimented with more than 300 psychiatric patients in asylums and clinics in Switzerland as well as normal persons. Many of the institutionalized patients had psychotic disorders, such as schizophrenia and manic-depressive psychosis, and so it is with these types of patients that Rorschach fine-tuned his famous test. He finally published the results of his studies in 1921 in his famous book *Psychodiagnostik* (Psychodiagnostics).

Projective tests for the purposes of diagnosing schizophrenia (or other mental disorders) has fallen into disrepute. From a scientific standpoint, they are unreliable.

Jung, C. G. *Experimental Researches: The Collected Works of C. G. Jung.* Vol. 2. Princeton, N.J.: Princeton University Press, 1973.

Rabin, A. I. "Projective Methods: A Historical Introduction." In *Assessment with Projective Techniques: A Concise Introduction,* edited by A. I. Rubin. New York: Springer, 1981.

Rorschach, H. *Psychodiagnostik.* Bern und Leipzig: Ernst Bircher Verlag, 1921.

Weiner, I. B. *Psychodiagnosis in Schizophrenia.* New York: Wiley, 1966.

prolonged sleep therapy See SLEEP TREATMENT.

Prolixin See ANTIPSYCHOTIC DRUGS.

propfschizophrenia A now-defunct term for a type of schizophrenia that was only thought to be found in a small number of persons who were mentally retarded. It was considered to have an onset after puberty and was characterized by paranoid episodes with delusions and hallucinations. *Propfhebephrenia* is another term formerly used for the same concept. *Oligophrenia* was a term used for "mental defective" or "idiots" (as the mentally retarded were termed earlier in this century), and propfschizophrenia was often referred to as a variety of this class of disorders.

propositus See PROBAND.

protein factors hypothesis Since the time of Emil KRAEPELIN, the search for a toxin or other substance that was to be found in the blood of schizophrenics has been reported from time to time. In many studies the blood or urine of schizophrenics has been analyzed, and substances that were assumed to be protein factors have been singled out as being possibly related to the cause of the disorder, or at least to the expression of its symptoms. Often these substances were isolated and then injected into other organisms (e.g., cells, plants, animals), which then changed their usual behavior, thus indicating that quite possibly these substances were affecting the behavior of humans.

See also AUTOINTOXICATION; TRANSMETHYLATION HYPOTHESIS.

Frohman, C. E., et al. "Evidence of a Plasma Factor in Schizophrenia," *Archives of General Psychiatry* 2 (1960): 255–262.

pseudoabstraction A characteristic of the thought and language of some schizophrenics who begin to use polysyllabic, highly abstract words, perhaps taken from philosophy or the sciences, but without using them meaningfully or in the proper context. Silvano ARIETI remarks that in a patient who is exhibiting pseudoabstraction, "If we ask him to explain what he means with these big words, he will be unable to do so. He will use other big words to accentuate the feeling of confusion. . . . Various German authors have very appropriately called this characteristic 'talking on stilts.'"

Arieti, S. *Interpretation of Schizophrenia.* 2nd ed. New York: Basic Books, 1974.

pseudocyesis See PREGNANCY DELUSIONS.

pseudodementia Sometimes a person may exhibit signs and symptoms of an ORGANIC MENTAL SYNDROME such as dementia without having any underlying brain disease process. Sometimes persons who are experiencing a major depressive episode may appear to have DEMENTIA due to the seriousness of the vegetative signs. In rarer cases, the PRODROMAL PHASE of schizophrenia may resemble dementia in extreme instances.

pseudodementia syndrome See GANSER'S SYNDROME.

pseudologia fantastica The clinical term for "pathological lying." The term is coined from two Greek words meaning "elaborate false speech."

pseudoneurotic schizophrenia See BORDERLINE SCHIZOPHRENIA.

pseudoschizophrenia syndrome A type of epilepsy that resembles schizophrenia and is supposedly characterized by its "hypnoid states." This concept has never gained wide usage. Although the relationship between convulsive disorders such as epilepsy and schizophrenia have been investigated, no support has ever been found for a pseudoschizophrenia syndrome.

Zec, N. R. "Pseudoschizophrenic Syndrome," *Psychiat. et Neurol.* 149 (1965): 197–209.

psychedelic experiences in schizophrenia With the advent of the "psychedelic revolution" in the mid-1960s, the metaphors supplied by the types of experiences reported by persons who had ingested hallucinogenic substances (e.g., LSD, mescaline) came to be applied to numerous areas of human experience. In particular, the psychedelic metaphors were applied to the subjective experience of psychosis. Because many persons in the PRODROMAL PHASE of schizophrenia and other psychotic disorders report perceptual anomalies and other phenomena related to ALTERED STATES OF CONSCIOUSNESS, many investigators during this period

began to turn their attention to the similarities between drug-induced hallucinatory states of consciousness and psychotic experience (see PERCEPTUAL ANOMALIES IN SCHIZOPHRENIA). The most notable attempt at such a comparison was published by Malcom Bowers and Daniel X. Freedman in 1966.

Due to a long-standing tradition of romanticizing "madness," psychotic experiences were compared with psychedelic experiences as possible "transcendent" experiences, notably by R. D. LAING. However, in a sharp critique of Laing's "psychedelic model" of schizophrenia, Miriam Siegler, Humphrey Osmond, and Harriet Mann constructed a detailed comparison of the subjective experiences of psychedelic experiences with those of schizophrenia and found many disturbing differences. They make the analogy of the difference between good dreams, bad dreams, and nightmares, with psychosis represented by the latter and psychedelic experiences by the first two. With the metaphoric fad of the 1960s no longer in fashion, the psychedelic model of schizophrenia is no longer discussed in the literature on this disorder.

See also SUBJECTIVE EXPERIENCES IN SCHIZOPHRENIA.

Bowers, M., and D. X. Freedman. "Psychedelic Experiences in Acute Psychosis," *Archives of General Psychiatry* 15 (1966): 240–248.

Laing, R. D. "Transcendental Experience in Relation to Religion and Psychosis," *Psychedelic Review* 6 (1965): 7–15.

Siegler, M., and H. Osmond. *Models of Madness, Models of Medicine.* New York: Macmillan, 1974.

Siegler, M., H. Osmond, and H. Mann. "Laing's Models of Madness." In *R. D. Laing and Anti-Psychiatry,* edited by R. Boyers and R. Orrill. New York: Harper & Row, 1971.

psychesthenia A disorder caused by the "exhaustion" of the nervous system. It is related to the concept of NEURASTHENIA in that the "wear and tear" of the "nerves" was thought to lead to a "nervous breakdown," which may result in some cases in more serious disorders such as schizophrenia or one of the other psychotic disorders. Pierre JANET introduced the term in 1903 in his book *Les obsessions et la psychasthénie.*

psychiatric social work In many instances, it is the nonmedical professionals such as social workers who are in the "frontlines" of the battle against the inhumane treatment of the mentally ill. It was only in the 1920s that the specialization of psychiatric social work came into existence, largely through the proliferation of "child guidance clinics" in the United States and England. In the decades since, psychiatric social workers have provided critical services for people with mental disorders in virtually every aspect of community care.

psychiatry The medical profession devoted to the study and treatment of mental disorders. The word *psychiatry* was first used in English in 1846 to refer to this profession. Other terms have been *medical psychologist* or *alienist,* and in an earlier age these physicians were also known as mad-doctors or lunatic doctors. The word is derived from the German term *psychiaterie,* which was first used in 1803 by the physician and student of mental illness Johannes Christian Reil (1759–1813) in a book entitled *Rhapsodies in the Application of Psychic Methods in the Treatment of Mental Disturbances.* The word *psychiatrie* was first used by Johann Christian Heinroth (1773–1843), and Ernst von Feuchtersleben (1806–1849) used the term *psychiatrics* for the profession in 1845.

Hunter, R. A., and I. Macalpine, eds. *Three Hundred Years of Psychiatry, 1535–1860: A History Presented in Selected English Texts.* Oxford: Oxford University Press, 1963.

psychoanalysis See DIRECT ANALYSIS.

psychoanalytic theories of schizophrenia Sigmund FREUD coined the term *psychoanalysis* in 1896 to refer to his philosophy and system of therapy that was based on a careful analysis of internal unconscious processes. Although Freud did treat some

manic-depressives, he never treated schizophrenic patients (unlike his colleague, C. G. JUNG, who held a position in a psychiatric hospital for nine years). Freud was very pessimistic about the treatment of schizophrenia with psychoanalysis and tended to discourage it. He left few writings on the subject, but this gap was filled by those psychoanalysts who came after him, notably Karl Abraham, Paul Federn, Melanie Klein, Frieda FROMM-REICHMANN, Leland Hinsie, John Rosen, Otto Fenichel, and Harold Searles.

According to Freud, schizophrenia involves a withdrawal of libido from the objects of the external world and into the self. This withdrawal of energy into the self was termed by Freud a regression into a state of primary narcissism similar to that found in infants in a period before there is any differentiation between ego, superego, or id and before there is any discriminative ability between the inner and outer worlds. Because of this, Freud believed no transference could take place between the schizophrenic patient and the analyst, and therefore no treatment could be possible. Because the regression to a state of primary narcissism characterized psychoses, he called them narcissistic neuroses (as opposed to transference neuroses, which were the usual phenomenon in psychoanalysis). Freud wrote in 1924 that in the narcissistic neuroses "the resistance is unconquerable" and that psychoanalytic techniques therefore "must be replaced by others; and we do not know yet whether we shall succeed in finding a substitute."

The central aspect of the schizophrenic experience, according to most psychoanalytic theorists, is the initial break with reality, after which the ego returns to its original infantile, undifferentiated state in which it is submerged or dissolved wholly or partially into the id. Although such regressions may be found in normals, the schizophrenic regresses to a fixation point in development that is further back than any encountered in the neuroses.

Psychoanalytic theories of schizophrenia dominated American psychiatry from the 1920s until the 1960s. Since biological research had turned up no definite cause of schizophrenia, psychoanalysts argued that this failure was in fact a confirmation of their anti-biological, anti-genetics, anti-laboratory science biases. Psychoanalysis continued to emphasize the exclusive master-apprentice model of medical training that had been challenged circa 1900 by those physicians who wanted to base medical therapeutics on laboratory findings, not general clinical "impressions" or vivid anecdotes. However, by 1980s it had become resoundingly clear that there was absolutely no empirical support from cognitive neuroscience research for any of the claims made by Freud, Jung, Adler, and their followers.

Historians of science now view psychoanalysis as a pseudoscience, not a scientific discipline. Psychoanalysis is to the 20th century what phrenology was to the l9th century and animal magnetism was to the 18th century.

Cioffi, F. *Freud and the Question of Pseudoscience.* Chicago: Open Court, 1998.

Crews, F. *Unauthorized Freud: Doubters Confront a Legend.* New York: Viking, 1998.

Dolnick, E. *Madness on the Couch: Blaming the Victim in the Heyday of Psychoanalysis.* New York: Simon & Schuster, 1998.

Gellner, E. *The Psychoanalytic Movement: The Cunning of Unreason.* Evanston, Ill.: Northwest University Press, 1996.

psychogenic psychoses See REACTIVE PSYCHOSES.

psychological research Although the search for the biological basis for schizophrenia and the psychotic disorders has been a primary focus of investigation since the 18th century (see ABLATION STUDIES), psychological experiments have given us much useful information on cognition, perception, learning, language, memory, and behavior in these disorders. The current trend is to correlate the overall findings of these studies and match this knowledge with the new discoveries gained by biochemical techniques, brain imaging, and other areas of scientific inquiry.

Francis Galton founded the first psychological laboratory in England in 1884, and his Anthropometric Laboratory collected data on more than 9,000 subjects. Galton charged his subjects a fee

for providing them with their test results. However, the first laboratory designated solely for the application of the experimental method to psychology was founded in Leipzig, Germany, by Wilhelm Wundt in 1879. In the 1880s, many Americans flocked to Germany to learn the experimental method (generally from Wundt), and subsequently between 1888 and 1895 many universities and hospitals set up "psychological laboratories" to conduct research. Harvard University was probably the first to do so in the United States, but the eminent American philosopher and psychologist William James (1842–1910), who taught at Harvard, was not impressed with the experimental method. Ridiculing the stereotypical obsessive-compulsive style of the Germans, James snidely remarks in the first volume of his landmark *Principles of Psychology* (1890), "This method taxes patience to the utmost, and could hardly have arisen in a country whose natives could be *bored*. Such Germans as Weber, Fechner, Vierordt and Wundt obviously cannot …"

Emil KRAEPELIN was an admiring disciple of Wilhelm Wundt and learned the techniques of psychological research from him. Kraepelin was one of the first to conduct psychological association experiments on subjects who were given various drugs. Since Kraepelin defined DEMENTIA PRAECOX, he was arguably the first to conduct experimental research on this disorder.

A useful summary of the psychological research on schizophrenia can be found in a review article by A. I. Rabin, Stuart Doneson, and Ricky Jentons in L. Bellak's *Disorders of the Schizophrenic Syndrome*.

Boring, E. G. *A History of Experimental Psychology.* New York: Century Company, 1929.

James, W. *The Principles of Psychology.* 2 vols. New York: Henry Holt, 1890.

Rabin, A. I., et al. "Studies of Psychological Functions in Schizophrenia." In *Disorders of the Schizophrenic Syndrome,* edited by L. Bellak. New York: Basic Books, 1979.

psychomotor agitation Excessive movement that is associated with inner tension. Often the activity is repetitious and nonproductive. When the agitation is at a high level, some persons may scream, shout, or complain loudly. People with psychomotor agitation can be seen pacing, pulling at their clothes or hair, wringing their hands, being unable to sit in one place for more than a few seconds, etc. When this type of behavior is a side effect of ANTIPSYCHOTIC DRUGS, the behavior is called AKATHISIA.

psychoneurosis A nonpsychotic mental disorder of a purely psychological (and not organic) origin. The word was introduced by Swiss neuropathologist Paul Charles Dubois (1848–1918) and was often used by Sigmund FREUD.

psychopathology The study of mental disorders. Despite the fact that mental disorders have been reported since antiquity, the clinical and descriptive categories now in use were only developed in the 19th century.

See also KAHLBAUM, KARL; NOSOLOGY.

Berrios, G. E. "Descriptive Psychopathology: Conceptual and Historical Aspects," *Psychological Medicine* 11 (1984): 677–688.

psychose passionelle See EROTOMANIA.

psychosis The term *psychosis* was coined by the Austrian physician and poet Ernst von FEUCHTERSLEBEN in 1845. Today psychosis refers to a MENTAL DISORDER in which there is gross impairment in reality testing (a "break with reality") and the creation of a new reality. Although the word *psychoses* first appeared in the early part of the 19th century, it has only been used in this sense since the end of that century, encompassing phenomena that were formerly described by the terms *insanity, alienation,* and *DEMENTIA.* Throughout most of the 19th century the word *neuroses* referred to an enormous class of diseases that included all the insanities, most neurological conditions, all the present-day neuroses, and some medical disorders—thus, they

were considered "organic" in origin. The word *psychoses* instead referred to psychological or experiential states, and the terms *neuroses* and *psychoses* were not dichotomous and did not depend upon one another for definition. By the end of the 1800s the new classificatory systems of Karl KAHLBAUM and especially Emil KRAEPELIN introduced the modern concept of psychosis and drastically reduced the number of the "insanities."

Two classification dichotomies that were popular in the late 19th century and survived into the early part of the 20th are (a) functional versus organic psychoses (see FUNCTIONAL PSYCHOSES), and (b) exogenous (in neurology, diseases due to toxins and infections) versus endogenous psychoses (due to inner or constitutional factors).

Beer, M. D. "The Importance of the Social and Intellectual Contexts in a Discussion of the History of the Concept of Psychosis," *Psychological Medicine* 25 (1995): 317–325.

Berrios, G. E. "Historical Aspects of Psychoses: 19th-century Issues," *British Medical Bulletin* 43 (1987): 484–498.

Feuchtersleben, E. von. *Lehrbuch der aerztlichen Seelenkunde.* Vienna: Carl Gerold, 1845.

psychosis gene See GENETICS STUDIES.

psychosis of association See FOLIE À DEUX.

psychosocial stressors Psychological or social sources of stress that can exacerbate mental disorders, including psychotic disorders. Severe tragedies (the death of loved ones) can even lead to the development of such disorders, as can the developmental phases of life (e.g., the stresses of adolescence, childbirth). The types of psychosocial stressors that clinicians are advised to document by severity are (a) conjugal (marital and nonmarital), for example, engagement, marriage, discord, separation, divorce, death of a spouse; (b) parenting; (c) other interpersonal problems; (d) occupational; (e) financial; (f) living circumstances, for example, change in residence; (g) developmental phases of life; (h) physical illness or injury; and (i) family factors.

psychosurgery The history of psychiatry can only be understood in the context of the history of medicine. As new biological discoveries, theories of disease, or treatments for disease were introduced into the practice of medicine, it was only natural that they be applied to the most mysterious class of diseases of all—the insanities. The advance of surgery as a technique for treating or curing disease began in earnest after the introduction of anesthesias (starting in 1846 with ether) and the general adoption of techniques of antisepsis (in the 1860s and 1870s) such as hand washing or the treating of the surgeon's hands with "Listerizing" preparations (the mouthwash Listerine is a descendant of these substances, bearing the name of Joseph Lister, a pioneer of antiseptic surgery). It was only natural that advances in surgical procedure would be applied to solving the problems of psychiatry. The three areas of the body that were the focus of psychosurgery were the brain, the mouth (dentistry), and the abdomen.

Brain surgery Although ancient peoples performed operations on the skulls and perhaps the brains of ill individuals (a phenomenon known as TREPHINING), the very first brain operation that specifically intended to treat or cure psychotic disorders was performed in Marin, Switzerland, in December 1888. Gottlieb Burckhardt (1836–1907), a Swiss psychiatrist and director of a private psychiatric clinic, operated (unsuccessfully) on the brains of six persons with psychotic disorders. He published his findings in an article in the *Allgemeine Zeitschrift für Psychiatrie* in 1891. No more brain operations to treat or cure mental disorders were performed for 47 years. It was not until November 1935 that neurologist EGAS MONIZ (1874–1955), working with neurosurgeon Almeida Lima, performed the first LEUCOTOMY on an asylum patient in Lisbon, Portugal. The following year, neuropathologist Walter FREEMAN (1895–1972) and neurosurgeon James Watts (1904–94) performed the first LOBOTOMY on a patient at George Washington University Hospital in Washington, D.C. After 1942, "psychosurgery" gained in prominence and was widely practiced in

the United States and Canada by the late 1940s. The development of the "icepick technique" of TRANSORBITAL LOBOTOMY by Freeman in 1946 led to the rapid spread of psychosurgical treatments for schizophrenia and other mental illnesses (including depression, anxiety, and other less severe conditions). Whereas major surgery in an operating room was required for traditional lobotomies, leucotomies, or TOPECTOMIES, a transorbital lobotomy only required a local anesthetic and could be performed in outpatient settings (which was where Freeman first tried it out). As historian Jack Pressman documented in his book, *Last Resort: Psychosurgery and the Limits of Medicine* (1998), psychosurgery "made sense" in the context of its era and was supported by some of the most important figures in medicine and psychiatry. Egas Moniz won the Nobel Prize in Medicine in 1949 for his leucotomy treatment. After the widespread introduction of ANTIPSYCHOTIC DRUGS in asylums after 1954, psychosurgery and other "somatic" treatments such as INSULIN COMA THERAPY and ELECTROSHOCK THERAPY began to decline in use. By the 1960s, brain operations to alleviate mental disorders had virtually disappeared (except for the treatment of severe seizure disorders).

Ovariotomies (oophorectomies) In 1872 an American surgeon, Robert Battey, published an article on "normal ovariotomy" in the *Atlanta Medical and Surgical Journal* that inspired the surgical removal of the ovaries in perhaps as many as 150,000 women in America, Britain, and Germany by 1906. These operations were much less welcome in France. Known as "Battey's operation," it was performed on otherwise normal, healthy women as a method of preventing later "incurable diseases." It was quickly adopted by psychiatrists who applied it to incurably insane women in asylums.

In 1893 the first large-scale experimental surgical program for the treatment of insanity was approved for a clinical trial at the Norristown Insane Asylum in Pennsylvania. The plan, proposed by Dr. Joseph Price, was to perform "oophorectomies" on "fifty patients selected as being cases likely to be benefited with this operation." However, when the fifth patient to be operated on died during surgery, the program was halted. The suspended program quickly became a political issue in Pennsylvania, leading to an investigation by the Lunacy Committee of the State Board of Charities. A member of the committee called the procedures "illegal . . . brutal and inhuman, and not excusable on any reasonable ground . . . it is regarded by the best medical authorities as a useless and improper expedient for the cure or relief of insanity, and the operation of oophorectomy in a public hospital upon indigent insane women must be regarded as largely experimental, and for that reason bound to reflect upon hospital authorities now boasting of modern humane methods."

The collapse of the clinical trial in Pennsylvania did not deter individual asylum superintendents from approving such surgeries on a limited case-by-case basis in their own institutions. In the mid-1890s ovariotomies, hysterectomies, and male castrations had been performed on asylum patients at a great many institutions, but by the end of that decade critics of the procedure slowed the spread of these experimental procedures. In the early 1900s such surgeries were still performed but as part of the eugenics program to halt DEGENERATION. This was especially true in the United States, where new state laws advocating forced sterilization for the "morally insane," the mentally ill, the mentally retarded, and criminals were in effect after 1907. After July 1918 Henry A. COTTON (1877–1933) of the New Jersey State Hospital at Trenton resumed this procedure along with a whole host of other forms of surgery to eliminate sites of FOCAL INFECTION AS A CAUSE OF MENTAL DISORDER.

Thyroid surgery Following the classic AUTOINTOXICATION theory that an overproduction of "internal secretions" from glands poisoned the brain and caused mental illness, Newdigate M. Owensby (1882–1952), chief physician at the Bay View Asylum in Baltimore, Maryland, hypothesized that the symptoms of DEMENTIA PRAECOX were caused by an oversecretion of the thyroid gland. The oversecretion was thought to be caused by diseased blood vessels in the gland. According to the December 20, 1907, edition of the *New York Times,* in July 1907 Owensby chose "the worst patient in the asylum," and cut away the diseased portion of the thyroid, "giving opportunity for new blood vessels to form." In October 1907 the man was discharged, symptom free. By December 1907 Owensby had operated on at least four

other patients, reporting therapeutic success in all of them. There is no indication that Owensby continued these experiments after 1907. Owensby later become one of the first psychiatrists in Georgia, achieving notoriety in 1940 for using metrazol convulsive therapy to attempt to reverse homosexuality in five male and one female patient.

Dental surgery In the very first years of the 20th century, reports that psychotic symptoms were reduced or eliminated after rotting or impacted teeth were pulled led to an increase in such procedures. As a site of focal infections that could spread from the mouth to the brain, the logic of removing teeth as a treatment method for the mentally ill "made sense" within an era dazzled by the "germ theory of disease." At Trenton, Henry Cotton installed a dental operating clinic in 1919 and routinely had all the teeth of newly admitted patients removed. He also convinced his wife and his two sons to have all their teeth removed as a preventive measure. The removal of teeth was also a major focus of treatment for psychiatrist Thomas C. Graves in Birmingham, England, in the 1920s and 1930s.

Abdominal surgery In May 1916, Chicago medical professor and specialist in the surgery of the abdomen and head, Bayard Taylor HOLMES, was the first to perform abdominal surgery specifically for the treatment and cure of dementia praecox (schizophrenia). The patient was his own son, Ralph Loring Holmes, who had developed dementia praecox in 1905 at the age of 17 as a first-year medical student. The previous year, Holmes had devised an AUTOINTOXICATION theory of the cause of dementia praecox based on the idea that fecal stasis in the colon led to the production of toxic amines (histamine) that was carried to the brain by the bloodstream and caused psychosis. Holmes or his associates performed a series of cecostomies on at least 22 persons diagnosed with dementia praecox, leaving a hole (stoma) open near the appendix through which a hose was inserted daily for constant irrigations. His son Ralph, the first to receive this experimental surgery for dementia praecox, died four days after the operation at Lakeside Hospital in Chicago. Abdominal surgeries involving the whole or partial removal of the colon, stomach, rectum, cervix, testes, and so on were performed on more than 2,000 patients at the New Jersey State Hospital at Trenton between 1918 and 1933. Hundreds died from postoperative infections and other complications. In England, Thomas Graves continued to perform such operations well into the 1930s.

Surgery on the brain, reproductive organs, mouth, and abdomen is no longer performed for the treatment of schizophrenia or any other mental disorder.

Anonymous. "An Experiment in Castration," *Medical Record* 43 (1893): 433–434.

Dally, A. *Fantasy Surgery 1880–1930.* Atlanta and Amsterdam: Rodopi, 1996.

Pressman, J. *Last Resort: Psychosurgery and the Limits of Medicine.* Cambridge: Cambridge University Press, 1998.

Reilly, P. R. *The Surgical Solution: A History of Involuntary Sterilization in the United States.* Baltimore: Johns Hopkins University Press, 1991.

Scull, A. *Madhouse: A Tragic Tale of Megalomania and Modern Medicine.* New Haven, Conn.: Yale University Press, 2005.

Stone, J. L. "Dr. Gottlieb Burckhardt—the Pioneer of Psychosurgery," *Journal of the History of the Neurosciences* 10 (2001): 79–92.

psychotherapy of schizophrenia Because people with schizophrenia have so many personal problems associated with daily living, most find themselves in some form of psychotherapy at some point in their lives, and this can be supportive for them. The earliest recorded cases of individual psychotherapy with schizophrenic persons can be attributed to Swiss psychiatrist and psychoanalyst C. G. JUNG at the BURGHÖLZI HOSPITAL in Switzerland. There is a vast literature on the psychotherapy of schizophrenia, and the various therapeutic modalities that have been tried include individual, group, family, and a whole host of "brand name" psychotherapeutic orientations.

Throughout most of the century the emphasis has been on the alleviation of the disease process itself with psychotherapy, but with the new emphasis on the organic basis of schizophrenia (and the discouraging results of psychotherapy on the disease itself), this goal is no longer deemed

justified. Instead, the focus has shifted to improving the psychosocial adaptation of individuals with schizophrenia, their vocational functioning, and the subjective well-being of these persons. Also, family therapy approaches have shifted away from viewing family dynamics as the cause of schizophrenia and now focuses instead on the potential influence of the family on the course of the illness and how family members may be taught strategies to make that influence more positive and reduce relapses (see EXPRESSED EMOTION).

In general, the well-controlled scientific research on the influence of psychotherapy on schizophrenics has tended to conclude that insight-oriented individual or group psychotherapy may be too intense for such individuals and perhaps worsen symptoms. Indeed, E. Fuller Torrey goes so far as to label psychoanalysis, insight-oriented therapy, and group psychotherapy as "ineffective treatments" in his book *Surviving Schizophrenia: A Family Manual* (1988). It is now generally recommended that psychotherapeutic treatments be psychoeducational and supportive in nature and used as an adjunct to treatment with ANTIPSYCHOTIC DRUGS.

See also FAMILY INTERACTION THEORIES; GROUP PSYCHOTHERAPY.

Mueser, K. T., and A. S. Bellack. "Psychotherapy for Schizophrenia." In *Schizophrenia,* edited by S. R. Hirsch and D. R. Weinberge. London: Blackwell Science, 1995, pp. 626–648.

psychotic disorders in *DSM-IV-TR* According to the most recent revision of the most widely used diagnostic manual for mental disorders in North America, *DSM-IV-TR* (2000), the disorders listed below are considered to be characterized by "psychosis" (a clear break with reality, often characterized by delusions, hallucinations, disorganized thought processes, bizarre and/or disorganized behavior, and a decline in social and occupational functioning). Entries for each can be found in this book.

- Schizophrenia (paranoid type, disorganized type, catatonic type, undifferentiated type, residual type)
- Schizophreniform Disorder
- Schizoaffective Disorder (bipolar type, depressive type)
- Delusional Disorder (erotomanic types, grandiose type, jealous type, persecutory type, somatic type, mixed type, unspecified type)
- Brief Psychotic Disorder (with marked stressors [brief reactive psychosis], without marked stressors, with postpartum onset)
- Shared Psychotic Disorder (Folie à Deux)
- Psychotic Disorder Due to a General Medical Condition
- Substance-induced Psychotic Disorder
- Psychotic Disorder Not Otherwise Specified

There may also be a primary diagnosis of a mood disorder that includes psychotic features. Psychotic features may be specified for Major Depressive Disorder, Single Episode; Major Depressive Disorder, Recurrent; Bipolar I Disorder, Single Manic Episode; Bipolar I Disorder, Most Recent Episode Manic; Bipolar I Disorder, Most Recent Episode Mixed; Bipolar I Disorder, Most Recent Episode Depressed; and Bipolar II Disorder, Depressed.

psychotic disorders in *ICD-10* According to the WORLD HEALTH ORGANIZATION, the following psychotic disorders included in *ICD-10* (1992) can be found in all countries of the world. Although this manual strives to be culture-free, it still reflects the major traditions of European PSYCHIATRY of the past 150 years. Entries for the major disorders below are included in this book.

- Schizophrenia (paranoid, catatonic, hebephrenic, residual, undifferentiated, simple, postschizophrenic depression)
- Schizotypal Disorder
- Persistent Delusional Disorder
- Acute and Transient Psychotic Disorders
- Induced Delusional Disorders
- Schizoaffective Disorder
- Other Non-organic Psychotic Disorders
- Unspecified Non-organic Psychosis

psychotic jealousy See OTHELLO SYNDROME.

psychotogenic drugs Literally, "psychosis-causing drugs." With the severe and widespread substance-abuse epidemic following the "psychedelic revolution" of the 1960s, psychiatric facilities around the world have been flooded with individuals, many of them young (see YOUNG ADULT CHRONIC PATIENTS), whose substance abuse has led to permanent psychotic disorders. Such persons with a psychotic disorder and a history of chronic substance abuse are called dually diagnosed patients. Current research studies are beginning to find that premorbid psychotogenic drug use (e.g., cocaine, PCP, LSD, marijuana) contributes to the development of psychotic disorders and may hinder the effectiveness of ANTIPSYCHOTIC DRUGS (a phenomenon called neuroleptic refractoriness), especially at the beginning of the illness.

Bowers, M. B., Jr., et al. "Psychotogenic Drug Use and Neuroleptic Response," *Schizophrenia Bulletin* 16 (1990): 81–87.

psychotomimetic Literally "psychosis-mimicking." Hallucinogenic (psychedelic) drugs were for a time referred to as "psychotomimetic drugs" because it was thought they could mimic the subjective experience of psychosis in anyone who ingested them. Prior to the banning of research using psychedelic drugs in the 1960s, some investigators administered such drugs to research subjects so as to better understand various dimensions of the psychotic disorders (see PSYCHOTOGENIC DRUGS). This sort of research has a long history dating from the 17th century. In Immanuel Kant's published lectures on "anthropology" (what we would now call empirical psychology), he cites the efforts of researchers to induce an "artificial insanity" through psychotomimetic drugs:

> On the other hand, attempts to observe oneself in a condition which approaches derangement, produced in oneself voluntarily and by physical means, in order to better understand the involuntary through such observations, indicate that one has understanding enough to investigate the sources of the phenomenon. But it is dangerous to perform experiments with the mind, and to make it disordered to a certain extent, for the sake of observing it and investigating its nature by means of the features which may be discovered in such experiments. Thus Helmont reports, after consuming a certain dose of *napell* (a poisonous root), having the unmistakable feeling as if he thought in his stomach. Another doctor increased his consumption of camphor, little by little, until it appeared to him as if everything along the street were in a great tumult. Still others have experimented on themselves with opium so long that they felt a weakening of the mind whenever they stopped using more of this brain-stimulant. An artificial insanity can easily become a real one.

See also TRANSMETHYLATION HYPOTHESIS.

Kant, I. *The Classification of Mental Disorders,* trans. C. T. Sullivan. Doylestown, Pa.: The Doylestown Foundation, 1964 [1798].

psychotropic See NEUROLEPTIC.

puerperal insanity Another name for POSTPARTUM PSYCHOSIS.

pulse Since the days of ancient Greece and Rome and well into the 19th century, it was commonly believed that a physician could diagnose mental disorders simply by taking the afflicted person's pulse and determining the heartbeat rate. In his famous textbook of 1812, American physician Benjamin RUSH of Philadelphia reports that: ". . . seven-eighths of all the deranged patients in the Pennsylvania Hospital in the year 1811 had frequent pulses, and that a pardon was granted to a criminal by the President of the United States, in the year 1794, who was suspected of counterfeiting madness, in consequence of its having been declared by three physicians that that symptom constituted an unequivocal mark of intellectual derangement."

The diagnostic importance of the pulse was still so highly regarded at the end of the last century that 20 columns were given to it in Daniel Hack Tuke's famous *Dictionary of Psychological Medicine.*

Rush, B. *Medical Inquiries and Observations upon the Diseases of the Mind.* Philadelphia: Kimber & Richardson, 1812.
Tuke, D. H. "Pulse." In *A Dictionary of Psychological Medicine,* edited by D. H. Tuke. London: Churchill, 1892.

purging One of Pinel's three USUAL TREATMENTS for MENTAL DISORDERS around 1800, purgatives were given to patients to help them expel bad humors or other bodily toxins that were thought to be the cause of mental illness. Purgatives have been used for thousands of years for the treatment of mental illness, and the herb *hellbore* was used for this purpose until the end of the 19th century.

pyknic type One of the four physiological types identified by Ernst Kretschmer in the 1920s. It was a thick-torsoed type with rounded shoulders that tended to resemble an orangutan. Most pyknic types were thought by Kretschmer to be "circulars" (manic-depressives).

See also ASTHENIC TYPE; ATHLETIC TYPE.

Q, R

quetiapine See ANTIPSYCHOTIC DRUGS.

race and schizophrenia In the United States, blacks have a higher rate of schizophrenia than do whites. This conclusion has been confirmed across many studies. However, psychiatrist E. Fuller Torrey argues in his book *Surviving Schizophrenia: A Family Manual* that this may have more to do with geography and socioeconomic status than with racial differences or racism. Most of the studies that have found a higher rate in blacks have been conducted in dense urban areas, but those studies done in rural areas find that the schizophrenia rates in whites and blacks are the same. Therefore, Torrey concludes, "This argues strongly against race as being the cause of the difference. Rather it suggests that it is because blacks live in the inner city, and not because they are black, that they have a higher schizophrenia rate."

Torrey, E. F. *Surviving Schizophrenia: A Family Manual.* New York: Harper & Row, 1988.

Ray, Isaac (1807–1881) An American physician and legal scholar, Ray was one of the original 13 founders of the AMERICAN PSYCHIATRIC ASSOCIATION. His classic textbook, *Treatise on the Medical Jurisprudence of Insanity* (1838), is considered to be perhaps the most influential American psychiatric text of the 19th century.

Hughes, J. S. *In the Law's Darkness: Isaac Ray and the Medical Jurisprudence of Insanity in Nineteenth Century America.* New York: Oceana Publications, 1986.

rCBF The acronym for regional cerebral blood flow, a measurement used to study the relationship between cerebral metabolism and psychiatric disorders.

See also BRAIN IMAGING STUDIES.

reactive psychoses It has long been noted that BRIEF PSYCHOTIC EPISODES sometimes result from the experience of trauma or extreme and prolonged stress. Conditions that produce such "reactions" include combat, imprisonment, and involuntary commitment to a mental hospital. Based on his study of the psychology of prisoners, August Wimmer (1872–1937), director of the St. Hans Psychiatric Hospital near Roskilde, Denmark, published a study on psychotic disorders that arose in reaction to stress and that were "psychogenic" rather than the result of hereditary DEGENERATION (as proposed by French psychiatrist Valentin Magnan) or a combination of heredity predisposition and glandular AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX (as believed by Emil KRAEPELIN and Wilhelm Weygandt). The title of Wimmer's 1916 study was *Psykogene Sindssygdomsformer* (Psychogenic Forms of Mental Disease). Following Wimmer, these psychotic disorders were originally called psychogenic, but they were more often called reactive throughout the 20th century, with the two terms being used interchangeably. The term *reactive* gained ascendancy after 1927 when the German psychiatrist Kurt Schneider proposed three "abnormal psychic reactions":

(1) emotional syndromes
(2) paranoid states
(3) syndromes with a disturbance of conscience

According to Wimmer, psychogenic (reactive) psychoses are independent of schizophrenia and

MANIC-DEPRESSIVE ILLNESS, develop in a person with a "predisposed foundation," are caused by psychosocial stressors, and end in full recovery with no lasting deficit. A similar diagnostic concept was added to *DSM-IV* in 1980 under the label "Brief Reactive Psychosis," but this changed to "Brief Psychotic Disorder" in 1992 in *DSM-IV.* Under the *DSM-IV* definition, a triggering stressor or trauma is not necessary, as there are causes of postpartum psychosis and other psychotic disorders that have no apparent trigger.

Pillman, F., and A. Marneros. "Brief and Acute Psychoses: The Development of Concepts," *History of Psychiatry* 14 (2003): 161–177.

Wimmer, A. "Psykogene Sindssygdomsformer." In *Jubilee Publication, St. Hans Hospital 1816–1916,* edited by A. Wimmer, 85–216. Copenhagen: Gad, 1916.

reactive schizophrenia See PROCESS-REACTIVE DISTINCTION IN SCHIZOPHRENIA, THE.

reality testing The ability to "test" or evaluate the external world ("reality") objectively and to distinguish it from the internal psychological state. It is also the ability to discriminate ego boundaries between what is the self and what is nonself (the "I" versus the "not-I"). The term was coined by Sigmund FREUD in 1911 as *Realitätsprüfung.* The hallmark of PSYCHOSIS is that reality testing is impaired.

recessive In GENETICS STUDIES, the opposite of DOMINANT.

recombination The process by which a pair of homologous chromosomes exchange sections yielding a new combination of genes.

recoverable psychosis According to the classification system of Emil KRAEPELIN, the group of recoverable psychoses was characterized by its primary entity, MANIC-DEPRESSIVE ILLNESS. These were psychotic disorders that had exacerbations and remissions but did not lead to the gross cognitive deterioration of chronic, progressively worsening disorders such as dementia praecox.

recovery with defect The term describes those persons whose basic personality is permanently altered after recovery from their primary mental disorder. Today, such a condition in schizophrenia might be termed the RESIDUAL PHASE. This term was coined by the German physician K. G. Neumann (1744–1850).

reference, ideas of See IDEAS OF REFERENCE.

refrigerator mother The name for the cold, rejecting mother who would thereby induce autism in her child.

See also AUTISM, INFANTILE.

regression A concept introduced by Sigmund FREUD in 1900 in his classic book *The Interpretation of Dreams,* although he did not use the word until much later. Essentially, regression means a reversion to earlier forms of thought, object-relationships, or behavior that the individual had previously experienced. Thus, according to PSYCHOANALYSIS, persons with psychotic disorders are "regressed" because they show signs of returning to infantile modes of thought, behavior and experience. In DEGENERATION THEORY, "reversions to type" were found in the physical stigmata of criminals, idiots, and the insane.

See also PSYCHOANALYTIC THEORIES OF SCHIZOPHRENIA.

relapse, signs of Those people with schizophrenia who seem to fare the best are those who are aware of the signs of an impending relapse of an active phase of the illness and who therefore seek help. In a useful study of relapse by Marvin Herz and Charles Melville published in 1980, they found the following signs and symptoms of relapse to be the most frequently reported by patients and their families:

Patients Reported	Percent
being tense and nervous	80
eating less	72
trouble concentrating	70
trouble sleeping	67
enjoying things less	65
restlessness	63
not able to remember things	63
depression	61
being preoccupied with one or two things	60
seeing friends less	60
being laughed at, talked about	60

Families Reported	Percent
being tense and nervous	83
restlessness	79
trouble concentrating	76
depression	76
talking in a nonsensical way	76
loss of interest in things	76
trouble sleeping	69
enjoying things less	68
being preoccupied with one or two things	65
not able to remember things	60
hearing voices, seeing things	60

It is extremely important for family members and persons with schizophrenia to recognize these signs of relapse and to seek medical help immediately.

Herz, M. "Prodromal Symptoms and the Prevention of Relapse in Schizophrenia," *Journal of Clinical Psychiatry* 46 (1985): 22–25.

Herz, M. I., and C. Melville. "Relapse in Schizophrenia," *American Journal of Psychiatry* 137 (1980): 801–805.

religious delusions Religious delusions are quite common in the psychotic disorders. Persons may believe, for example, that they are God, Jesus Christ, or a prophet who relates messages from God to the world. Many of these delusions are also grandiose in nature.

remission The abatement of an illness. In schizophrenia, the period after a remission may still evidence residual deficits from the illness. Full remissions from schizophrenia apparently do occur, but they are extremely rare, and the few that are on record are an issue of controversy. A return to full premorbid functioning is also rare in schizophrenia.

See also RESIDUAL PHASE.

Renfield's syndrome A term first used by Richard Noll (1991) to refer to CLINICAL VAMPIRISM, since contemporary reports of people with this delusional disorder seem to develop the same sequence of symptoms as the human vampire Renfield in Bram Stoker's novel *Dracula* (1897).

Noll, R. *Vampires, Werewolves and Demons: Twentieth Century Case Reports in the Psychiatric Literature.* New York: Brunner/Mazel, 1991.

repression A term used by Sigmund FREUD (*Verdrängung* in the original German) for a psychological operation in which a person attempts to push away, expel, or keep in the unconscious representations (thoughts, images, memories) that are connected to an instinct. Repression occurs when it is determined that the expression of an instinctual urge, which is probably in itself pleasurable (e.g., sex), may have painful consequences. Repression is considered one of the most basic defense mechanisms for keeping threatening materials out of conscious awareness. Freud once wrote that "the theory of repression is the cornerstone on which the whole structure of psychoanalysis rests." According to psychoanalytic theory, the failure of repression in the psychotic disorders leads to HALLUCINATIONS and bizarre and inappropriate behavior.

See also PSYCHOANALYTIC THEORIES OF SCHIZOPHRENIA.

Laplanche, J., and J. B. Pontalis. *The Language of Psychoanalysis,* trans. D. Nicholson-Smith. New York: Norton, 1973.

research diagnostic criteria (RDC) In an effort to ensure that diagnostic groups of persons with

mental disorders have the same characteristics across different studies performed in different settings, several attempts have been made to set standard guidelines for selecting subjects for research. An early system was the FEIGHNER RESEARCH CRITERIA, but currently the most widely accepted criteria is the Research Diagnostic Criteria developed at the New York Psychiatric Institute. When research studies refer to "RDC schizophrenics," they are referring to schizophrenic subjects that fit the RDC definitional guidelines.

Endicott, J., et al. "Diagnostic Criteria for Schizophrenia: Reliabilities and Agreement between Systems," *Archives of General Psychiatry* 39 (1982): 864–889.

Spitzer, R. L., J. Endicott, and E. Robins. "Research Diagnostic Criteria: Rationale and Reliability," *Archives of General Psychiatry* 35 (1978): 773–782.

Reserpine See antipsychotic drugs.

residual phase The residual phase follows the active phase of the illness. In many ways, the clinical picture of the residual phase resembles many of the signs and symptoms of the initial PRODROMAL PHASE, except that the blunting or flattening of affect and a marked impairment in social and occupational functioning are found. Some DELUSIONS and HALLUCINATIONS may persist in the residual phase, but they may not be accompanied any longer by strong affect (e.g., a strong screaming reaction to the hearing of voices may not be found in the residual phase). The most common course of schizophrenia is a disease process characterized by acute exacerbations of symptoms followed by periods of residual impairment between active phases of the illness. During the first years of the disorder (some say five to 10 years), the residual impairment between episodes increases and then seems to plateau at some point for the remainder of the person's life. Depression is often present in the residual phase.

restraints See CHEMICAL RESTRAINTS; MECHANICAL RESTRAINTS.

retrospective ruminative jealousy A (usually) nonpsychotic delusional disorder related to the OTHELLO SYNDROME in which a person is obsessed with the past sexual activities of the current sexual partner or spouse. However, there is no delusion about present infidelity.

RFLP See MOLECULAR MARKERS.

right to refuse treatment In the United States, the legal principle has developed over a series of cases since 1975 that holds that no one admitted to a psychiatric facility for treatment, whether the commitment was voluntary or involuntary, can be forced to submit to any form of treatment against his or her will unless it is determined that a life-and-death emergency exists.

Applebaum, P. S. "The Right to Refuse Treatment with Antipsychotic Medications: Retrospect and Prospect," *American Journal of Psychiatry* 145 (1988): 413–419.

right to treatment In the United States, the legal principle has developed that when a psychiatric facility has assumed the responsibility of providing treatment for a person, that facility is then legally obligated to provide adequate treatment for that individual.

risk factors Most of what we have learned about the potential causes, courses, and outcomes of schizophrenia comes from epidemiological studies. In current epidemiological research in medicine, a distinction is being made between risk indicators or proxy markers and risk modifying factors. Risk indicators are any variables that precede an outcome (e.g., the first episode of schizophrenia) but are not causally related to that outcome (e.g., season of birth). *Risk modifying factors* is a term reserved for factors that appear to contribute to the cause of the outcome. Risk modifying factors can be fixed (for example, gender) or variable (e.g., amount and frequency of cannibis use), endogenous (e.g., genetics) or exogenous

(e.g., obstetric complications, maternal exposure to infections).

Family history/genetics The strongest risk factor correlated to developing schizophrenia is family history. Being biologically related to a person with schizophrenia has been found to be the greatest risk factor in developing schizophrenia in the future. Genetic relatedness is a key factor: the closer the blood relationship, the greater the risk for developing schizophrenia. Having a biological parent with schizophrenia is the strongest predictor of outcome for adult psychiatric disorders. This is one of the very few firm facts we know about schizophrenia.

Environment There is no single environmental factor that predicts a higher risk of developing schizophrenia. In persons who are biologically related to someone with schizophrenia, certain environmental or nongenetic risk factors have been identified as possible risk indicators or risk modifying factors. These are as follows:

Age and sex The vast majority of people who develop schizophrenia have their first episode somewhere between 15 and 24 years of age. For the vast majority of males the peak age of onset is 20 to 24 years old, then the rate remains at a constant low rate. In contrast, there is a small peak for females between 20 and 24 years old, followed by a constant low rate until age 35, after which it begins rising. Cases of late-onset schizophrenia are predominantly women.

Perinatal factors (maternal obstetric complications) Birth complications have been correlated with the later development of schizophrenia in studies dating back to the mid-1960s. The strongest findings are, in order:

(1) perinatal brain damage (any cause)
(2) brain damage due to hypoxia (lack of oxygen)
(3) Rh incompatibility
(4) pre-eclampsia
(5) low birth weight

Prenatal factors The strongest prenatal risk factor found thus far, ranking third behind family history and perinatal brain damage, is maternal bereavement. Unwantedness, famine, flood, and maternal depression are much lesser factors.

Infection Exposure to various infections during pregnancy have been linked to the later development of schizophrenia in the unborn child. Of the various infectious agents studied, rubella (German measles) carries the strongest risk, followed by influenza, respiratory infections, and the polio virus. More recent research has focused on exposure to toxoplasmosis (a virus transmitted from cats to humans) as a possible viral risk factor.

Premorbid intelligence Low IQ and the risk of developing schizophrenia have been linked in several studies.

Place and time of birth Being born in urban environments confers a higher risk than being born in a rural setting. Also, the SEASONALITY OF BIRTHS effect for persons born in the Northern Hemisphere confers a greater risk for developing schizophrenia if one is born in the winter and spring months (particularly February to May). Both findings have been linked to the greater presence of viruses, but no one really knows what causes this effect. Interestingly, season of birth effects have also been found for bipolar disorder, autism, attention deficit disorder, alcoholism, stillbirths, diabetes, Alzheimer's disease, and Down's syndrome. No one knows how to interpret these facts either.

Migrant status and ethnic minorities In some groups (such as African-Caribbean immigrants to the United Kingdom), being an immigrant and ethnic minority confers a higher risk for developing schizophrenia.

Epidemiological research into the risk factors associated with the development of schizophrenia will continue to be a vital area of research. Genetics alone cannot explain schizophrenia, and it is only through the clues revealed through the study of correlated environmental factors that new hypotheses about the causes of schizophrenia will emerge.

Murray, R. M., et al. *The Epidemiology of Schizophrenia.* Cambridge: Cambridge University Press, 2003.

Risperdal See ANTIPSYCHOTIC DRUGS.

risperidone See ANTIPSYCHOTIC DRUGS.

ritualistic behavior Sometimes people with schizophrenia are described as engaging in ritualistic behavior—that is, they repeat stereotyped actions based, perhaps, on MAGICAL THINKING. For example, such a person may repeatedly take off all his or her clothes, crouch down on the floor in a praying position, and then get up and put the clothes back on, only to repeat continually these actions over and over again for long periods of time.

Rorschach test See PROJECTIVE TESTS.

rotatory machines See CIRCULATING SWING; GYRATOR.

Rush, Benjamin (1746–1813) The first American physician to specialize in mental disorders. In fact, his profile appears in the logo of the AMERICAN PSYCHIATRIC ASSOCIATION. He graduated from the Presbyterian College of New Jersey (later renamed Princeton) when he was 15 years old and later went to Edinburgh and received a medical degree from the university there in 1768. During his stay in Scotland and England, Rush visited the major psychiatric hospitals of his day, including the BETHLEM ROYAL HOSPITAL, and was influenced by English physician William Cullen's ideas on the classification and treatment of mental disorders. Rush was a signer of the Declaration of Independence, and as physician at the Pennsylvania Hospital in Philadelphia (starting in 1783), he was the leading American physician of his day. Rush's own son John became insane at the age of 30 and was admitted to the Pennsylvania Hospital as a "lunatic," and he remained there until his death 27 years later.

Besides conducting an abundance of research on all aspects of medicine, Rush took a particular interest in diseases of the human mind. Rush's treatments covered a wide range from the "moral treatment" (influenced in Philadelphia, no doubt, by the Quakers) of institutionalized patients to some fairly terrifying methods of BLEEDING and MECHANICAL RESTRAINT, including his famous invention the stationary "coercion-chair" or TRANQUILLIZER and the GYRATOR. His 1812 textbook was the only American textbook on psychiatry for more than 70 years.

Goodman, N. G. *Benjamin Rush: Physician and Citizen, 1746–1813.* Philadelphia: University of Pennsylvania Press, 1934.

Rush, B. *Medical Inquiries and Observations on the Diseases of the Mind.* Philadelphia: Kimber & Richardson, 1812.

S

Sakel, Manfred Joshua (1906–1957) The inventor of INSULIN COMA THERAPY for schizophrenia.

Salpêtrière, la The famous Paris asylum for insane females. Although it was a place of incarceration for socially undesirable females since 1656, following the French Revolution of the early 1790s it became primarily a hospital for mentally ill women. The Salpêtrière played an important role in the history of psychiatry, for Philippe PINEL made many of his clinical observations as head of the institution in the 1790s and Jean Martin Charcot established a neurological clinic there in 1878. It was there that Charcot developed an interest in hypnotism and HYSTERIA.

Scandinavia The Scandinavian countries contain areas with some of the highest prevalence rates of schizophrenia in the world. This fact was observed as early as 1862 in a book by W. Charles Hood, *Statistics of Insanity,* in which he reported that the northern European countries had the highest rates of insanity and the southern European countries had the lowest. The Scandinavian countries, particularly Sweden, have been found to have prevalence rates for schizophrenia that are two to three times that of the United States. The highest prevalence rates for any area of the world have been found in northern Sweden in two studies that were conducted 25 years apart by J. A. Böök and colleagues. The rural area of Sweden that was north of the Arctic Circle was found by Bvvk to have a prevalence rate of 9.5 per 1,000. Other Swedish studies have found lower rates, but these are still quite high when compared with other areas of the world. High rates have also been found in areas of Norway and Finland, but somewhat less so for Denmark.

Böök, J. A. "Schizophrenia in a Northern Swedish Population, 1900–1975," *Clinical Genetics* 14 (1978): 373–394.

Torrey, E. F. "Prevalence Studies of Schizophrenia," *British Journal of Psychiatry* 150 (1987): 598–608.

schizoaffective disorder The term *schizoaffective* was coined by Jacob S. Kasanin (1897–1946) in 1933 to describe cases of BORDERLINE SCHIZOPHRENIA. Kasanin's concept was accepted for a time as a possible fifth subtype of schizophrenia. It is now a psychotic disorder that has symptoms of both a schizophrenic and a mood disturbance, and at other times with psychotic symptoms but without mood symptoms. The diagnosis is made only if the criteria for schizophrenia or for a mood disorder cannot be met and if it cannot be determined if an organic factor is responsible for this confusing mixture of symptoms. Family studies indicate that schizoaffective disorder is distinct from BIPOLAR DISORDER but that it may bear a closer relationship to schizophrenia. There are two subtypes of schizoaffective disorder: schizoaffective disorder, bipolar type, which, with its current or previous manic episode, makes it more closely related to a mood disorder than to schizophrenia; and schizoaffective disorder, depressive type, which does seem to be more closely related to schizophrenia.

The typical age of onset for schizoaffective disorder is early adulthood. The course of the disorder tends to be chronic, but the prognosis is better than that for schizophrenia and worse than that for a mood disorder. It is not known how prevalent this disorder is, but it is less common than schizo-

phrenia. Some family studies have indicated that there is an increased risk of schizophrenia in the first-degree biological relatives of people with this disorder.

See also ATYPICAL PSYCHOTIC DISORDERS.

Bertelsen, A., and I. I. Gottesman. "Schizoaffective Psychoses: Genetical Clues to Classification," *American Journal of Medical Genetics* 60 (1995): 7–11.

Kasanin, J. "The Acute Schizo-affective Psychoses," *American Journal of Psychiatry* 97 (1933): 97–106.

schizoid personality disorder According to *DSM-IV-R* (1994), the defining characteristic of this nonpsychotic mental disorder is "a pervasive pattern of indifference to social relationships and a restricted range of emotional experience and expression, beginning in early adulthood and present in a variety of contexts." These people appear to be cold and aloof, and they do not seem to desire or enjoy close relationships with other people. They almost always choose solitary activities and occupations, and they express little desire for sexual relationships with others. A person who meets the criteria for schizoid personality disorder must have demonstrated a lifelong course, and even though many of the signs and symptoms may resemble the PRODROMAL PHASE of schizophrenia, it is not thought that persons with this personality disorder go on to develop schizophrenia.

See also SCHIZOTYPAL PERSONALITY DISORDER.

schizomimetic Behavior in a person that mimics or resembles the signs and symptoms of schizophrenia but in fact is not due to the presence of that disorder.

schizophrene An obsolete term for persons with schizophrenia. We now call them schizophrenics. An analogous outmoded term for persons with bipolar disorder is *circulars.*

schizophrenia A term coined by Swiss psychiatrist Eugen BLEULER to replace the term *DEMENTIA PRAECOX* for the most prevalent group of the psychotic disorders. In 1899 Emil KRAEPELIN had unified what were previously separate disorders—hebephrenia, catatonia, and paranoia (of a specific type)—under the general heading of dementia praecox, which he regarded as all chronic and progressively degenerative diseases. Thus, the basis of Kraepelin's classification was the *prognosis* of these disorders.

Bleuler disagreed with the overtly negative prognosis as the defining characteristic of this disorder and instead renamed it schizophrenia (from two Greek words meaning "to split" and "mind") to stress what for him was the fundamental nature of these psychotic disorders: the splitting or dissociation of psychic functions (for which Bleuler used the German word *Spaltung*).

Although Bleuler had been using the word *schizophrenia* in clinical presentations and lectures at the BURGHÖLZI HOSPITAL in Zurich, Switzerland, where he was the chief physician, he introduced the concept in print in a 1908 article titled "The Prognosis of Dementia Praecox: The Group of Schizophrenias" (*Die Prognose der Dementia Praecox—Schizophreniegruppe*). In the first paragraph of that historic article, in which he questions the importance of Kraepelin's idea of prognosis, Bleuler writes:

> In using the term dementia praecox I would like it to mean what the creator of the concept meant it to mean. To treat the subject from any other point of view would serve no purpose, but I would like to emphasize that Kraepelin's dementia praecox is not necessarily either a form of dementia or a disorder of early onset. For this reason, and because there is no adjective or noun that can be derived from the term dementia praecox, I am taking the liberty of using the word *schizophrenia* to denote Kraepelin's concept. I believe that the tearing apart or splitting of psychic functions is a prominent symptom of the whole group and I will give my reasons for this elsewhere.

So what is "split" (*Spaltung*) in schizophrenia? Bleuler argues that it is primarily encountered in the disturbance of associations that characterize normal trains of thought, although there are

also splits in the normal functions of affect and of behavior (especially relating to the external world). Thus, the FOUR A'S (associations disturbances, autism, ambivalence, affective disturbances) that constitute the FUNDAMENTAL SYMPTOMS OF SCHIZOPHRENIA according to Bleuler are all manifestations of the splitting of psychic functions.

In 1911 Bleuler published his classic book that still influences our current thinking about schizophrenia: *Dementia Praecox oder die Gruppe der Schizophrenien (Dementia Praecox, or the Group of Schizophrenias)*. In it, Bleuler defines his conception of the disease in the following way:

> By the term "dementia praecox" or "schizophrenia" we designate a group of psychoses whose course is at times chronic, at times marked by intermittent attacks, and which can stop or retrograde at any stage, but does not permit a full *restitutio ad integrum*. The disease is characterized by a specific type of alteration of thinking, feeling, and relation to the external world which appears nowhere else in this particular fashion.

Bleuler divided the clinical picture of schizophrenia into its "fundamental symptoms" (*Grundsymptome*), which were caused directly by the disease process itself, and its accessory symptoms (*akzessorische Symptome*). The fundamental symptoms (the "four A's") are present to some degree during the entire course of the illness, whereas the secondary symptoms (delusions, hallucinations, transient catatonic episodes, behavioral disturbances) come and go throughout the course of the illness and are found in other mental disorders as well. In addition, Bleuler added a fourth subtype of the disease—"simple schizophrenia"—that had been proposed by Otto Diem in 1904.

Bleuler's dementia praecox Bleuler had believed he was further developing Kraepelin's concepts of dementia praecox rather than inventing an entirely new disorder. Bleuler's objections to Kraepelin's dementia praecox were many, however. He objected (as many others did, particularly British psychiatrists) that there was no dementia in the classical, organic sense of the term (for example, as in today's Alzheimer's disease), but instead an intellectual deterioration that may or may not end up looking like dementia. He noted the deterioration was not progressive, with episodes of partial remission or complete recovery occurring in some cases. The term *praecox* was also objectionable to Bleuler since he had encountered cases of schizophrenia that occurred during midlife (currently named LATE-ONSET SCHIZOPHRENIA). There were also cases of LATENT SCHIZOPHRENIA, according to Bleuler, in which the psychotic disorder was not triggered by an endogenous disease process but by personal experiences, such as trauma. Bleuler went so far as to believe that cases of latent schizophrenia were more common than cases of manifest schizophrenia. Bleuer also noted the existence of people with paranoid personality disorders who resembled cases of dementia praecox. Bleuler widened Kraepelin's concept of dementia praecox by arguing that these cases, too, should be considered part of the disease (an idea that has taken hold in our current notions of schizophrenia spectrum disorders, especially SCHIZOTYPAL PERSONALITY DISORDER). Influenced by his associate Carl Gustav Jung (1875–1961) and by Freud and the psychoanalytic movement, Bleuler believed in the possibility of psychogenic or reactive triggers for schizophrenia, which Kraepelin did not allow.

In sum, Bleuler greatly widened the circumference of persons whom he considered should be diagnosed with dementia praecox. He also left open the possibilities for various courses and outcomes, and better prognoses, than Kraepelin did. He emphasized the heterogeneous nature of schizophrenia, with the possibility that multiple disease processes may underlie it, whereas Kraepelin held to the conviction that dementia praecox was one disease with at least three forms. It was therefore Bleuler's wider concept of schizophrenia that took hold, especially in America, and dominated psychiatry until 1980. In that year, the narrower diagnostic criteria and pessimistic prognosis for schizophrenia became the official diagnosis of this disorder in *DSM-III*. This narrower, "neo-Krapelinian" definition of schizophrenia persists today.

Symptoms and Diagnostic Path

Schizophrenia remains a disease of unknown cause, with no single identifiable pathophysiol-

ogy, no truly effective treatment for most, and no known cure. There is no objective medical test for diagnosing this disorder. No blood test or brain scan can confirm a diagnosis. The current diagnostic criteria for this book from both the North American *DSM-IV-TR* (2000) and the European *ICD-10* (1992) can be found in an appendix to this book. Sometimes schizophrenia may resemble other psychotic disorders, especially MANIC-DEPRESSIVE ILLNESS or BIPOLAR DISORDER.

Reviews of the significant epidemiological, biological, and clinical features of this disease can be found in the following entries in this book: COURSE AND OUTCOME OF SCHIZOPHRENIA; PRODROMAL PHASE; RESIDUAL PHASE; RISK FACTORS; BRAIN ABNORMALITIES IN SCHIZOPHRENIA; NEUROPSYCHOLOGICAL STUDIES OF SCHIZOPHRENIA; SUBJECTIVE EXPERIENCES IN SCHIZOPHRENIA.

Treatment Options and Outlook

The treatment of schizophrenia is primarily based on the administration of ANTIPSYCHOTIC DRUGS. Severe side effects of these drugs, such as TARDIVE DYSKINESIA, PARKINSONISM, or NEUROLEPTIC MALIGNANT SYNDROME are also discussed in detailed entries. Other than programs that educate family members about the disease, and how to alter their own behavior to prevent relapse in their relative with schizophrenia (see EXPRESSED EMOTION), there is no form of psychotherapy that has been shown to be effective for the long term for people with schizophrenia. Antipsychotic drugs do not seem to delay or reverse the natural course of the schizophrenia disease process. Antipsychotic drugs do not improve NEGATIVE SYMPTOMS or cognitive deficits (for example, attention, working memory, and goal-directed thinking).

No one knows the cause or pathophysiology of schizophrenia. However, the most prominent theory generating research at present is the NEURODEVELOPMENTAL MODEL OF SCHIZOPHRENIA. Schizophrenia does not seem to follow the pattern of being a neurodegenerative disease like Alzheimer's disease, so neurodevelopmental theories are prominent almost by default. The strongest evidence for a biological cause for schizophrenia seems to lie in the evidence provided in GENETICS STUDIES. There is no single environmental factor that has been strongly linked to the cause and development of schizophrenia.

Risk Factors and Preventive Measures

There are no known preventive measures for schizophrenia.

See also RISK FACTORS.

Bleuler, E. *Dementia Praecox oder die Gruppe der Schizophrenien.* A volume in *Handbuch der Geisteskrankheiten,* edited by G. Aschaffenburg. Leipzig: F. Deuticke, 1911.

———. "Die Prognose der Dementia Praecox—Schizophreniengruppe," *Allgemeine Zeitschrift für Psychiatrie* 65 (1908): 436–464.

Cutting, J., and M. Shepherd, eds. *The Clinical Roots of the Schizophrenia Concept: Translations of Seminal European Contributions on Schizophrenia.* Cambridge: Cambridge University Press, 1987. (Contains an almost complete translation of Bleuler's 1908 article.)

schizophrenia spectrum disorders See SCHIZOTYPAL PERSONALITY DISORDER.

schizophreniform disorder According to *DSM-IV-TR* (2000), a person must be given the diagnosis of schizophreniform disorder if they manifest the characteristic symptoms of the active phase of schizophrenia for a period of one month but not more than six months and there is a full recovery. If symptoms persist after six months, they are given the diagnosis of schizophrenia. Schizophreniform disorder is perhaps nothing more than a conceptual bridge, based on duration of symptoms, between BRIEF PSYCHOTIC DISORDER and schizophrenia. Although it is in *DSM-IV-TR,* there is no scientific evidence to support schizophreniform disorder as a distinct diagnostic category. For this reason it does not appear in the WORLD HEALTH ORGANIZATION'S *ICD-10* (1992).

schizophreniform psychoses A term for persons with an ATYPICAL PSYCHOTIC DISORDER with a good prognosis that was often misdiagnosed as "genuine" or "process" schizophrenia, another syndrome that had a chronic and deteriorating

course. Persons who developed schizophreniform psychoses were well-adjusted prior to becoming ill. The onset of psychotic symptoms was sudden, and in response to identifiable causes such as stress or trauma. Although the psychotic symptoms resembled those of schizophrenia, there were also elements of an AFFECTIVE DISORDER such as manic-depression and a clouding of consciousness. Unlike persons with true schizophrenia, persons with a schizophreniform psychosis were responsive to treatments such as electroshock therapy. The concept was introduced into psychiatry by Gabriel Langfeldt (1895–1983), a psychiatrist in Vinderen, Norway, in his 1939 book, *The Schizophreniform States*. From the 1940s to the 1980s Langfeldt's concept of schizophreniform psychoses was popular in psychiatry, particularly in Europe and Scandinavia. Langfeldt's term lives on as SCHIZOPHRENIFORM DISORDER in *DSM-IV-TR*, although the clinical picture differs sharply from his suggested symptoms for the disorder. Reanalyses of the 100 case histories documented by Langfeldt as schizophreniform have found that his cases more closely match affective or mood disorders with psychotic features.

Langfeldt, G. *The Schizophreniform Disorders.* Copenhagen: Munsksgaard; Oxford: Oxford University Press, 1939.

schizophrenogenic mother Due to the influence of psychoanalysis and, later, FAMILY INTERACTION THEORIES, it was thought that the behavior of certain family members—particularly the mother—was responsible for causing a schizophrenic breakdown in children. The term *schizophrenogenic mother* (although previously used in a paper by Frieda FROMM-REICHMANN) was introduced into the mainstream by psychoanalytic psychiatrist Trude Tietze in a 1949 published study of 25 mothers of schizophrenic patients. They were all seen as "domineering" and with "warped psychosexual development" that psychologically injured their children. In the 1950s and early 1960s medical students training in psychiatry were routinely taught that mothers were "pathogens." One of the most prominent figures in clinical psychology, Paul Meehl, likewise believed in this. A useful review of the long and tragic course of the idea of the schizophrenogenic mother in American culture and psychiatry was published by C. E. Hartwell in 1996. Today, it is clear that there is no scientific evidence to support the notion of the schizophrenogenic mother.

Hartwell, C. E. "The Schizophrenogenic Mother Concept in American Psychiatry," *Psychiatry* 59 (1996): 274–279.

Tietze, T. "A Study of Mothers of Schizophrenic Patients," *Psychiatry* 12 (1949): 55–65.

schizotaxia A term coined by psychologist Paul Meehl in 1962 to refer to the genetically transmitted "neural integrative defect" that predisposes a whole class of individuals to develop SCHIZOTYPY or SCHIZOPHRENIA. Schizotaxia, according to Meehl, is the only thing that is inherited in schizophrenics, and it does not necessarily lead to the development of this disorder unless there are certain environmental factors that also push the individual in the direction of psychopathology. Schizotypy refers to the unusual personality organization that these environmental influences may cause, but persons who are schizotypes still may not necessarily develop schizophrenia. Instead, Meehl suggests: "It seems likely that the most important causal influence pushing the schizotype toward schizophrenic decompensation is the schizophrenogenic mother."

Meehl first proposed these ideas in a Presidential Address to the AMERICAN PSYCHOLOGICAL ASSOCIATION in September 1962, and the idea of "schizotaxia, schizotypy, schizophrenia" was important in developing later diathesis stress models of schizophrenia and of the role of genetics in SPECTRUM DISORDERS.

Meehl, P. "Schizotaxia, Schizotypy, Schizophrenia," *American Psychologist* 17 (1962): 827–838.

schizotypal personality disorder This type of personality disorder best exemplifies what Paul Meehl meant by "SCHIZOTYPY" (see SCHIZOTAXIA). The person with schizotypal personality disorder displays a "pervasive pattern of peculiarities of

ideation, appearance, and behavior and deficits in interpersonal relatedness, beginning by early adulthood and present in a variety of contexts, that are not severe enough to meet the criteria for schizophrenia." These persons may exhibit IDEAS OF REFERENCE, be extremely uncomfortable in social situations, exhibit extremely odd beliefs or engage in magical thinking, may look odd or unkempt, talk to themselves, speak oddly, have no close friends, have silly or inappropriate affect, or perhaps even be a little suspicious or paranoid. It is estimated that approximately 3 percent of the population of the United States has this disorder and that it is more common among the FIRST-DEGREE RELATIVES of persons with schizophrenia.

Historical Background

When Eugen BLEULER proposed his concept of SCHIZOPHREHNIA in 1908, he widened the circumference of the definition DEMENTIA PRAECOX to include persons who had dementia praecox–like symptoms that were much less severe and who had a much better prognosis than those identified by Emil KRAEPELIN. He also referred to persons who had "latent dementia praecox" that might worsen into cases of full, active schizophrenia under stress or the experience of trauma. Later, in 1911, he would add a fourth form of dementia praecox that loosely corresponded to this group, SIMPLE SCHIZOPHRENIA. The New York psychoanalyst Sandor Rado was the first to use the term *SCHIZOTYPAL DISORDERS* in the *American Journal of Psychiatry* in 1953 to refer to persons who were genetically predisposed to schizophrenia but who did not go on to develop the full disorder. These persons appeared to have stable if bizarre personality traits rather than a psychotic disorder, therefore beginning with *DSM-III* in 1980, this diagnostic group was renamed Schizotypal Personality Disorder and included in a "cluster" with two other similar personality disorders: Paranoid Personality Disorder and Schizoid Personality Disorder. Schizoid personality disorder and schizotypal personality disorder are part of what was termed *schizophrenia spectrum disorders* by Seymour Kety and David Rosenthal of the NATIONAL INSTITUTE OF MENTAL HEALTH in Bethesda, Maryland, in the early 1970s. A significant finding of their initial 1968 report of the Danish adoption studies was that some relatives of persons with schizophrenia who did not have the disorder nonetheless exhibited symptoms or traits of a "borderline state" of schizophrenia. GENETICS STUDIES of schizophrenia that have followed Kety and Rosenthal's work have replicated this finding, indicating that close biological relatives of persons with schizophrenia may share the same genes underlying the predisposition to the disorder ("schizotaxia") but may express watered-down or less severe symptoms or traits of schizophrenia ("schizotypy"). Although the current assumption in modern genetics studies is that schizotypal personality disorder is a form of "subthreshold" schizophrenia," similarities between the symptoms of the two disorders do not necessarily mean they have a common etiology (cause). However, as a recent survey of the experimental research on schizotypal personality disorder (SPD) by O'Flynn, et al., concluded in 2003, "Studies of the phenomenology, genetics, biology, cognition, outcome and treatment response of SPD have consistently supported a close relationship of SPD to schizophrenia."

In clinical practice as well as research studies, the "cluster A" personality disorders (paranoid, schizoid, and schizotypal) are highly overlapping and often difficult to distinguish in practice. The high comorbidity of these disorders is interpreted by some schizophrenia researchers as an indication that there may be gradations along the schizophrenia spectrum rather than distinct disorders. From least in severity to worst, the gradation would go from schizoid to paranoid to schizotypal personality disorders to schizophrenia.

The terms *schizotypal, schizotypy,* and *schizophrenia spectrum disorders* are all used interchangeably in the literature on schizophrenia research.

In *ICD-10* (1992), schizotypal disorder is not a personality disorder but is one of the five categories of ATYPICAL PSYCHOTIC DISORDERS.

See also BORDERLINE CASES; BORDERLINE SCHIZOPHRENIA; LATENT SCHIZOPHRENIA.

O'Flynn, K. O., J. Gruzelier, A. Bergman, and L. J. Siever. "The Schizophrenia Spectrum Personality Disorders." *Schizophrenia.* 2nd ed., edited by S. R. Hirsch and D. Weinberger. Cambridge: Blackwell, 2003.

schizotypy See SCHIZOTYPAL PERSONALITY DISORDER.

schizovirus According to the VIRAL THEORIES OF SCHIZOPHRENIA, there is a possibility that some individuals with schizophrenia develop the disorder due to a chronic infectious agent of the nervous system. Although such a possibility had been noted by Emil KRAEPELIN at the turn of the century, the hypothesis was not investigated seriously until E. Fuller Torrey resurrected this notion with a series of studies at the NATIONAL INSTITUTE OF MENTAL HEALTH in the 1970s. In a 1988 article, he reports, "My psychiatric research colleagues regarded the efforts whimsically as the search for the 'schizovirus' or 'schizococcus.'" However, as Torrey admits, there is yet very little direct evidence to link viruses with schizophrenia. Yet, he writes, "The search for the putative 'schizovirus' continues. Whether the quest will eventually lead to Jason's fabled Golden Fleece, or merely be another blind alley down which schizophrenia research has wandered, remains to be seen."

Torrey, E. F. "Stalking the Schizovirus," *Schizophrenia Bulletin* 14 (1988): 223–229.

Torrey, E. F., and M. R. Peterson. "Slow and Latent Viruses in Schizophrenia," *Lancet* 2 (1973): 22–24.

Schnauzkrampf Interest in the PHYSIOGNOMY of mental illness was a major concern in the 19th century. In schizophrenic people with CATATONIA, it was reported by German psychiatrist Karl KAHLBAUM that they tended to exhibit a protrusion of the lips that resembled an animal snout (*Schnauzkrampf*).

Scotland Scotland has a higher prevalence rate for schizophrenia than England, its neighbor to the south. The observation that there has always been more "insanity" among the Scottish dates at least from the mid-19th century. A schizophrenia prevalence study by Mayer-Gross in Scotland, in which 56,231 persons were surveyed, found a prevalence rate of 4.2 per 1,000.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

seasonal affective disorder The observation that DEPRESSION and MANIA are sensitive to seasonal and environmental influences has been reported for at least 2,000 years. Hippocrates noted in the fourth century B.C. that "it is chiefly in the changes of season which produce diseases, and in the seasons the great changes are from cold or heat." As early as 1801, French ALIENIST Philippe PINEL noted winter and summer onsets for mood disorders. *DSM-III-R* (1987) included criteria for "seasonal pattern" in mood disorders such as BIPOLAR DISORDER or recurrent major depression in which it must be established that, through the years, there has been a regular appearance of an episode of the disorder in a given 60-day period of the year. In a 1989 review of all the research studies that link seasonal patterns to mood disorders, it was found that there are two primary, opposite seasonal patterns of annual mood disorders, namely depression: those with winter depression (onset during September, October, and November) and summer depression (onset during March, April, and May). It is estimated that seasonal affective disorder has been found to occur in about 16 percent to 38 percent of all persons who experience recurrent depression. The vast majority of persons (83 percent) who develop SAD (the apt acronym for seasonal affective disorder) are females in their 30s. It is generally important to identify those persons who suffer from recurrent winter depression because they have been found to respond to a novel form of treatment—phototherapy (bright light administered to such persons for varying lengths of time and intensity of brightness).

Rosenthal, N. E., and M. C. Blehar, eds. *Seasonal Affective Disorder and Phototherapy.* New York: Guilford, 1989.

Rosenthal, N. E., and T. A. Wehr. "Seasonal Affective Disorders," *Psychiatric Annals* 17 (1987): 670–674.

Wehr, T. A., and N. E. Rosenthal. "Seasonality and Affective Illness," *American Journal of Psychiatry* 146 (1989): 829–839.

seasonality of births in the psychotic disorders One of the most consistent findings in the epidemiology of the psychotic disorders is that there is a seasonal excess of births in the winter and early spring months (roughly December through May) of people

who go on to develop schizophrenia and/or bipolar disorder later in life. The very first published study to document this remarkable phenomenon appeared in 1929. In it, a Swiss psychiatrist named Tramer analyzed birth data for 3,100 patients with psychotic disorders institutionalized in Swiss clinics.

Since then, the most vigorous proponent of this hypothetical risk factor for schizophrenia is E. Fuller Torrey. In a comprehensive review article on this issue published in *Schizophrenia Research* in 1997, Torrey and his colleagues analyzed more than 250 studies on seasonality of birth that covered 29 Northern and five Southern Hemisphere countries. A consistent finding across studies was a 5 percent to 8 percent winter-spring excess of births of people who later went on to develop schizophrenia or bipolar disorder. Of the 86 studies dealing specifically with schizophrenia, a total of 437,710 individuals with schizophrenia were analyzed. According to Torrey et al., "The schizophrenia birth excess, therefore, may be said to be predominantly from December to May, with its maximum peak in January and February." In BIPOLAR DISORDER, those with mania have a December to March peak, and those with major depression have a March to May peak.

This birth-excess effect was also found for persons diagnosed with SCHIZOAFFECTIVE DISORDER (December–March), major depression (March–May), and autism (March). However, no other major psychiatric disorders seemed to be related to the season of a person's birth.

The seasonality of birth effect is not correlated with gender, social class, race, measurable pregnancy and birth complications, clinical subtypes, or neurological, neuropsychological, or neuroimaging measures.

What, then, causes this remarkable effect? Torrey and colleagues offer the following hypotheses: seasonal effects of genes, subtle pregnancy and birth complications, sunlight's effect on the internal chemistry of the body, toxins, nutrition, temperature/weather, infectious agents (such as viruses), or a combination of any number of these environmental and genetic factors.

Torrey, E. F., et al. "Seasonality of Births in Schizophrenia and Bipolar Disorder: A Review of the Literature," *Schizophrenia Research* 28 (1997): 1–38.

Tramer, M. "Uber die biologische Bedeutung des Geburtsmonates, insbesondere für die Psychoseerkrankung," *Schweitzer Archiv für Neurologie and Psychiatrie* 24 (1929): 17–24.

secondary process See PRIMARY PROCESS.

secondary symptoms of schizophrenia See ACCESSORY SYMPTOMS.

segregation analysis This is a major statistical method used in population genetics research that compares the observed frequency of an illness in a pedigree with a pattern that would occur if a hypothesized mode of genetic inheritance (e.g., one of the patterns of monogenetic transmission or polygenetic transmission) were accurate. Although there are limitations to segregation analyses, such analyses on diverse phenotypes in relevant pedigrees have been able to reject the "single-locus model" (that is, the idea that all cases of schizophrenia have a common single cause and that no familial resemblance is environmentally determined). It has also ruled out the strict polygenetic inheritance model (that is, that schizophrenia is caused by the additive effect of many genes in all cases).

Garver, D. L., et al. "Schizophrenia and the Question of Genetic Heterogeneity," *Schizophrenia Bulletin* 15 (1989): 421–430.

seleniasmus Yet another synonym for lunacy. The word is derived from the name for the Greek goddess of the moon, Selene.

self-image in schizophrenia According to Silvano ARIETI, a person's self-image consists of three components: body image, self-identity, and self-esteem. In schizophrenia, all three of these components are disrupted. There are body image distortions and perceptual anomalies, GENDER-IDENTITY CONFUSION, and a loss of self-esteem

that can be so severe that it may precipitate the PREPSYCHOTIC PANIC that may then lead to a psychosis. American psychiatrist Harry Stack Sullivan devoted considerable work to exploring the development of self and self-image, which he felt originated in the child's passive incorporation of reflected appraisals from significant adults. Several papers on the transformation of self-image in the person stricken with schizophrenia were published in a special issue of *Schizophrenia Bulletin* (vol. 15, no. 2) in 1989 devoted to the theme "Subjective Experiences of Schizophrenia and Related Disorders."

Estroff, S. E. "Self, Identity, and Subjective Experiences of Schizophrenia," *Schizophrenia Bulletin* 15 (1989): 189–198.

self-injurious behavior, or self-mutilation The deliberate cutting, scratching, burning, tearing, or other action performed against one's own body. Self-mutilation is a serious sign of extreme internal distress in many of the persons who do it. It is a side effect of many psychiatric disorders, especially in the psychotic disorders, the DISSOCIATIVE DISORDERS, BORDERLINE PERSONALITY DISORDER, sexual masochism, and the eating disorders bulimia and anorexia nervosa. Self-injurious behavior (SIB) is also quite commonly seen in the mentally retarded, and studies have reported that as many as 40 percent of the institutionalized mentally retarded, especially those with a rare enzyme deficiency known as Lesch-Nyhan syndrome, bang their heads; chew their fingers, lips, or the skin of other parts of their body; and abuse themselves in a multitude of other ways.

Favazza, A. *Bodies under Siege: Self-Mutilation in Culture and Psychiatry.* Baltimore: Johns Hopkins University Press, 1990.

sensorimotor gating This is one of the oldest theories in studies of schizophrenic cognition but has been given new life under a new name with the neuropathological and neuroimaging studies of the 1980s and 1990s. The idea is that the brain of a person with schizophrenia cannot screen out relevant from irrelevant sensations. The metaphorical "gate" that lets sensory and motor messages in and out of the cortex is broken. This failure in "gating" to "screen out" irrelevant stimuli leads to a disruption in the ability of a person with schizophrenia to willfully focus his or her ATTENTION. The person feels flooded by irrelevant sensations, feelings, and thoughts and, in an effort to cope, can "shut down" and become unresponsive. Genes that seem to be linked to sensorimotor gating have been found in mice (in 1998) and are suspected to exist in humans as well.

Swerdlow, N. R., and M. A. Geyer. "Using an Animal Model of Deficient Sensorimotor Gating to Study the Pathophysiology and New Treatments of Schizophrenia," *Schizophrenia Bulletin* 24 (1998): 285–301.

Serentil See ANTIPSYCHOTIC DRUGS.

Seroquel See ANTIPSYCHOTIC DRUGS.

serotonin hypothesis Serotonin is a neurotransmitter that functions in both the central and the peripheral nervous systems. In the peripheral nervous system (PNS) it functions as a vasoconstrictor. In the central nervous system (CNS) it has many functions, primarily the inhibition of certain brain areas during sleep.

The chemical name for serotonin is 5-hydroxytryptamine, or 5HT. Serotonin was the basis for the first theory of a NEUROTRANSMITTER DISORDER AS A CAUSE OF SCHIZOPHRENIA, which was proposed in a paper by biochemists D. W. Wooley and E. Shaw in 1954.

Many of the ATYPICAL ANTIPSYCHOTICS introduced in the 1990s act on serotonergic pathways in the brain to alleviate the symptoms of schizophrenia. However, given that more than 100 different neurotransmitters in the brain have now been found, it is no longer argued by schizophrenia researchers that serotonin (or dopamine or norepinepherine or glutamine) can act alone in the disease processes of schizophrenia.

Baumeister, A. A., and M. F. Hawkins. "The Serotonin Hypothesis of Schizophrenia: A Historical Case Study on the Heuristic Value of Theory in Clinical Neuroscience," *Journal of the History of the Neurosciences* 13 (September 2004): 277–291.

Wolley, D. W., and E. Shaw. "A Biochemical and Pharmacological Suggestion about Certain Mental Disorders," *Proceedings of the National Academy of Sciences of the United States of America* 40 (1954): 228–231.

sertindole See ATYPICAL ANTIPSYCHOTICS.

sex differences in schizophrenia See GENDER DIFFERENCES IN SCHIZOPHRENIA.

sexual jealousy See OTHELLO SYNDROME.

shamanism and schizophrenia Shamanism is a magico-religious tradition that has been reported for centuries in simple societies that are based on hunting, gathering, and fishing. The shaman is an individual who deliberately enters an altered state of consciousness (through drugs, drumming, dancing, fasting) in order to induce visionary states in which he performs certain culturally prescribed actions, usually either healing or divination. Unfortunately, especially prior to the "psychedelic era" of the 1960s, the only frame of reference most anthropologists possessed for understanding the unusual experiences these people had during their visions was psychiatric diagnostic manuals. Thus, such experiences were long interpreted as signs of psychosis, and the myth grew that shamans were nothing more than severely disturbed individuals who may even be psychotic but whose society has a role for them and therefore they are accepted and "healed" to some extent.

A widely cited 1967 paper by Julian Silverman did much to promote this pathologizing of shamans by comparing the experiences of the altered states of consciousness in the early training of the shaman with the symptoms of acute schizophrenia. Unfortunately, Silverman's paper was taken as the final word on the issue for almost two decades. However, a 1983 paper by clinical psychologist Richard Noll strongly criticized this assumption on phenomenological grounds, and now anthropological studies of religion no longer view the experiences of shamans as "schizophrenic" or "psychotic."

Noll, R. "Shamanism and Schizophrenia: A State-Specific Approach to the 'Schizophrenia Metaphor' of Shamanic States," *American Ethnologist* 10 (1983): 443–459.

———. "What Have We Really Learned about Shamanism?" *Journal of Psychoactive Drugs* 21 (1989): 47–50.

Silverman, J. "Shamanism and Acute Schizophrenia," *American Anthropologist* 69 (1967): 21–31.

shared delusional (or paranoid) disorder See FOLIE À DEUX.

shared psychotic disorder See FOLIE À DEUX.

shock therapy See ELECTROSHOCK THERAPY.

sibship The group of all siblings of the afflicted person and their parents.

sign The sign of an illness is an objective indicator of a pathological condition. This differs from a SYMPTOM in that the sign of a disorder is observed by an examiner and is not a subjective report by the individual. For example, a runny nose is the sign of the common cold, whereas the feeling of discomfort or fever are symptoms of this illness.

silly dementia See HEBEPHRENIA.

simple schizophrenia The fourth subtype of schizophrenia added by Eugen BLEULER to the original three of paranoia, hebephrenia, and catatonia grouped together in 1899 by Emil KRAEPELIN as DEMENTIA PRAECOX. This subtype was outlined by Swiss psychiatrist Otto Diem in 1903. Diem

worked under Bleuler at the BURGHÖLZI HOSPITAL, and the idea for his article may have been suggested by Bleuler as an elaboration of an earlier idea by Czech psychiatrist Arnold Pick (1851–1924). In the English translation (in Cutting and Shepard's book) of his original article, Diem acknowledges the "characteristic mental debility" of Kraepelin's dementia praecox in the three original subtypes and then proposes that "there is one further condition which leads to the same end state, to the same disorder of intelligence and affect." Diem calls this *dementia simplex,* or "simple schizophrenia." Diem notes that, after puberty, "the onset of this particular form of the illness is habitually simple, insidious, and without warning signs, and the illness progresses without acute progressive attacks and remissions. There are no definite affective disturbances of a manic or a melancholic nature, no hallucinations or delusional ideas, and none of the other characteristic symptoms of the other forms of dementia praecox . . . such as catalepsy, affectations, mannerisms, stereotypies, negativism and mutism." The term *simple schizophrenia* entered the official psychiatric diagnostic manuals and remained there for many years. In *DSM-IV-TR* (2000), it is no longer considered one of the four main subtypes of schizophrenia and is instead currently referred to as schizotypal personality disorder. Simple schizophrenia still exists as a subtype in *ICD-10* (1992).

Black, D. W., and T. J. Boffeli. "Simple Schizophrenia: Past, Present, Future," *American Journal of Psychiatry* 146 (1989): 1,267–1,273.

Diem, O. "The Simple Dementing Form of Dementia Praecox," ("Die einfach demente Form der Dementia praecox"), *Archiv Für Psychiatrie und Neruenkrankheiten* 37 (1903): 111–187. Translated and reprinted in J. Cutting and M. Shepherd, eds. *The Clinical Roots of the Schizophrenia Concept.* Cambridge: Cambridge University Press, 1987.

simulated insanity See FEIGNED INSANITY.

sleep studies It has often been remarked how "dreamlike" the hallucinatory and confusional states of some persons with schizophrenia seem to be. This has led researchers to explore the psychophysiology of sleep and to see if people with schizophrenia manifest any significant differences in the normal stages of sleep or in REM (rapid eye movement) sleep that is associated with dreaming. A 1977 review of this vast experimental literature by Mendelson et al. concluded that investigators "have failed to establish any unique or even consistent abnormalities in the sleep of schizophrenic patients." However, a later reassessment of this conclusion by Buchsbaum in 1979 suggests that the highly contradictory results of the study of sleep in persons with schizophrenia may simply indicate the great diversity in the sleep neurophysiology of persons with psychotic disorders and perhaps warrants more carefully controlled studies with larger sample sizes of schizophrenic subjects. Although the issue of REM sleep differences in schizophrenics when compared with normals is still controversial, Buchsbaum does suggest that one fairly consistent finding is that people with schizophrenia have much lower amounts of delta, or stage IV, sleep than do people without this disorder.

Buchsbaum, M. S. "Neurophysiological Aspects of the Schizophrenic Syndrome." In *Disorders of the Schizophrenic Syndrome,* edited by L. Bellak. New York: Basic Books, 1979.

Mendelson, W. B., J. C. Gillin, and R. J. Wyatt. *Human Sleep and Its Disorders.* New York: Plenum, 1977.

Reich, L., et al. "Sleep Disturbance in Schizophrenia," *Archives of General Psychiatry,* 32 (1975): 51–55.

sleep treatment In 1922 Swiss psychiatrist Jakob Kläsi (1883–1980) introduced the first somatic treatment specifically for schizophrenia. It was referred to as "prolonged sleep therapy." He used barbiturates to induce continuous periods of sleep of one week or longer in persons with schizophrenia. They were only allowed to be awakened for eating and performing other bodily functions. Kläsi reported good results with his sleep treatment, but it never became an accepted treatment. The strong sedatives he used were rather toxic and would result in respiratory complications, espe-

cially pneumonia. This form of treatment was used until the 1950s.

Kläsi, J. "Ober die therapeutische Anwendung per 'Dauernarkose' mittels sominifens bei Schizophrenen," *Z. Neurol. Psychiatr.* 74 (1922): 557–592.

sluggish schizophrenia In the former Soviet Union, perhaps 40 percent of all persons labeled with schizophrenia are within the form of the disorder identified as "sluggish schizophrenia." In many ways this concept is compatible with Eugen BLEULER's concept of LATENT SCHIZOPHRENIA, which he presented in 1911. In Soviet psychiatry, there is a long-established tradition of studying "soft" forms of schizophrenia. In 1969 A. V. Snezhnevsky and colleagues published an influential book that introduced a new classification system for the various schizophrenias, including the new concept of "sluggish schizophrenia." Sluggish schizophrenia is not viewed as an initial or PRODROMAL PHASE of schizophrenia, but instead it is an independent diagnostic category characterized by a slowly progressive course, subclinical manifestations in the latent period, overt psychopathological symptoms in the active period. Then follows a period in which the POSITIVE SYMPTOMS decrease and the NEGATIVE SYMPTOMS predominate the clinical presentation during the stabilization of the patient. In the United States, "sluggish schizophrenia" may have been called SIMPLE SCHIZOPHRENIA or by its currently accepted name, SCHIZOTYPAL PERSONALITY DISORDER.

The diagnosis of "sluggish schizophrenia" has long been claimed by Soviet dissidents to be the excuse for putting countless political prisoners into Soviet mental hospitals for punishment. During the week of June 30, 1989, the Reuters news agency reported from Moscow that the current issue of an influential Moscow journal, the *Literary Gazette*, published an article by writer Leonid Zagalsky that for the first time publicly named and condemned the two top Soviet psychiatric authorities and their mentor, A. V. Snezhnevsky, for condoning the imprisonment in mental hospitals of otherwise healthy persons under the label "sluggish schizophrenia."

See also ABUSE OF PSYCHIATRIC PATIENTS; BORDERLINE SCHIZOPHRENIA.

Smulevich, A. B. "Sluggish Schizophrenia in the Modern Classification of Mental Illness," *Schizophrenia Bulletin* 15 (1989): 533–539.

Snezhnevsky, A. V., ed. *Shizofrenia: Klinika i Patogenez.* Moscow: Meditsina, 1969.

smoking and schizophrenia As anyone who has ever visited or worked in a psychiatric hospital will know, persons with schizophrenia tend to smoke a great deal. Some have even been seen to smoke two or more cigarettes at a time, and many persons chain-smoke so much that their lips and fingers are stained with nicotine. Cigarettes are the currency of the psychiatric hospital, and all sorts of economic transactions (including prostitution) are based on them. One study of outpatients with schizophrenia found that 88 percent of them were regular smokers, a number three times higher than the nonpsychiatric control group subjects in the study and still far higher than persons who are diagnosed with other psychiatric disorders. It is not known why nicotine addiction is so prevalent in persons with schizophrenia, nor is it known why, paradoxically, lung cancer does not seem to be a major cause of death among schizophrenics despite their years of heavy daily smoking.

See also PHYSICAL DISEASE AND SCHIZOPHRENIA; RISK FACTORS.

Hughes, J. R., et al. "Prevalence of Smoking among Psychiatric Outpatients," *American Journal of Psychiatry* 143 (1986): 993–997.

social drift theory See SOCIOECONOMIC STATUS AND SCHIZOPHRENIA.

social skills training The poor social interactions of people who develop schizophrenia adds considerably to the often terrible quality of their lives and alienates them from other members of the community. Social adjustment has repeatedly been found to be a relatively strong predictor of

relapse, rehospitalization, and long-term outcome. Therefore, since the 1970s and 1980s in particular, there has been a strong emphasis on teaching persons with schizophrenia certain "social skills" that may help prevent relapse or rehospitalization as they continue to adjust to life with such a chronic and debilitating disease. Social skills that are often trained are learned abilities such as making eye contact, the content of speech, voice inflection, and facial expression. The training techniques often include modeling new behaviors, role playing, homework and even training in social perception in order to help keep such persons from misinterpreting the expressions and actions of others.

Many studies have indicated that social skills training procedures are effective in teaching some persons with schizophrenia new skills, and that such newly learned behaviors can be maintained for varying periods of time. Some studies have even associated some forms of social skills training with reduced rates of relapse. However, due to the organic nature of the disease, it is difficult to maintain such learned skills once the person with schizophrenia is no longer monitored and trained consistently within a structured program, and therefore those persons who would most benefit from such training are strongly encouraged to be involved in such programs as often as possible.

Bellak, A. S., ed. *Schizophrenia: Treatment, Management, Rehabilitation.* New York: Grune & Stratton, 1984.

Penn, D. L., and K. T. Mueser. "Research Update on the Psychosocial Treatment of Schizophrenia," *American Journal of Psychiatry* 153 (1996): 607–617.

socioeconomic status and schizophrenia One of the most overwhelming pieces of evidence that we have about schizophrenia is that it occurs at an unusually high rate in the lowest socioeconomic strata of urban communities. However, there are several different interpretations of this finding. One of them is the famous "social drift" explanation—that is, that persons who develop schizophrenia tend not to be able to function very well in the social or occupational spheres and therefore tend to "drift" downward to the lower socioeconomic layers of society. An alternative hypothesis asserts that it is the unhealthful and stressful living conditions of persons of low socioeconomic levels (e.g., living in a ghetto) that produces the disorder.

Perhaps another explanation may involve a mixture of these two theories, in that if schizophrenia is a genetic disease, then previous generations have gotten sick and have already drifted downward in socioeconomic status over the generations, and therefore a higher concentration of persons with this disorder should be found at these lower levels of society.

Faris and Dunham published the first major study of the relationship between schizophrenia and socioeconomic status in 1939 and gave the first evidence for the inverse relationship between class and schizophrenia. Their research was corroborated by Hollingshead and Redlich in 1958, in their famous book *Social Class and Mental Illness,* in which they present the "social drift" hypothesis. In 1980 epidemiologist W. W. Eaton published a review of 17 studies conducted throughout the world and found that 15 of them confirmed the same conclusion that Faris and Dunham reached in 1939: that schizophrenia forms a concentric pattern, with the highest admission rates for schizophrenia in the central slum areas of the city with the lowest socioeconomic status and then diminishing rates as one looks farther and farther from the inner-city slums to the higher-status suburbs.

It is not likely that one's socioeconomic class actually causes schizophrenia, and this is a conclusion reached in 1992 in a major review of the issue in *Science.*

Dohrenwald, B. P., et al. "Socioeconomic Status and Psychiatric Disorders: The Causation-selection Issue," *Science* 255 (1992): 946–952.

Faris, R. E. L., and H. W. Dunham. *Mental Disorders in Urban Areas.* Chicago: Chicago University Press, 1939.

Hollingshead, A. B., and F. C. Redlich. *Social Class and Mental Illness: A Community Study.* New York: Wiley, 1958.

Solian See ANTIPSYCHOTIC DRUGS.

somatic delusions Delusions involving the body. An example is the delusion that one has a hole in the middle of one's body through which the wind is blowing. Another type may be a PREGNANCY DELUSION.

See also DELUSIONAL DISORDER.

somatic type One of the subtypes of the psychotic disorder known as DELUSIONAL DISORDER in which a person may have the delusion that he or she has some physical defect, disorder or disease.

spectrum disorders Influenced by Paul Meehl's DIATHESIS-STRESS THEORY of "schizotaxia, schizotypy, schizophrenia" and by the later GENETICS STUDIES of David Rosenthal and Seymour Kety, it has been suggested that many persons may inherit a genetic defect (schizotaxia, in Meehl's words) that may then give rise to a spectrum of disorders, all the way from a schizoid personality disorder to schizotypal personality disorder to schizophrenia. In other words, a spectrum of related disorders from the least serious to the most serious may be due to similar or related genetic factors. The evidence supporting a spectrum concept of schizophrenia is that first-degree biological relatives of persons with schizophrenia have a greater risk of developing schizotypal personality disorder or paranoid personality disorder or other schizophrenia-spectrum disorders.

See also SCHIZOTAXIA; SCHIZOTYPAL PERSONALITY DISORDER.

spinning chair See CIRCULATING SWING.

Spitzer, Robert (1932–) An American psychiatrist from New York who is perhaps second only to Emil KRAEPELIN in changing the language and classification systems of psychiatry. Spitzer led the task force that produced *DSM-III* in 1980. This revision of the diagnostic manual completely changed clinical research and practice and is regarded as the most influential psychiatric text of the 20th century. Many of the changes were either proposed or personally approved by him.

Spiegel, A. "The Dictionary of Disorder: How One Man Revolutionized Psychiatry," *New Yorker,* January 3, 2005, pp. 56–63.

spontaneous remission Although many clinicians have reported rare cases of spontaneous remission in cases of schizophrenia, *DSM-IV* (1994) cautions that "a return to full premorbid functioning in this disorder is not common. Full remissions do occur, but their frequency is currently a subject of controversy."

spread eagle cure In 19th-century America, this was a technique used in all asylums and prisons for agitated patients or inmates. The procedure involved stripping the violent patient of all clothes and throwing him flat on his back. Four men would take hold of each of the limbs and spread them out at right angles from the body. A physician or an attendant would then stand up on a chair or a table and pour buckets of ice-cold water on the restrained person's face until he was completely subdued. In some instances, the shock was so great that death resulted. A picture of this torturous procedure appears in Emil KRAEPELIN's book *One Hundred Years of Psychiatry.*

Kraepelin, E. *One Hundred Years of Psychiatry,* trans. W. Baskin. 1917. Reprint, New York: Philosophical Library, 1962.

stadium melancholicum This is the 19th-century term for the depression that sometimes precedes the onset of a psychotic disorder. German psychiatrist Wilhelm GRIESINGER writes in his 1861 book, *Mental Pathology and Therapeutics:* "The *stadium melancholicum* which precedes insanity is by some physicians designated as the period of incubation, or prodromal stadium . . . (that) the stage of incubation has almost always a depressive character is interesting and of great importance."

See also PRODROMAL PHASE.

Griesinger, W. *Mental Pathology and Therapeutics.* 2nd ed., trans. C. L. Robertson. New York: William Wood, 1882.

State Care Act of 1890 This was the legislative act passed by Congress that divided each of the United States into districts and mandated a state hospital for each of the districts. With this act, the term *asylum* was replaced by the term *hospital* in reference to these institutions.

Stelazine See ANTIPSYCHOTIC DRUGS.

stereotypy Long observed to be a behavioral sign of psychotic disorders, particularly schizophrenia, stereotypy refers to seemingly meaningless repetitive acts that are rigidly performed over and over again, as if engaged in an idiosyncratic ritual. One of the first psychiatrists to find a symbolic meaning in the stereotypies of psychotic individuals was C. G. JUNG, who, in his autobiography, *Memories, Dreams, Reflections* (1962), relates the story of a quiet old woman who made strange repetitive sewing motions with her hands. In trying to understand what possible meaning the action could have had for her, he investigated her past and found out that many years previously, the woman had suffered the onset of her psychosis after losing a lover who happened to make shoes—hence the source of her sewing motions. Psychoanalyst Frieda FROMM-REICHMANN writes in a 1942 paper that "the seemingly meaningless and inappropriate stereotyped actions of schizophrenics are meaningful, as are the rest of their communications. They serve to screen the appropriate emotional reactions that are at their bottom. . . . They are a means of defense against non-acceptance and rebuff."

Fromm-Reichmann, F. "A Preliminary Note on the Emotional Significance of Stereotypes in Schizophrenics" (1942). In *Psychoanalysis and Psychotherapy: Selected Papers of Frieda Fromm-Reichmann,* edited by D. M. Bullard. Chicago: Chicago University Press, 1959.

Storch's theory of schizophrenic cognition Alfred Storch was a German psychologist who published one of the first comprehensive studies of the peculiarities of thought and language in schizophrenia. Storch was a pupil of the comparative psychologist Heinz Werner. In his 1922 book (published in an English translation in 1924), Storch compared the similarities between the thought processes of schizophrenics and those of persons in primitive societies. He compared the magical worlds of persons living in such societies and the delusional worlds of schizophrenics, especially their preoccupations with religious and mystical issues. Such comparisons are today considered invalid due to the ethnocentrism that colors them. Persons who live in preliterate societies are as "normal" in their thought processes as "normal" persons are in our own, and mental illness is known in these societies and is recognized as such.

Storch, A. *The Primitive Archaic Forms of Inner Experiences and Thought in Schizophrenics.* New York and Washington, D.C.: Nervous and Mental Disease Publishing Company, 1924.

straitjacket, or straight-waistcoat A form of MECHANICAL RESTRAINT invented by a man named MacBride in England in the 1700s for restraining agitated patients in asylums. The heavy canvas coat had sleeves that wrapped around the body and could be tied in the back. Such forms of restraint were used well into the 20th century and may still be in use in some places even today.

See also CAMISOLE.

street drug psychosis A psychotic disorder whose onset is related to the use of PSYCHOTOGENIC DRUGS.

See also SUBSTANCE ABUSE; SUBSTANCE-INDUCED PSYCHOTIC DISORDER.

street people A term for vagrants of all sorts, but especially the homeless mentally ill persons who live on the streets. It is an American term that came into vogue in the 1980s. A 19th-century term for the same class of individuals was PAUPER LUNATICS.

stress It is clear that stress is related to the onset and relapse of many mental and physical disorders.

However, a direct connection between stressful life events and the development of schizophrenia has not been demonstrated. Given that about 80 percent of the vulnerability to schizophrenia is now estimated to be from genetic factors (see GENETICS STUDIES), it is probably true that part of the remaining 20 percent may be related to physically or emotionally stressful environmental influences that contribute to the exacerbation of the disease process. However, a major review of the stress issue in schizophrenia published in 1985 has concluded that "there is no good evidence that life stress is causally related to episodes of schizophrenia."

Gruen, R., and M. Biron. "Stressful Life Events and Schizophrenia," *Neuropsychobiology* 12 (1984): 206–208.

Tennant, C. C. "Stress and Schizophrenia: A Review," *Integrative Psychiatry* (1985): 248–261.

strong rooms See OUBLIETTES.

subjective experiences of schizophrenia With its emphasis on biological and biochemical factors in the development of mental disorders (and the psychotic disorders in particular), psychiatry has been criticized for ignoring the actual experience of an illness by the afflicted person. Indeed, psychiatry has been accused of viewing the notion of the "self" as perhaps a bit mystical, and most professional psychiatric journals today have less and less space for detailed "case histories" of individual experiences. Most studies of the subjective experience of schizophrenia agree on the alterations in the sense of "self" that the disease process produces. Hearing voices, perceptual anomalies, odd beliefs, intrusive thoughts, strange feelings (or lack thereof)—all these highly self-threatening phenomena have been documented in the various reports of persons with psychotic disorders (see PERCEPTUAL ANOMALIES IN SCHIZOPHRENIA). By understanding what actually goes on inside the thoughts and emotions of a person with schizophrenia, we can all develop a deeper empathy for the afflicted person and interact with him or her in a much more genuinely supportive manner.

Based on their work in the United Kingdom, McGhie and Chapman's 1961 paper on attention disturbances is an exemplary study of the inner experiences of schizophrenics and what these reports may mean from a theoretical point of view. The "psychedelic era" generated new interest in purported PSYCHEDELIC EXPERIENCES IN SCHIZOPHRENIA, which then led to a series of studies comparing drug-induced states with psychotic states of consciousness. In the United States, psychiatrist Malcom Bowers's book, *Retreat from Sanity: The Structure of Emerging Psychosis,* published in 1974, provided clinicians and the general public with a series of vivid case histories of what it must be like to undergo a psychotic episode. An excellent collection of historical accounts of the subjective experience of mental illness, particularly of institu- tionalization, was published by Dale Peterson in 1982, containing a comprehensive bibliography of first-person accounts of experiences with "madness." Indeed, most of the major attempts to study the subjective experiences of people with schizophrenia were published in the 1960s and 1970s—prior to the revolution in BRAIN IMAGING TECHNIQUES and GENETICS STUDIES that have shifted the focus to the purely organic view of this disease. In an effort to resurrect interest in the more human and experiential side, in 1989 *Schizophrenia Bulletin* (vol. 15, no. 2) devoted an entire special issue to the theme "Subjective Experiences of Schizophrenia and Related Disorders."

Historical Background

Beginning at least with German psychiatrist Karl Ludwig Kahlbaum's 1874 book on catatonia, psychiatry has been concerned with psychopathology in a very specific way: the objective identification and classification of symptoms of mental illness that could then be grouped into syndromes. A disease was constructed from its symptoms. A second approach in psychiatry, that of nosology, assumed that there are underlying disease processes that exist prior to the appearance of symptoms, and the disease determines the symptoms. Both approaches are still quite influential in psychiatry. However, the subjective human experience of being a particular mentally ill person is lost in these approaches. Both emphasize what is common and

universal across persons (symptoms) and not how a particular form of a symptom (e.g., an auditory hallucination of voices) is actually experienced by a particular person in the course of his or her life. Individual patients are thus objectified, reduced to collections of interchangeable modular components of mental illness stripped of any connection to the meaning of one's personal history.

In 1913 the German psychiatrist Karl Jaspers (1883–1969) transformed the psychopathology approach by applying the philosophical methods of phenomenology to psychiatry in his book *Allgemeine Psychopathologie.* Jaspers was interested in the ways in which patients experienced their consciousness of themselves, the meaning they attached to their symptoms and their illness as a whole, and their feelings. From 1908 to 1915 Jaspers was associated with the psychiatric clinic at the University of Heidelberg in Germany and later was appointed a professor of philosophy there. His work inspired a "phenomenology" movement in psychiatry that was centered in Heidelberg and included such prominent German psychiatrists as Karl Wilmanns (1873–1945); Hans Walther Gruhle (1880–1958); Wilhelm Mayer-Gross (1889–1961), who wrote his paper on "the phenomenology of abnormal feelings of happiness"; Kurt Beringer (1893–1949), who wrote a 1924 monograph on the "dream-like (oneiroid)" forms of experience in psychotic disorders; and Hans Prinzhorn (1886–1933), who compiled a vast collection of the "art of the insane" as evidence of the inner, subjective world of madness, and published an influential book on the subject (see ART, SCHIZOPHRENIC). From 1945 to 1955, Kurt Schneider (1887–1967) became chair of the department. Schneider's FIRST-RANK SYMPTOMS of schizophrenia are a product of this phenomenological tradition at Heidelberg that started with Jaspers.

In the 1950s the subjective experiences of persons with schizophrenia again became a focus of understanding by psychiatrists influenced by the philosophy of existentialism. Prominent among this group was Ludwig Binswanger (1881–1966), who developed a method of psychotherapy based on existential principles, *DASEINANALYSE*. This work influenced British psychiatrist R. D. LAING and the antipsychiatry movement.

Phenomenological and existential approaches to the inner experiences of persons with schizophrenia were always more popular in Europe and the rest of the world than in the United States, where there is a traditional aversion among psychiatrists to any philosophical tradition other than its homegrown pragmatism of William James and John Dewey. Other than its 70-year (1910–80) flirtation with Freudian psychoanalysis and its murky metaphysical ideas, abstract European philosophical concepts have generally been avoided like cholera by anti-intellectual Americans.

Beginning in the 1990s, clinical psychologist Louis Sass of Rutgers University in New Jersey and psychiatrist Josef Parnas of Denmark have been promoting a return to the study of the inner world of schizophrenia by redefining it as a "self-disorder" or an "ipseity disorder" from the Latin, *ipse,* for "self" or "itself." Relying on European phenomenological psychiatry, cognitive science, and phenomenological philosophy, they argue that schizophrenia is characterized by "complementary distortions of the act of awareness: hyperreflexity and diminished self-affection." *Ipseity* is defined as "the experiential sense of being a vital and self-identical *subject* of experience or *first person perspective* on the world." Whether the reframing of schizophrenia as an ipseity disorder proves to have direct application in clinical practice and research remains to be seen.

Bowers, M. *Retreat from Sanity: The Structure of Emerging Psychosis.* New York: Human Sciences Press, 1974.

Freedman, B. J. "The Subjective Experience of Perceptual and Cognitive Disturbances in Schizophrenia," *Archives of General Psychiatry* 30 (1974): 333–340.

Freedman, B. J., and L. J. Chapman. "Early Subjective Experience in Schizophrenia Episodes," *Journal of Abnormal Psychology* 82 (1973): 46–54.

Kleinman, J. E., et al. "A Comparison of the Phenomenology of Hallucinogens and Schizophrenia from Some Autobiographical Accounts," *Schizophrenia Bulletin* 3 (1977): 560–586.

McGhie, A., and J. Chapman. "Disorders of Attention and Perception in Early Schizophrenia," *British Journal of Medical Psychology* 34 (1961): 103–115.

Peterson, D., ed. *A Mad People's History of Madness.* Pittsburgh: University of Pittsburgh Press, 1982.

Sass, L. A., and J. Parnas. "Schizophrenia, Consciousness, and the Self," *Schizophrenia Bulletin* 29 (2003): 427–444.

substance abuse Psychiatric facilities the world over have been deluged since the 1960s with a new type of patient—the "dual diagnosis" patient who is often young, a substance abuser, and perhaps even schizophrenic. Considering the prevalence of illicit drug use in our society by adolescents, and given the fact that it is usually in late adolescence or early adulthood that the first serious onset of schizophrenia has been documented for almost a century, the combination ("comorbidity") of schizophrenia and substance abuse is perhaps the rule and not the exception in today's treatment centers. The issues that are often raised are whether certain drugs actually do initiate the onset of schizophrenia, how they affect its course, and how a history of substance abuse with PSYCHOTOGENIC DRUGS may affect treatment, especially with antipsychotic drugs.

In a major review of the impact of substance abuse on schizophrenia, researchers Winston Turner and Ming T. Tsuang arrived at the following conclusions regarding the present state of scientific knowledge about this relationship:

1. It is evident that substance abuse may profoundly affect the course and outcome of schizophrenia, but the true impact remains largely undefined.
2. There is some evidence that drugs tend to hasten the age of onset of psychosis, but it is unclear whether the effect is to precipitate latent or subliminal psychotic behavior or to initiate psychosis in persons who would not have had a psychotic episode if they did not abuse drugs.
3. Drug abuse just before hospitalization is fairly common, and the drugs of choice do not appear to be random, but it has yet to be determined whether the specific benefits the schizophrenic patients are receiving from the drugs differ from those experienced by persons who do not have schizophrenia.
4. The relationship between characteristics of drug abuse (drug type, quantity, and frequency of drug abuse) and the degree of psychopathology, manifestations of the disease, and long-term outcome has yet to be addressed.
5. Drugs may be precipitating relapse and subsequent rehospitalization among those persons with schizophrenia who are in remission and who would otherwise remain outside of the hospital.

At the end of the 20th century, one of the greatest obstacles to the effective treatment of schizophrenia was the fact that so many young patients used drugs and alcohol. An estimate by Lisa Dixon speculates that half of persons in the United States with schizophrenia may also be battling a diagnosable drug or alcohol disorder. Those persons with schizophrenia at greater risk for addiction tend to be of younger age, of male gender, and have a lower grade of completed education. It is clear now from research studies that persons with schizophrenia who also have a substance abuse problem have poorer outcomes. Furthermore, when compared to other persons diagnosed with schizophrenia, they have more psychotic symptoms, poorer treatment compliance, they tend to be more violent, they are more likely to be homeless, and they are more likely to have medical problems (including HIV infection). Integrating substance abuse treatment (AA, etc.) with mental health services is currently the only viable treatment option.

In the early 1990s the WORLD HEALTH ORGANIZATION conducted a 10-country study of the comorbidity of substance abuse and schizophrenia. It was found that 57 percent of males with schizophrenia abused alcohol. Illegal drugs, primarily cannabis (marijuana) and cocaine, were found to be in use by 24 to 41 percent of all persons with schizophrenia surveyed in the study. In a two-year follow-up study the WHO found that cannabis use was a major risk factor for relapse in schizophrenia. In clinical practice it is not unusual to meet young persons who experienced their first episode of schizophrenia after smoking marijuana, and this connection has long been part of the anecdotal lore of mental health professionals. There is no strong evidence as to whether smoking marijuana is actually a causal factor in the onset of schizophrenia, but the evidence concerning its correlation to increased rates of relapse suggests this may be a precipitating factor in the illness of some young persons.

See also COMORBIDITY.

Dixon, Lisa. "Dual Diagnosis of Substance Abuse in Schizophrenia: Prevalence and Impact on Outcomes," *Schizophrenia Research* 35 (1999): 93–100.

Turner, W. M., and M. T. Tsuang. "Impact of Substance Abuse on the Course and Outcome of Schizophrenia," *Schizophrenia Bulletin* 16 (1990): 87–95.

substance-induced psychotic disorder A *DSM-IV-TR* diagnostic category for persons who develop a psychotic disorder during, or within a month of, substance intoxication or withdrawal. The symptoms must be severe and in excess of what would normally be expected from intoxication or withdrawal. To receive this diagnosis there can be no evidence of a preexisting psychotic disorder.

subtype An identifiable variant of a particular disease.

suicide and schizophrenia Persons with schizophrenia live, on average, 10 to 15 years less than persons in the general population. The main causes of this are deaths due to suicide and to accidents. The single most common cause of death in persons with schizophrenia is suicide. Current estimates place the suicide rate in schizophrenia as equal to, or greater than, the risk of suicide in persons suffering from major depression. In 1995 a study conducted in Scotland found that the suicide rate for persons with schizophrenia was increasing, with the most dangerous period being the first year following discharge from the hospital.

See also COMORBIDITY; MORTALITY IN SCHIZOPHRENIA; RISK FACTORS.

Geddes, J. R., and E. Juszczak. "Period Trends in Rate of Suicide in First 28 Days after Discharge from Psychiatric Hospitals in Scotland, 1968–1992," *British Medical Journal* 311 (1995): 357–360.

surgery See AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX, COLUMBIA-GREYSTONE PROJECT; FOCAL INFECTION A CAUSE OF SCHIZOPHRENIA; LEUCOTOMY; LOBECTOMY; LOBOTOMY; PSYCHOSURGERY; TOPECTOMY; TRANSORBITAL LOBOTOMY.

Sweden See SCANDINAVIA.

swinging chair See CIRCULATING SWING.

symbiotic psychosis This was a syndrome proposed by child psychoanalyst Margaret Mahler to describe a psychotic disorder of childhood that may resemble schizophrenia. It has also been called the "Mahler syndrome." According to Mahler, it occurs in children who have reached a level of development in which they are able to differentiate and individualize from the mother (usually ages two to four) but cannot proceed to a full separation. Whenever separation is attempted, panic ("separation anxiety") sets in. Mahler writes: "The symbiotic psychotic syndrome is aimed at restoring the symbiotic-parasitic delusion of oneness with the mother and thus serves a function diametrically opposite to that of the autistic mechanism." Mahler says that the psychosis may be insidious and may not be detected until school age. The primary symptoms of REGRESSION are catatonia-like temper tantrums and states of panic.

Mahler, M. S. *On Human Symbiosis and the Vicissitudes of Individuation.* Vol. 1, *Infantile Psychosis.* New York: International Universities Press, 1968.

symptom Generally, a symptom is any manifestation of a pathological condition. Although a strict interpretation of this word is that it refers only to subjective complaints of distress, it may, in some instances, also refer to objective pathological conditions.

See also SIGN.

syndrome A cluster of symptoms that commonly appear together and constitute a recognizable condition. The term *syndrome* is often less specific than the words *disease* or *disorder. Disease* is used when

a specific etiology (cause) of an illness is known, or if its specific organic disease process is known. Most mental disorders therefore are in fact syndromes rather than diseases.

synesthesia A condition in which a sensory experience normally associated with one modality occurs when another modality is stimulated. For example, a loud, sudden sound might produce visual images of lights flashing or swirling colors. Such experiences have been reported with the use of hallucinogens and in acute psychotic episodes.

See also PSYCHEDELIC EXPERIENCES IN SCHIZOPHRENIA.

syphilitic psychosis See GENERAL PARALYSIS OF THE INSANE.

T

tactile hallucinations A hallucination of "touch." Often a tactile hallucination involves something that is felt on or under the skin, and a delusional interpretation of the sensory experience usually accompanies a tactile hallucination. FORMICATION is a specific type of tactile hallucination in which something (usually "bugs") is felt to be crawling just below the surface of the skin. Formication is commonly reported in alcohol withdrawal delirium and in withdrawal from cocaine intoxication.

Taiwan The prevalence rate for schizophrenia in Taiwan has been found to be 2.2 per 1,000. Studies of prevalence rates for schizophrenia among the aboriginal population has been found to be among the lowest rates in the world—0.9 per 1,000.

Torrey, E. F. *Schizophrenia and Civilization.* New York: Jason Aronson, 1980.

tangentiality A feature of the peculiar thought processes found in schizophrenia and in schizotypal personality disorder in which a person does not stick to one topic when speaking but gets pulled off into tangential currents of thought. Usually these are topics that are unrelated to the main point of the conversation, but the person seems unable to focus attention enough to stay consistent with the main topic.

taraxein hypothesis In 1957 a research study by Heath and coworkers announced that they had isolated an abnormal blood protein in the serum of people with schizophrenia that they called taraxein. When they injected this protein into monkeys, it apparently produced abnormal behavior. Furthermore, when injected into normal human subjects, Heath claimed that this substance induced a temporary psychotic disorder that mimicked schizophrenia. It was claimed that taraxein was in the gamma immunoglobulin (IgG) of persons with schizophrenia and that it acted as an antibody against antigens that were present in the person's own limbic system in the brain. Therefore, since it interfered with brain functioning, it was argued that taraxein was a probable cause of schizophrenia, making it an autoimmune disease. Heath's findings have not been replicated by other laboratories.

See also IMMUNE SYSTEM ALTERATION IN SCHIZOPHRENIA.

Heath, R. G., and I. M. Krupp. "Schizophrenia as an Immunologic Disorder: Demonstration of Antibrain Globulins by Fluorescent Antibody Techniques," *Archives of General Psychiatry* 16 (1967): 1–9.

Heath, R. G., et al. "Effect on Behavior in Humans with the Administration of Taraxein," *American Journal of Psychiatry* 114 (1957): 14–24.

tardive dyskinesia This is an involuntary movement disorder directly caused by brain changes resulting from the long-term use of ANTIPSYCHOTIC DRUGS. It appears either during treatment with antipsychotic drugs or shortly (four to eight weeks) after terminating such treatment.

Symptoms and Diagnostic Path

The TD syndrome is characterized by abnormal movements in the following areas of the body, as summarized by M. Marsalek in an article published in 2000:

- Tongue: rolling, arrhythmic tongue protrusions (fly catching sign), tongue producing a bulge in the cheek (the bon-bon sign)
- Lips: pouting, smacking, puckering, sucking
- Mouth: chewing movements
- Face: grimacing, paroxysms of rapid eye-blinking
- Neck: arrhythmic head nodding
- Trunk: irregular rocking movements of the upper torso
- Upper extremities: abnormal stereotypic movements in the fingers may look as though the patient is playing an invisible guitar (also formerly known as the "pill-rolling" movement)
- Lower extremeties: flexing, rotation of the ankles, involuntary stamping movements, retroflexion of the toes

Treatment Options and Outlook

Tardive dyskinesia is a chronic disorder. At present there are no uniformly safe and effective treatments for it.

Marsalek, M. "Tardive Drug-induced Extrapyramidal Syndromes," *Pharmacopsychiatry* 33 (2000): 14–33.

temperament See FUNDAMENTAL STATES OF MANIC-DEPRESSIVE INSANITY.

temporary psychosis See ATYPICAL PSYCHOTIC DISORDERS.

theomania A type of MONOMANIA identified by J. E. D. ESQUIROL in 1938 for the category of persons with a psychotic disorder that includes those "who believe that they are God, who imagine that they have conversations and intimate communications with the Holy Spirit, angels and saints, and who pretend to be inspired, and to have received a commission from heaven to convert men." This disorder is in distinction to CACODEMONOMANIA, which involves the delusional belief of contact with "evil" forces.

Esquirol, J. E. D. *Mental Maladies: A Treatise on Insanity,* trans. E. K. Hunt. 1838. Reprint, Philadelphia: Lea and Blanchard, 1945.

therapeutic community See MILIEU THERAPY.

thioridazine See ANTIPSYCHOTIC DRUGS.

thiothixene See ANTIPSYCHOTIC DRUGS.

thioxanthenes See ANTIPSYCHOTIC DRUGS.

Thorazine The trade name for CHLORPROMAZINE. It is named after the Norse god of Thunder, Thor.
See also ANTIPSYCHOTIC DRUGS.

thought broadcasting A delusion common in schizophrenia in which the person believes or experiences his or her own internal thoughts as being broadcast from one's head as they are occurring so that others can hear them.

thought disorder See FORMAL THOUGHT DISORDER.

thought insertion Another common delusion found in persons in schizophrenia, it is the delusion that thoughts belonging to other persons or entities are being inserted into one's mind.

thought withdrawal One of the most common delusions found in schizophrenia, "thought withdrawal" is the belief that thoughts have been removed from one's head.

thrashing See FLOGGING.

Three Christs of Ypsilanti Social psychologist Milton Rokeach published his famous study of the impact that three paranoid schizophrenic men, who all believed they were Jesus Christ, had on one another when they were placed together in the same bedroom, same workplace, and same cafeteria table at Ypsilanti State Hospital in Michigan

from July 1959 to August 1961. The purpose was to record the changes in each of the men, who all claimed the same delusional identity. Although no one improved in any overall sense, two of the Christs modified their self-identities a bit to avoid conflict, whereas the third ended up becoming more firmly entrenched in his identity, even to the point of denying that the other two were alive (see COTARD'S SYNDROME). Rokeach concludes in the final sentence of his books: "And, finally, we have learned that even when a summit of three is composed of paranoid men, deadlocked over the ultimate in human contradiction, they prefer to seek ways to live with one another in peace rather than destroy one another."

Rokeach, M. *The Three Christs of Ypsilanti: A Psychological Study.* New York: Alfred A. Knopf, 1964.

thyroid disease masking as psychosis See MEDICAL DISORDERS THAT MIMIC PSYCHOTIC DISORDERS.

token economy See BEHAVIOR THERAPY.

topectomy A PSYCHOSURGERY procedure invented by J. Lawrence Pool, a research assistant in the Department of Neurology at Columbia University in 1947. The term is derived from two Greek words meaning "place" and "excision." An attempt to create a more conservative form of psychosurgery, topectomy involved destroying parts of the frontal cortex itself rather than severing the white fibers below (as in a LEUCOTOMY). It considerably reduced the chances of hemorrhaging and therefore the likelihood that a patient would become a zombie-like vegetable, as was the case in many psychosurgical patients of Walter FREEMAN. The topectomy was one of the forms of psychosurgery studied by the COLUMBIA-GREYSTONE PROJECT in 1947 and was performed on patients of the New Jersey State Hospital in Greystone Park.

Tory rot An 18th- and early 19th-century American psychotic disorder identified by Benjamin RUSH to refer to those "insane" persons who did not believe in the value of the American Revolution. Rush was convinced that these people were mentally ill and that they died from their insanity. It is not known if Rush involuntarily committed any of these people to the Pennsylvania Hospital in Philadelphia, which would have made them political prisoners.

Lloyd, J. H. "Benjamin Rush and His Critics," *Annals of Medical History* 2 (1930): 470–475.

toxin theory See AUTOINTOXICATION AS A CAUSE OF DEMENTIA PRAECOX (SCHIZOPHRENIA).

tranquillizer A form of MECHANICAL RESTRAINT invented by American physician Benjamin RUSH in 1808. Also called a "coercion chair," it was designed to restrain agitated or violent patients. The device was an instrument of torture in which a person would sit upright in a chair, arms shackled to the arms of the chair and feet clasped by the ankles in a device at the bottom of the chair; it had a wooden block that could be raised or lowered and would fit over the head of the person, making him or her completely immobile. In his 1812 treatise, Rush extols the virtues of the use of the "tranquillizer" for violent patients:

> Confinement by means of a strait waistcoat or of a chair which I have called a tranquillizer. He submits to them both with less difficulty than to human force, and struggles less to disengage himself from them. The tranquillizer has several advantages over the straight waistcoat or mad shirt. It opposes the impetus of blood towards the brain, it lessens muscular actions every where, it reduces the force and the frequency of the pulse, it favours the application of cold water and ice to the head, and warm water to the feet, both of which I shall say presently are excellent remedies in this disease; it enables the physician to feel the pulse and to bleed without any trouble, or altering the erect position of the patient's body; and, lastly, it relieves him, by means of a close stool, half filled with water, over which he con-

stantly sits, from the festor and filth of his alvine evacuations.

Since Rush's time, the word *tranquillizer* has been part of the slang of asylums and mental hospitals, referring to just about any method that quiets an agitated patient. It is thought that this is the source of our use of the word *tranquilizer* for sedative medications. A graphic reproduction of the famous illustration of Rush's device appears on the cover of the book cited below by Sander Gilman.

Gilman, S. L. *Seeing the Insane.* New York: Wiley, 1982.
Rush, B. *Medical Inquiries and Observations upon the Diseases of the Mind.* Philadelphia: Kimber & Richardson, 1812.

transcultural studies of schizophrenia See CROSS-CULTURAL STUDIES.

transmethylation hypothesis Based on studies of how hallucinogenic drugs, particularly LSD-25, worked on the brain to produce "psychotogenic" (psychosis-causing) effects, from at least 1957 to the mid-1970s the dominant theories of schizophrenia were based on various "inappropriate methylation" or transmethylation hypotheses. The term *transmethylation* was coined by the organic chemist John Harley-Mason of Cambridge University in England in 1951. The first publication advocating this hypothesis was published in 1952 in the *Journal of Mental Science* and coauthored by Humphrey Osmond (1917–2004) and John Smythies. They suggested that schizophrenia was caused by a toxic hallucinogenic substance, produced in the brain, through the faulty methylation of adrenaline. Throughout the 1950s Osmond was joined by Abram Hoffer (1917–) in this research at the mental hospital in Weyburn, Saskatchewan, Canada. Osmond coined the term *psychedelic* in 1957 for hallucinogenic drugs such as LSD-25 and mescaline, which he had personally introduced to the British author Aldous Huxley (1894–1963) in 1953. In 1959 Osmond and Hoffer revised their transmethylation theory, claiming the toxic substance was adrenochrome. Replication attempts by others could not find adrenochrome in the bodily fluids of persons with schizophrenia. However, Hoffer's suggestion that the production of adrenochrome could be blocked by administering high doses of niacin (vitamin B_3) led to the fad of MEGAVITAMIN THERAPY for schizophrenia and a new but marginal discipline known as orthomolecular psychiatry.

The assumption was that if the body of a person with schizophrenia was producing LSD-like or mescaline-like substances, then metabolites of these chemicals should be detectable in the blood or urine. For two decades schizophrenia researchers searched for enzymes that converted one biochemical molecule into another less-active substance or its detectable metabolite after breakdown. A prominent proponent of this line of research during this era of "metabolic psychiatry" was Seymour Kety (1915–2000), the head of the neuroscience laboratories at the National Institute of Mental Health.

No endogenous psychotogen or psychosis-causing metabolite was ever found in persons with schizophrenia. However, the basic research conducted within the framework of the transmethylation hypotheses led to many useful discoveries, including the metabolites of dopamine and serotonin, which had applications to other fields of research, such as psychopharmacology. By the late 1960s the focus of research had shifted from the search for toxic metabolites to instabilities of the methylation process itself. By the late 1970s, the TRANSMETHYLATION HYPOTHESIS had been replaced by a new one: the DOPAMINE HYPOTHESIS. Research into the various transmethylation hypotheses slowed to a trickle and had virtually disappeared by the 21st century. The last such publication in this tradition appeared in 1999, reporting the "experimental psychosis" induced by the ingestion of Ayahoasca, a South American hallucinogenic beverage prepared by boiling two plants found in the Amazon region.

See also BIOCHEMICAL STUDIES OF SCHIZOPHRENIA; METABOLIC DISORDER HYPOTHESIS.

Hoffer, A., and H. Osmond. "The Adrenochrome Model and Schizophrenia," *Journal of Nervous and Mental Disease* 123 (1959): 18–35.
Luchins, D., et al. "A Review of Nicotinic Acid, N-methylated Indoleamines and Schizophrenia," *International Pharmacopsychiatry* 13 (1978): 16–33.

Osmond, H., and J. R. Smythies. "Schizophrenia: A New Approach," *Journal of Mental Science* 98 (1952): 309–315.

Pomilio, A. B., et al. "Ayahoasca: An Experimental Psychosis That Mirrors the Transmethylation Hypothesis of Schizophrenia," *Journal of Ethnopharmacology* 65 (April 1999): 29–51.

transorbital lobotomy The famous "ice-pick technique" of PSYCHOSURGERY invented by psychiatrist Walter FREEMAN in 1946 as an alternative to the formal surgical procedures that involved the opening of the skull. Transorbital lobotomies avoided this by lodging an ice pick–type instrument behind the orbit of the eye and into the frontal lobes, where a few quick strokes could damage enough of the brain tissue to achieve the desired tranquilizing effect. Freeman first used this technique on outpatients in his Washington, D.C., office in 1946 against the advice of his associate, James Watts, who refused to cooperate with him. For these first patients Freeman did use an actual ice pick from his kitchen drawer at home, and this historic kitchen utensil is in the collection of the James W. Watts and Himmelfarb Health Sciences Library of George Washington University in Washington, D.C. The development of the transorbital lobotomy technique led to the mass brain damaging of thousands of institutionalized psychiatric patients in the 1940s and 1950s.

treatment-resistant schizophrenia Despite the many positive reports about the beneficial effects of treating people with schizophrenia with ANTIPSYCHOTIC DRUGS, there are still patients who are refractory to this form of therapy. Those who are not helped by antipsychotic drugs range in estimates from 20 to 33 percent of schizophrenics. These estimates do not include the 15 percent or so of schizophrenic patients who improve with just placebo treatment in double-blind studies of antipsychotic drugs.

Research on persons who develop treatment-resistant schizophrenia have found the following characteristics:

(1) there is no clear relationship between initial symptoms, positive or negative, and outcome (a fact that rejects the claims of CROW'S HYPOTHESIS regarding Type II schizophrenia)
(2) poor premorbid functioning
(3) early age of onset of illness
(4) male gender
(5) presence of neurological "soft signs" in males
(6) early cognitive impairment

The duration of time during which the illness was left untreated has no apparent relationship to being treatment-resistant. Research on the new atypical ANTIPSYCHOTIC DRUGS indicates many of them may be as useful as clozapine as a form of maintenance therapy. All in all, the reasons why so many persons with schizophrenia simply do not respond to current medication remain a mystery.

Barnes, T. R. E., P. Buckley, and S. C. Schulz. "Treatment-resistant Schizophrenia." In *Schizophrenia. 2nd ed.*, edited by S. R. Hirsch and D. Weinberger. Cambridge: Blackwell, 2003.

trepanation (or trephination) Perhaps the earliest form of PSYCHOSURGERY for epilepsy and mental disorders, this technique involved the removal of a (usually) circular piece of the skull for the purposes of surgical treatment of the brain. Trephined skulls dating from Neolithic times have been found in Europe and among the ruins of the great civilizations of the world, including the ancient Incas. During the Middle Ages trepanning continued as a treatment and was done by using carpenters' drills. Sir William Osler (1848–1919) writes in a 1921 book, *The Evolution of Modern Medicine*, that "the operation was done for epilepsy, infantile convulsions, headache and various cerebral disease believed caused by confined demons, to whom the hole gave a ready method of escape."

Horrax, G. *Neurosurgery—An Historical Sketch.* Springfield, Ill.: Charles C. Thomas, 1952.

trichtillomania An infrequently observed but not uncommon behavior observed in people with psychotic disorders (and with other types of mental disorders) is the compulsive pulling out of one's

hair, resulting in bald patches on the scalp or on other parts of the body. In *DSM-III-R* trichtillomania is included among the impulse control disorders. Trichtillomania was first described by the French physician Hallopeau in 1889. Most studies of trichtillomania have concluded that it is (1) a chronic disorder that (2) frequently involves multiple hair sites, and (3) that is highly correlated with the presence of another mental disorder (for example, major depression, the mental disorder with which trichtillomania is most closely correlated).

Christenson, G. A., et al. "Characteristics of 60 Adult Chronic Hair Pullers," *American Journal of Psychiatry* 148 (1991): 365–370.

Hallopeau, M. "Alopcie par grattage (trichomanie ou trichtillomanie)," *Annales Dermatol. Venerol.* 10 (1889): 440–441.

trifluoperazine See ANTIPSYCHOTIC DRUGS.

Trilafon See ANTIPSYCHOTIC DRUGS.

tuberculosis and psychosis The idea has often been put forth that certain diseases are incompatible and cannot be found in the same person. This was the untested hypothesis behind the CONVULSIVE THERAPY idea in the 20th century that epilepsy and schizophrenia could not be found together in the same person. In the 18th and 19th centuries, it was believed that those persons who developed pulmonary tuberculosis were not likely to develop a psychotic disorder. No scientific support for this theory has ever been put forth.

However, in the 1930s the opposite hypothesis was put forth: namely, that tuberculosis might be the cause of certain mental diseases, including schizophrenia. In 1933 Austrian researcher E. Löwenstein published a paper describing a new and more sensitive technique for the detection of Koch's bacillus (the cause of tuberculosis) and suggested that he could establish a diagnosis of tuberculosis in cases that may not, on first appearance, look like tuberculosis. Included among these were some mental disorders, including schizophrenia. For a few years following this announcement, the hypothesis was discussed that schizophrenia and tuberculosis may be related after all, but no confirming evidence was ever put forth.

See also PHYSICAL DISEASE; SCHIZOPHRENIA.

Hunter, R. A., and J. G. Widdicombe. "Tuberculosis and Insanity: Historical and Experimental Observations on the Straight-waistcoat as Collapse Therapy," *St. Bart's Hospital Journal* 61 (1957): 113–119.

Löwenstein, E. "Über Tuberkelbasillämie bei Nervenkrankheiten," *Wein. Klin. Wchschr.* 46 (1933): 228–231.

twins method and studies Studying pairs of twins in which one or both members have schizophrenia or bipolar disorder has been an important area in GENETICS STUDIES of these psychotic disorders. Indeed, they have been so fruitful that NIMH genetics researcher David Rosenthal has concluded that "the twins studies probably have contributed our most reliable data regarding the inheritance of schizophrenia."

Twins studies compare the CONCORDANCE RATE for schizophrenia in pairs of MONOZYGOTIC ("identical") TWINS with the rate found in DIZYGOTIC ("fraternal") TWINS. In fact, it was Rosenthal himself who pioneered the scientific study of schizophrenic twins for their possible information regarding genetic transmission, publishing the first study using the strategy of comparing the concordance rate of monozygotic twins in 1962. In some later studies, the rate in first-degree biological relatives is also compared.

There are two major assumptions behind the twins studies: (a) that monozygotic twins share all the same genes, whereas dizygotic twins only have about half of their genes in common, and (b) that both varieties of twin pairs are exposed to the same prenatal and postnatal environmental influences. Therefore, given these two assumptions, it would be expected that monozygotic twins would show a greater concordance for genetically transmitted diseases of all types than dizygotic twins—which is, indeed, the case.

According to a review of genetics studies of schizophrenia by K. S. Kendler in 1986, the twins studies of schizophrenia have fairly consistently

reported a three-times greater risk for developing schizophrenia in the monozygotic twins of persons with schizophrenia than in the dizygotic twins of afflicted persons. Furthermore, the risk for developing schizophrenia is 40 percent to 60 percent greater in these monozygotic twins than in the general population. Other studies have demonstrated that monozygotic twins reared apart from each other are concordant for schizophrenia (that is, both twins have it) at about the same rate as those who are raised together, thus strongly confirming the role of genetics over the environment. Still, there are monozygotic twins who are discordant for schizophrenia, and future research must determine why this is so if schizophrenia is a genetically transmitted disease.

For bipolar disorder, twins studies also point to a strong genetic component for the transmission of the illness. A famous Danish twins study of manic-depressive disorders published in 1977 found that there was a 79 percent concordance rate for bipolar illness in the monozygotic twins of persons diagnosed with this disorder, in contrast to a concordance rate of only 19 percent in the dizygotic twins of persons diagnosed with bipolar disorder. Reanalysis of the Danish data by others found these rates to be too high. Other studies of bipolar disorder find the rates for MZ twins to be closer to 44 percent.

One of the most intriguing studies using the twins method was conducted by E. Fuller Torrey and his colleagues. Finding large numbers of pairs of twins that were discordant (one twin had the disease, the other didn't) for schizophrenia or bipolar disease, Torrey and his colleagues conducted a series of neuropsychological, neurophysiological, genetic, and neuroimaging studies to answer the age-old question: "Why is one twin sick and the other one isn't if X is a genetic disease?" Although they did not find the answer to this question, the data they collected will be a valuable contribution to solving that riddle in the 21st century.

See also GENETICS STUDIES.

Bertelsen, A., et al. "A Danish Twin Study of Manic-Depressive Disorders," *British Journal of Psychiatry* 130 (1997): 330–351.

Kendler, K. S. "Genetics of Schizophrenia." In *Psychiatry Update: American Psychiatric Association Annual Review.* Vol. 5, edited by A. J. Frances and R. J. Hales. Washington, D.C.: American Psychiatric Press, 1986.

Rosenthal, D. "Problems of Sampling and Diagnosis in the Major Twin Studies of Schizophrenia," *Journal of Psychiatric Research* 1 (1962): 116–134.

Torrey, E. F., A. E. Bowler, E. H. Taylor, and I. I. Gottesman. *Schizophrenia and Manic-Depressive Disorder: The Biological Roots of Mental Illness as Revealed by the Landmark Study of Identical Twins.* New York: Basic Books, 1994.

two-syndrome concept of schizophrenia See CROW'S HYPOTHESIS.

Type I/Type II schizophrenia See CROW'S HYPOTHESIS.

U

undifferentiated type This is one of the four subtypes of schizophrenia currently recognized by *DSM-IV* (1994), and it is probably the most common diagnosis given to people with schizophrenia (with the paranoid subtype close behind). The essential features of this subtype are prominent psychotic features such as delusions, hallucinations, formal thought disorder, incoherence, or grossly disorganized behavior, but it may combine features of two or more of the other subtypes, or features that simply cannot fit into the diagnostic descriptions of the other subtypes. Hence, "undifferentiated type" is a garbage pail diagnosis.

unitary psychosis See *EINHEITSPSYCHOSE*.

United States Worldwide prevalence rates for schizophrenia have been found to range from less than 1 to 17 per 1,000 persons. However, most studies conducted worldwide—including those in the United States—fall within the 2 to 5 per 1,000 range. In the United States, specific prevalence rates from research studies have ranged from 1.1 (among the rural Hutterites, a closed religious community) to 4.7 (if age corrected, from 2.1 to 6.4) per 1,000. The highest rates of schizophrenia are found in the urban areas and among the lowest socioeconomic strata of American society. E. Fuller Torrey has suggested that preliminary evidence shows that the prevalence rate for schizophrenia in the United States may have risen since 1950 and recommends that more comprehensive research be carried out to investigate this possibility.

Torrey, E. F. "Prevalence Studies of Schizophrenia," *British Journal of Psychiatry* 150 (1987): 598–608.

"usual treatment, the" Philippe Pinel's phrase that he used several times in his 1801 book, *A Treatise on Insanity,* to describe the treatment of institutionalized persons with mental disorders in the 18th and early 19th centuries—namely, "bleeding, bathing and purging."

Utica crib A form of mechanical restraint originally developed in France by a physician named Aubanel in 1845 but first used in the United States at the Utica State Hospital in New York State upon the recommendation of its superintendent, Amariah Brigham, one of the original 13 founders of the AMERICAN PSYCHIATRIC ASSOCIATION. It was a crib bed but with a hinged lid that could be locked, keeping the patient confined in a horizontal position.

V

V.A. hospitals Hospitals in the United States for veterans of military service. They are managed under the auspices of the Veterans Administration, and their psychiatric wards serve as an adjunct to the state hospital system for the mentally ill.

vampirism, clinical Although it is quite rare, there have been actual case reports of people with psychotic disorders engaging in clinical vampirism—that is, the ingestion of blood, whether one's own or the blood of others. Clinical vampirism is actually a "blood fetish" that often develops in childhood, when the child finds the taste of his own blood enjoyable. Then, after puberty, these pleasurable feelings become associated with sexual activities, usually masturbation. The typical course starts with autovampirism, causing bleeding from one's own body through simple cuts or scrapes, to then opening major blood vessels to drink one's own blood. In some people, the fetish graduates to true clinical vampirism—the desire to drink the blood of others. Psychologist Richard Noll has suggested this delusional syndrome be named RENFIELD'S SYNDROME, after the character in Bram Stoker's *Dracula*. People with schizophrenia have been reported to have engaged in clinical vampirism, but this is an extremely rare occurrence.

Benezech, M., et al. "Cannibalism and Vampirism in Paranoid Schizophrenia," *Journal of Clinical Psychiatry* 42 (1981): 7.

Noll, R. *Vampires, Werewolves and Demons: Twentieth Century Case Reports in the Psychiatric Literature.* New York: Brunner/Mazel, 1991.

Prins, H. "Vampirism—A Clinical Condition," *British Journal of Psychiatry* 146 (1985): 666–668.

variable expressivity In GENETICS STUDIES, if the same genetically transmitted abnormality produces different manifestations for either genetic or nongenetic reasons, it is said that this abnormality is characterized by variable expressivity. For example, the finding in schizophrenia research that smooth-pursuit eye movement abnormalities have been found in 60 percent of persons with schizophrenia and in 55 percent of their first-degree biological relatives might be an example of variable expressivity, because in many instances there are persons with schizophrenia who do not have abnormal smooth-pursuit eye movement but their nonschizophrenic relatives do (see EYE MOVEMENT ABNORMALITIES IN SCHIZOPHRENIA). All this may really mean is that an underlying process (or "latent trait," perhaps) may induce a disorder in the brain that produces either schizophrenia, smooth-pursuit eye movement abnormalities, or both. These three possibilities illustrate the variable expressivity of this underlying process or trait.

Holzman, P. S. "Eye Movement Dysfunction and Psychosis," *International Review of Neurobiology* 27 (1985): 179–205.

vascular-inflammatory theory of schizophrenia See BLOOD VESSEL ALTERATIONS IN SCHIZOPHRENIA.

ventriculomegaly Literally, "enlarged ventricles," a common characteristic of some persons with schizophrenia. Ventricle size in the majority of schizophrenics is within the normal range.

See also BRAIN ABNORMALITIES IN SCHIZOPHRENIA.

verbigeration A term for the repetitious, meaningless speech of persons with psychotic disorders. It was first introduced by German psychiatrist Karl KAHLBAUM in 1874. In the English translation of the fourth edition of Eugen BLEULER's famous textbook on psychiatry, he defines this psychotic behavior in the following way: "The stereotype of speech, or *verbigeration*, always repeats the same words or sentences, often entirely senseless ones."

violence and schizophrenia Contrary to the popular negative stereotype of the mentally ill as "psycho killers," it is probably not true that persons with schizophrenia are more violent toward others than those persons who do not have this disease. It is true that those persons with schizophrenia that do tend to be violent toward others are of the paranoid subtype or have transient paranoid delusions, are undermedicated or have ingested street drugs of some sort. It is also true that persons with schizophrenia have a higher rate of crimes against property than persons in the general population. In addition, persons with schizophrenia have higher rates of violence against themselves in the form of suicide when compared with the general population, and perhaps even for acts of self-mutilation, although there are no statistics for this latter observation. Although a prior history of violence is the best predictor of future violence in individual cases, it is still next to impossible for clinicians to accurately predict future acts of "dangerousness" or of violence.

McNiel, D. E., and R. L. Binder. "Predictive Validity of Judgments of Dangerous in Emergency Civil Commitment," *American Journal of Psychiatry* 144 (1987): 197–200.

Rada, R. T. "The Violent Patient: Rapid Assessment and Management," *Psychosomatics* 22 (1981): 101–109.

Weaver, K. E. "Increasing the Dose of Antipsychotic Medication to Control Violence," *American Journal of Psychiatry* 140 (1983): 1,274.

Yesavage, J. A. "Inpatient Violence and the Schizophrenic Patient: An Inverse Correlation between Danger-Related Events and Neuroleptic Levels," *Biological Psychiatry* 17 (1982): 1,331–1,337.

viral theories of schizophrenia Since the turn of the century, it has often been suggested that infectious agents might be the cause of schizophrenia. Both Emil KRAEPELIN and Eugen BLEULER commented on the fact that infectious processes might play a role in the development of schizophrenia. When it was discovered conclusively at around that time that the syndrome known as the GENERAL PARALYSIS OF THE INSANE was caused by tertiary syphilis, similar infectious agents were sought for dementia praecox (schizophrenia). Most of the research centered on bacteria (see FOCAL INFECTION AS CAUSE OF PSYCHOTIC DISORDERS and TUBERCULOSIS AND PSYCHOSIS), since viruses were not well understood at the time.

After the First World War, worldwide outbreaks of influenza and Von Economo's encephalitis drew attention once again to this hypothesis, since post-encephalitic patients seem to have the same signs and symptoms of schizophrenia. However, after the 1920s, the rise of psychoanalytic, psychosocial, and family interaction theories of the causes of schizophrenia drew attention away from possible organic causes, such as viruses. It wasn't until the 1950s that interest once again briefly revived, only to subside until the 1970s, when research on the role of infectious agents in the development of many physical diseases began to uncover some promising results.

E. Fuller Torrey is responsible for drawing attention once again to the viral hypothesis of schizophrenia, after he became aware of some research that demonstrated that "slow" or latent viruses could cause central nervous system diseases after remaining latent in the body for perhaps 20 years or more. Such research continues into the possible viral causes of multiple sclerosis and many other diseases of the central nervous system. Torrey began research at the National Institute of Mental Health in the early 1970s by collecting the blood and cerebral spinal fluid (CSF) from persons with schizophrenia and then analyzing these fluids to detect evidence of a viral presence. His first publication on this viral hypothesis appeared in 1973.

Although other infectious agents such as bacteria, rickettsiae, and fungi cannot be ruled out, viruses are prime suspects in schizophrenia for

several reasons: (1) their frequent neurotropism, that is, their affinity for neural tissue, (2) their ability to remain latent in brain tissue for many years, perhaps even decades, (3) they can attack very specific areas of the brain (often the limbic system, which is implicated in schizophrenia) and leave others untouched, (4) their propensity to produce relapses and remissions, and (5) their ability to alter the enzymatic functions of brain cells without causing visible structural damage to the cells that could be picked up, for example, by BRAIN IMAGING TECHNIQUES or neuropathological methods. They have even been found to cause changes in the neurotransmitters of the brain, perhaps even producing the biochemical changes that produce the symptoms of schizophrenia.

There are several viral models as possible causes of schizophrenia. Some of them are based on the idea that an *in utero* infection of the fetus may affect fetal neural development and therefore result in schizophrenia later in life. This theory fits in with the research on perinatal factors as contributing causes to schizophrenia. Other theories propose that the mother or even the father may be an asymptomatic carrier that transmits the virus across the placenta during pregnancy. The SEASONALITY OF BIRTHS of persons who develop schizophrenia also fits well with a viral theory, since many viral infections are seasonal, and the excess of schizophrenic births in late winter to spring may be a reflection of prenatal infection. The fact that schizophrenia runs in families may be attributed to viral theories as well, since persons may be inheriting a genetic predisposition to being affected by a particular virus, or the virus may actually be transmitted on the gene itself (as is the case in retroviruses).

However, despite the logic of viral theories of schizophrenia, the research has not been very fruitful. In 1988 E. Fuller Torrey concluded in his review of the issue: "Despite the theoretical attractiveness of infectious agents as etiologic models, there is as yet little direct evidence with which to link them to schizophrenia. This may be because laboratory technology is not yet sensitive enough, we have not yet looked for the correct infectious agent, or the infectious hypothesis is simply wrong. In addition, adoption studies suggest that if infectious agents are involved in such cases, transmission of the agent must occur in utero or at birth."

Throughout the 1990s the search for a virus that may be related to schizophrenia continued to fail. Using the long latency period of the human immunodeficiency virus (HIV) as a model (since it takes so many years for symptoms to appear in infected persons), schizophrenia researchers used the new tools of genetics research to find evidence of the presence of a retrovirus in persons with schizophrenia. In one major study, DNA and RNA was extracted from the brain tissue of deceased persons with schizophrenia and also from controls. The new PCR (polymerase chain reaction) procedure was used because it can allow for the detection of small amount of genetic material from viruses present in the blood, urine, or tissue of humans. The researchers used PCR with primers from 12 different viruses, some of them retroviruses, all of them speculated to be involved in schizophrenia at one time or another. Absolutely no trace of any genes from any of these viruses were found. The search for the "schizovirus" continues.

See also CATS AND SCHIZOPHRENIA.

Taller, A. M., et al. "Search for Viral Nucleic Acid Sequences in Brain Tissues of Patients with Schizophrenia Using Nested Polymerase Chain Reaction," *Archives of General Psychiatry* 53 (1996): 32–40.

Torrey, E. F. "Stalking the Schizovirus," *Schizophrenia Bulletin,* 14 (1988): 223–229.

Torrey, E. F., and M. R. Peterson. "Slow and Latent Viruses in Schizophrenia," *Lancet* 2 (1973): 22–24.

visual hallucinations Hallucinations of sight. These may include formed images (such as people or alligators) or unformed images (such as flashes of light). Visual hallucinations have often been attributed to an organic cause, such as the presence of drugs in the person's system, or perhaps a metabolic disorder or an infection. In schizophrenia, auditory hallucinations have been the most commonly reported type. However, a 1989 study found that visual hallucinations may occur in 32 percent to 56 percent of persons with schizophrenia at some point in their illness, and that they are usually associated with auditory hallucinations,

delusions, and thought disorder. They found that visual hallucinations were slightly more prevalent in the nonparanoid forms of schizophrenia than in the paranoid forms but that this difference was not statistically significant in the study. They suggest that most clinicians do not ask about visual hallucinations (the most common interview question is often, "Do you hear voices?"), and that probably accounts for why they are so infrequently discussed in the literature of schizophrenia.

Bracha, H. S., et al. "High Prevalence of Visual Hallucinations in Research Subjects with Chronic Schizophrenia," *American Journal of Psychiatry* 146 (1989): 526–528.

vorbeireden See GANSER'S SYNDROME.

vulnerability model of schizophrenia What do all the various theories of schizophrenia (genetic, environmental, developmental, learning, neurophysiological) have in common? Can they be unified in some way? These were the questions asked by researchers Joseph Zubin and Bonnie Spring, who propose in a 1977 paper that the concept of vulnerability is the common link between all these theories. They write: "The vulnerability model proposes that each of us is endowed with a degree of vulnerability that under suitable circumstances will express itself in an episode of schizophrenia illness." However, the researchers "distinguish between *vulnerability* to schizophrenia, which we regard as a relatively permanent, enduring trait, and *episodes* of schizophrenic disorder, which are waxing and waning states." Thus, they suggest that both vulnerability and episodic "markers" (biological, genetic, environmental) must be found. Since the publication of this article, the concept of vulnerability in this wider, more general sense is often referred to in the literature of schizophrenia.

Zubin, J., and B. Spring. "Vulnerability—A New View of Schizophrenia," *Journal of Abnormal Psychology* 86 (1977): 103–126.

W

water drinking, excessive, in persons with schizophrenia See POLYDIPSIA.

water therapy See HYDROTHERAPY.

wet sheets See PACKING (AS TREATMENT).

whipping See FLOGGING.

Williamsburg Eastern Lunatic Asylum The first official asylum for the mentally ill to be founded in the United States. It was established in Williamsburg, Virginia, in 1773, and was open to all levels of society except slaves.

witchcraft It has often been reported, especially in psychiatric textbooks, that the most prevalent theory of the causes of mental illness (and particularly the psychotic disorders) was a supernatural one based on "demons" or malevolent "spirits." Furthermore, it has often been reported that most of those people who died during the Great Witch Hunt in Europe, between about 1500 and 1650, were mentally ill. However, research by psychologist Thomas Schoeneman has demonstrated that these assertions, despite wide report in psychiatric textbooks, are untrue and that the evidence shows that most of the people who were executed for witchcraft were poor women with a sharp tongue and a bad temper, or old and unmarried—or that, in some areas, just about anyone was suspect.

Schoeneman, T. J. "The Mentally Ill Witch in Textbooks of Abnormal Psychology: Current Status and Implications of a Fallacy," *Professional Psychology: Research and Practice* 15 (1984): 299–314.

withdrawal, social This is one of the most commonly reported signs of schizophrenia and is present long before the definite outbreak of a psychosis in many persons. Social withdrawal is therefore part of the PRODROMAL PHASE of schizophrenia and can later develop into one of the chronic NEGATIVE SYMPTOMS of this disorder. Such persons may shun contact with others, for example, or be unable to interact or make eye contact when in the presence of others.

word salad A very descriptive term for an abnormality of language that can be found in some persons with schizophrenia or with certain types of aphasias. A person speaking word salad just seems to toss out words without regard to their meaning, making unusual and meaningless combinations and perhaps even creating NEOLOGISMS.

work (as therapy) See FARMING (AS TREATMENT); OCCUPATIONAL THERAPY.

World Health Organization One of the semiautonomous organizations created by the United Nations, the World Health Organization (WHO) has been instrumental in sponsoring epidemiological and CROSS-CULTURAL STUDIES of schizophrenia and other mental disorders.

World Psychiatric Association An international association made up of national associations of psychiatrists from various countries. It was founded in 1961.

Y, Z

York Retreat The famous humane institution for the insane founded in 1792 by the Religious Society of Friends in York, England. Founded by William Tuke (1732–1822), it helped to put into practice the MORAL TREATMENT of the institutionalized mentally ill in England, as was shortly thereafter the case in Philippe PINEL's France and Vincenzo CHIARUGI's Italy. The emphasis was on occupational therapy and good food and sanitary conditions, with MECHANICAL RESTRAINTS used rarely, if at all. William Tuke's grandson, Samuel Tuke (1784–1857), wrote a glowing description of the treatment of the mentally ill at the Retreat, and after its publication in 1813 it helped influence Parliament to investigate conditions in British asylums.

Daniel Hack Tuke (1827–95), one of the leading psychiatrists in England in the 19th century, was the son of Samuel and the grandson of William Tuke.

Tuke, S. *Description of the Retreat.* London: 1813.

young adult chronic patient With the ever-increasing problem of patients presenting with the dual diagnosis of a traditional psychotic disorder (schizophrenia, bipolar disorder, schizoaffective disorder) and a history of substance abuse since the 1960s, more and more young persons who are nonetheless following a chronic course of illness have made up a large percentage of the admissions to psychiatric facilities. This person has been labeled by psychiatrist Bert Pepper as the "young adult chronic patient." A young adult chronic patient is defined as one who is between 18 and 35 years old, abuses alcohol and drugs, is sexually active, has unpredictable and sometimes violent behavior, has frequent suicidal thoughts, often has children with whom there is little or no relationship, often has been arrested, cannot seem to hold down a job, and is attention-seeking but also tends to reject treatment.

See also SUBSTANCE ABUSE.

Pepper, B. "The Young Adult Chronic Patient: Population Overview," *Journal of Clinical Psychopharmacology* 5 (1985): 3S to 7S.

ziprasidone See ANTIPSYCHOTIC DRUGS.

Zyprexa See ANTIPSYCHOTIC DRUGS.

APPENDIXES

I. North American Diagnostic Criteria for Schizophrenia

II. European Diagnostic Criteria for Schizophrenia

III. Sources of Information Concerning Schizophrenia

IV. Directory

APPENDIX I

NORTH AMERICAN DIAGNOSTIC CRITERIA FOR SCHIZOPHRENIA

DSM-IV-TR (2000)

Source: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision.* Washington, D.C.: American Psychiatric Press, 2000.

DIAGNOSTIC CRITERIA

A. *Characteristic symptoms:* Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

1. delusions
2. hallucinations
3. disorganized speech (e.g., frequent derailment or incoherence)
4. grossly disorganized or catatonic behavior
5. negative symptoms, i.e., affective flattening, alogia, or avolition

Note: Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other.

B. *Social/occupational dysfunction:* For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. *Duration:* Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D. *Schizoaffective and mood disorder exclusion:* Schizoaffective Disorder and Mood Disorder With Psychotic Features have been ruled out because either (1) no Major Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.

E. *Substance/general medical condition exclusion:* The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

F. *Relationship to a pervasive developmental disorder:* If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only

if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).

PARANOID TYPE

A type of Schizophrenia in which the following criteria are met:

A. Preoccupation with one or more delusions or frequent auditory hallucinations.
B. None of the following is prominent: disorganized speech, disorganized or catatonic behavior, or flat or inappropriate affect.

CATATONIC TYPE

A type of Schizophrenia in which the clinical picture is dominated by at least two of the following:

1. motoric immobility as evidenced by catalepsy (including waxy flexibility) or stupor
2. excessive motor activity (that is apparently purposeless and not influenced by external stimuli)
3. extreme negativism (an apparently motiveless resistance to all instructions or maintenance of a rigid posture against attempts to be moved) or mutism
4. peculiarities of voluntary movement as evidenced by posturing (voluntary assumption of inappropriate or bizarre postures), stereotyped movements, prominent mannerisms, or prominent grimacing
5. echolalia or echopraxia

DISORGANIZED TYPE

A type of Schizophrenia in which the following criteria are met:

A. All of the following are prominent:
   1. disorganized speech
   2. disorganized behavior
   3. flat or inappropriate affect
B. The criteria are not met for Catatonic Type.

UNDIFFERENTIATED TYPE

A type of Schizophrenia in which symptoms that meet Criterion A are present, but the criteria are not met for the Paranoid, Disorganized, or Catatonic Type.

RESIDUAL TYPE

A type of Schizophrenia in which the following criteria are met:

A Absence of prominent delusions, hallucinations, disorganized speech, and grossly disorganized or catatonic behavior.
B. There is continuing evidence of the disturbance, as indicated by the presence of negative symptoms or two or more symptoms listed in criterion A for Schizophrenia, present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

APPENDIX II

EUROPEAN DIAGNOSTIC CRITERIA FOR SCHIZOPHRENIA

ICD-10

Source: World Health Organization. *International Classification of Diseases, Tenth Edition (ICD-10).* Geneva: WHO, 1992.

F20 SCHIZOPHRENIA

The schizophrenic disorders are characterized in general by fundamental and characteristic distortions of thinking and perception, and by inappropriate or blunted affect. Clear consciousness and intellectual capacity are usually maintained, although certain cognitive deficits may evolve in the course of time. The disturbance involves the most basic functions that give the normal person a feeling of individuality, uniqueness, and self-direction. The most intimate thoughts, feelings, and acts are often felt to be known to or shared by others, and explanatory delusions may develop, to the effect that natural or supernatural forces are at work to influence the afflicted individual's thoughts and actions in ways that are often bizarre. The individual may see himself or herself as the pivot of all that happens. Hallucinations, especially auditory, are common and may comment on the individual's behaviour or thoughts. Perception is frequently disturbed in other ways: colours or sounds may seem unduly vivid or altered in quality, and irrelevant features of ordinary things may appear more important than the whole object or situation. Perplexity is also common early on and frequently leads to a belief that everyday situations possess a special, usually sinister, meaning intended uniquely for the individual. In the characteristic schizophrenic disturbance of thinking, peripheral and irrelevant features of a total concept, which are inhibited in normal directed mental activity, are brought to the fore and utilized in place of those that are relevant and appropriate to the situation. Thus thinking becomes vague, elliptical, and obscure, and its expression in speech sometimes incomprehensible. Breaks and interpolations in the train of thought are frequent, and thoughts may seem to be withdrawn by some outside agency. Mood is characteristically shallow, capricious, or incongruous. Ambivalence and disturbance of volition may appear as inertia, negativism, or stupor. Catatonia may be present. The onset may be acute, with seriously disturbed behaviour, or insidious, with a gradual development of odd ideas and conduct. The course of the disorder shows equally great variation and is by no means inevitably chronic or deteriorating (the course is specified by five-character categories). In a proportion of cases, which may vary in different cultures and populations, the outcome is complete, or nearly complete, recovery. The sexes are approximately equally affected but the onset tends to be later in women.

Although no strictly pathognomonic symptoms can be identified, for practical purposes it is useful to divide the above symptoms into groups that have special importance for the diagnosis and often occur together, such as:

(a) thought echo, thought insertion or withdrawal, and thought broadcasting;
(b) delusions of control, influence, or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception;
(c) hallucinatory voices giving a running commentary on the patient's behaviour, or discussing the patient among themselves, or other types of hallucinatory voices coming from some part of the body;
(d) persistent delusions of other kinds that are culturally inappropriate and completely impossible, such as religious or political identity, or superhuman powers and abilities (e.g. being able to control the weather, or being in communication with aliens from another world);
(e) persistent hallucinations in any modality, when accompanied either by fleeting or half-formed delusions without clear affective content, or by persistent over-valued ideas, or when occurring every day for weeks or months on end;
(f) breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech, or neologisms;
(g) catatonic behaviour, such as excitement, posturing, or waxy flexibility, negativism, mutism, and stupor;
(h) "negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses, usually resulting in social withdrawal and lowering of social performance; it must be clear that these are not due to depression or to neuroleptic medication;
(i) a significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of interest, aimlessness, idleness, a self-absorbed attitude, and social withdrawal.

DIAGNOSTIC GUIDELINES

The normal requirement for a diagnosis of schizophrenia is that a minimum of one very clear symptom (and usually two or more if less clear-cut) belonging to any one of the groups listed as (a) to (d) above, or symptoms from at least two of the groups referred to as (e) to (h), should have been clearly present for most of the time during a period of 1 month or more. Conditions meeting such symptomatic requirements but of duration less than 1 month (whether treated or not) should be diagnosed in the first instance as acute schizophrenia-like psychotic disorder and are classified as schizophrenia if the symptoms persist for longer periods.

Viewed retrospectively, it may be clear that a prodromal phase in which symptoms and behaviour, such as loss of interest in work, social activities, and personal appearance and hygiene, together with generalized anxiety and mild degrees of depression and preoccupation, preceded the onset of psychotic symptoms by weeks or even months. Because of the difficulty in timing onset, the 1-month duration criterion applies only to the specific symptoms listed above and not to any prodromal nonpsychotic phase.

The diagnosis of schizophrenia should not be made in the presence of extensive depressive or manic symptoms unless it is clear that schizophrenic symptoms antedated the affective disturbance. If both schizophrenic and affective symptoms develop together and are evenly balanced, the diagnosis of schizoaffective disorder should be made, even if the schizophrenic symptoms by themselves would have justified the diagnosis of schizophrenia. Schizophrenia should not be diagnosed in the presence of overt brain disease or during states of drug intoxication or withdrawal.

F20.0 PARANOID SCHIZOPHRENIA

This is the commonest type of schizophrenia in most parts of the world. The clinical picture is dominated by relatively stable, often paranoid, delusions, usually accompanied by hallucinations, particularly of the auditory variety, and perceptual disturbances. Disturbances of affect, volition, and speech, and catatonic symptoms, are not prominent.

Examples of the most common paranoid symptoms are:

(a) delusions of persecution, reference, exalted birth, special mission, bodily change, or jealousy;
(b) hallucinatory voices that threaten the patient or give commands, or auditory hallucinations

without verbal form, such as whistling, humming, or laughing;

(c) hallucinations of smell or taste, or of sexual or other bodily sensations; visual hallucinations may occur but are rarely predominant.

Thought disorder may be obvious in acute states, but if so it does not prevent the typical delusions or hallucinations from being described clearly. Affect is usually less blunted than in other varieties of schizophrenia, but a minor degree of incongruity is common, as are mood disturbances such as irritability, sudden anger, fearfulness, and suspicion. "Negative" symptoms such as blunting of affect and impaired volition are often present but do not dominate the clinical picture.

The course of paranoid schizophrenia may be episodic, with partial or complete remissions, or chronic. In chronic cases, the florid symptoms persist over years and it is difficult to distinguish discrete episodes. The onset tends to be later than in the hebephrenic and catatonic forms.

DIAGNOSTIC GUIDELINES

The general criteria for a diagnosis of schizophrenia (see introduction to F20 above) must be satisfied. In addition, hallucinations and/or delusions must be prominent, and disturbances of affect, volition and speech, and catatonic symptoms must be relatively inconspicuous. The hallucinations will usually be of the kind described in (b) and (c) above. Delusions can be of almost any kind of delusions of control, influence, or passivity, and persecutory beliefs of various kinds are the most characteristic.

Includes:

- paraphrenic schizophrenia

Differential diagnosis It is important to exclude epileptic and drug-induced psychoses, and to remember that persecutory delusions might carry little diagnostic weight in people from certain countries or cultures.

Excludes:

- involutional paranoid state (F22.8)
- paranoia (F22.0)

F20.1 HEBEPHRENIC SCHIZOPHRENIA

A form of schizophrenia in which affective changes are prominent, delusions and hallucinations fleeting and fragmentary, behaviour irresponsible and unpredictable, and mannerisms common. The mood is shallow and inappropriate and often accompanied by giggling or self-satisfied, self-absorbed smiling, or by a lofty manner, grimaces, mannerisms, pranks, hypochondriacal complaints, and reiterated phrases. Thought is disorganized and speech rambling and incoherent. There is a tendency to remain solitary, and behaviour seems empty of purpose and feeling. This form of schizophrenia usually starts between the ages of 15 and 25 years and tends to have a poor prognosis because of the rapid development of "negative" symptoms, particularly flattening of affect and loss of volition.

In addition, disturbances of affect and volition, and thought disorder are usually prominent. Hallucinations and delusions may be present but are not usually prominent. Drive and determination are lost and goals abandoned, so that the patient's behaviour becomes characteristically aimless and empty of purpose. A superficial and manneristic preoccupation with religion, philosophy, and other abstract themes may add to the listener's difficulty in following the train of thought.

DIAGNOSTIC GUIDELINES

The general criteria for a diagnosis of schizophrenia (see introduction to F20 above) must be satisfied. Hebephrenia should normally be diagnosed for the first time only in adolescents or young adults. The premorbid personality is characteristically, but not necessarily, rather shy and solitary. For a confident diagnosis of hebephrenia, a period of 2 or 3 months of continuous observation is usually necessary, in order to ensure that the characteristic behaviours described above are sustained.

Includes:

- disorganized schizophrenia
- hebephrenia

F20.2 CATATONIC SCHIZOPHRENIA

Prominent psychomotor disturbances are essential and dominant features and may alternate between

extremes such as hyperkinesis and stupor, or automatic obedience and negativism. Constrained attitudes and postures may be maintained for long periods. Episodes of violent excitement may be a striking feature of the condition.

For reasons that are poorly understood, catatonic schizophrenia is now rarely seen in industrial countries though it remains common elsewhere. These catatonic phenomena may be combined with a dream-like (oneiroid) state with vivid scenic hallucinations.

DIAGNOSTIC GUIDELINES

The general criteria for a diagnosis of schizophrenia (see introduction to F20 above) must be satisfied. Transitory and isolated catatonic symptoms may occur in the context of any other subtype of schizophrenia, but for a diagnosis of catatonic schizophrenia one or more of the following behaviours should dominate the clinical picture:

(a) stupor (marked decrease in reactivity to the environment and in spontaneous movements and activity) or mutism;
(b) excitement (apparently purposeless motor activity, not influenced by external stimuli);
(c) posturing (voluntary assumption and maintenance of inappropriate or bizarre postures);
(d) negativism (an apparently motiveless resistance to all instructions or attempts to be moved, or movement in opposite direction);
(e) rigidity (maintenance of a rigid posture against efforts to be moved);
(f) waxy flexibility (maintenance of limbs and body in externally imposed positions); and
(g) other symptoms such as command automatism (automatic compliance with instructions), and perseveration of words and phrases.

In uncommunicative patients with behavioural manifestations of catatonic disorder, the diagnosis of schizophrenia may have to be provisional until adequate evidence of the presence of other symptoms is obtained. It is also vital to appreciate that catatonic symptoms are not diagnostic of schizophrenia. A catatonic symptom or symptoms may also be provoked by brain disease, metabolic disturbances, or alcohol and drugs, and may also occur in mood disorders.

Includes:

1. catatonic stupor
2. schizophrenic catalepsy
3. schizophrenic catatonia
4. schizophrenic flexibilitas cerea

F20.3 UNDIFFERENTIATED SCHIZOPHRENIA

Conditions meeting the general diagnostic criteria for schizophrenia (see introduction to F20 above) but not conforming to any of the above subtypes, or exhibiting the features of more than one of them without a clear predominance of a particular set of diagnostic characteristics. This rubric should be used only for psychotic conditions (i.e. residual schizophrenia and post-schizophrenic depression are excluded) and after an attempt has been made to classify the condition into one of the three preceding categories.

DIAGNOSTIC GUIDELINES

This category should be reserved for disorders that:

(a) meet the diagnostic criteria for schizophrenia;
(b) do not satisfy the criteria for the paranoid, hebephrenic, or catatonic subtypes;
(c) do not satisfy the criteria for residual schizophrenia or post-schizophrenic depression.

Includes:

- atypical schizophrenia

F20.4 POST-SCHIZOPHRENIC DEPRESSION

A depressive episode, which may be prolonged, arising in the aftermath of a schizophrenic illness. Some schizophrenic symptoms must still be present but no longer dominate the clinical picture. These persisting schizophrenic symptoms may be "positive" or "negative," though the latter are more common. It is uncertain, and immaterial to the diagnosis, to what extent the depressive symptoms have merely been uncovered by the resolution of earlier psychotic symptoms (rather than being a new development)

or are an intrinsic part of schizophrenia rather than a psychological reaction to it. They are rarely sufficiently severe or extensive to meet criteria for a severe depressive episode, and it is often difficult to decide which of the patient's symptoms are due to depression and which to neuroleptic medication or to the impaired volition and affective flattening of schizophrenia itself. This depressive disorder is associated with an increased risk of suicide.

DIAGNOSTIC GUIDELINES

The diagnosis should be made only if:

(a) the patient has had a schizophrenic illness meeting the general criteria for schizophrenia (see introduction to F20 above) within the past 12 months;
(b) some schizophrenic symptoms are still present; and
(c) the depressive symptoms are prominent and distressing, fulfilling at least the criteria for a depressive episode, and have been present for at least 2 weeks.

If the patient no longer has any schizophrenic symptoms, a depressive episode should be diagnosed. If schizophrenic symptoms are still florid and prominent, the diagnosis should remain that of the appropriate schizophrenic subtype.

F20.5 RESIDUAL SCHIZOPHRENIA

A chronic stage in the development of a schizophrenic disorder in which there has been a clear progression from an early stage (comprising one or more episodes with psychotic symptoms meeting the general criteria for schizophrenia described above) to a later stage characterized by long-term, though not necessarily irreversible, "negative" symptoms.

DIAGNOSTIC GUIDELINES

For a confident diagnosis, the following requirements should be met:

(a) prominent "negative" schizophrenic symptoms, i.e. psychomotor slowing, underactivity, blunting of affect, passivity and lack of initiative, poverty of quantity or content of speech, poor nonverbal communication by facial expression, eye contact, voice modulation, and posture, poor self-care and social performance;
(b) evidence in the past of at least one clear-cut psychotic episode meeting the diagnostic criteria for schizophrenia;
(c) a period of at least 1 year during which the intensity and frequency of florid symptoms such as delusions and hallucinations have been minimal or substantially reduced and the "negative" schizophrenic syndrome has been present;
(d) absence of dementia or other organic brain disease or disorder, and of chronic depression or institutionalism sufficient to explain the negative impairments.

If adequate information about the patient's previous history cannot be obtained, and it therefore cannot be established that criteria for schizophrenia have been met at some time in the past, it may be necessary to make a provisional diagnosis of residual schizophrenia.

Includes:

- chronic undifferentiated schizophrenia
- "Restzustand"
- schizophrenic residual state

F20.6 SIMPLE SCHIZOPHRENIA

An uncommon disorder in which there is an insidious but progressive development of oddities of conduct, inability to meet the demands of society, and decline in total performance. Delusions and hallucinations are not evident, and the disorder is less obviously psychotic than the hebephrenic, paranoid, and catatonic subtypes of schizophrenia. The characteristic "negative" features of residual schizophrenia (e.g. blunting of affect, loss of volition) develop without being preceded by any overt psychotic symptoms. With increasing social impoverishment, vagrancy may ensue and the individual may then become self-absorbed, idle, and aimless.

DIAGNOSTIC GUIDELINES

Simple schizophrenia is a difficult diagnosis to make with any confidence because it depends on

establishing the slowly progressive development of the characteristic "negative" symptoms of residual schizophrenia without any history of hallucinations, delusions, or other manifestations of an earlier psychotic episode, and with significant changes in personal behaviour, manifest as a marked loss of interest, idleness, and social withdrawal.

Includes:

- schizophrenia simplex

APPENDIX III

SOURCES OF INFORMATION CONCERNING SCHIZOPHRENIA

INFORMATION, SUPPORT, AND ADVOCACY ORGANIZATIONS

Since information on schizophrenia and its treatments changes rapidly, please check the Web sites of these organizations to get the most up-to-date information. Some of these organizations maintain Web sites that are tremendously rich sources of current information.

NAMI (Formerly called THE NATIONAL ALLIANCE FOR THE MENTALLY ILL)

NAMI is the national umbrella organization for more than 1,100 local support and advocacy groups for families and individuals affected by serious mental illnesses. NAMI is the first place for families to turn when a loved one has been diagnosed with schizophrenia or another serious mental disorder. All local chapters are listed on NAMI's Web site.

NAMI
2107 Wilson Boulevard
Suite 300
Arlington, VA 22201-3042
(800) 950-NAMI (6264)
http://www.nami.org

STANLEY RESEARCH FOUNDATION / NAMI RESEARCH INSTITUTE
5430 Grosvenor Lane
Suite 200
Bethesda, MD 20814
(301) 571-0770
http://www.stanleyresearch.org

NATIONAL ALLIANCE FOR RESEARCH ON SCHIZOPHRENIA AND AFFECTIVE DISORDERS (NARSAD)
60 Cutter Mill Road
Suite 404
Great Neck, NY 11021
(516) 829-0091
http://www.mhsource.com

NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)
Office of Communication and Public Liaison
Information Resources and Inquiries Branch
6001 Executive Boulevard
Room 8184, MSC 9663
Bethesda, MD 20892-9663
(301) 443-4279
http://www.nimh.nih.gov

NIMH SCHIZOPHRENIA GENETICS INITIATIVE

For the latest information on the genetics of schizophrenia, regularly check out the Web site of the NIMH Schizophrenia Initiative, as they gather data from large numbers of families of people with the illness.
http://www.grb.nimh.nih.gov/gi.html

WORLD WIDE WEB SOURCES OF INFORMATION

http://www.schizophrenia.com

By far the best Web site devoted solely to schizophrenia. Besides basic information for families and persons who have schizophrenia,

there are multiple links to other schizophrenia-related Web sites and discussion and chat areas.

www.ncbi.nlm.nih.gov/pubmed

PubMed is a search service provided by the National Library of Medicine in Bethesda, Maryland, as part of its MEDLINE medical Web site. Scientific and medical journals that publish articles on schizophrenia or the other psychotic disorders are added to the PubMed data base daily. This is the best place to look for (literally) up-to-the-minute scientific research on schizophrenia and the psychotic disorders. One must first register to use the service, but there is no registration fee. One can order copies of scientific and medical articles and have them sent via the mail, but there is a rather steep fee for this service.

http://www.mentalhealth.com

An information source and a search engine maintained by Internet Mental Health. Quite useful.

OTHER ONLINE RESOURCES

British Columbia Schizophrenia Society
http://www.bcss.org

The Experience of Schizophrenia
http://www.chovil.com

Mental Health Infosource
http://www.mhsource.com/narsad.html

Public Citizen: eLetter on Drugs for Severe Psychiatric Illness
http://www.citizen.org/eletter

Schizophrenia Society of Canada
http://www.schizophrenia.ca

Treatment Advocacy Center
http://www.psychlaws.org

APPENDIX IV
DIRECTORY

Academy for Eating Disorders
60 Revere Drive
Suite 500
Northbrook, IL 60062-1577
(847) 498-4274
http://www.aedweb.org

Academy of Psychosomatic Medicine
5272 River Road
Bethesda, MD 20816
(301) 718-6520
http://www.apm.org

American Academy of Addiction Psychiatry
1010 Vermont Avenue, NW
Suite 710
Washington, DC 20005
(202) 393-4484
(202) 393-4419 (fax)
http://www.aaap.org

American Academy of Child and Adolescent Psychiatry
3615 Wisconsin Avenue, NW
Washington, DC 20016-3007
(202) 966-7300
(202) 966-2891 (fax)
http://www.aacap.org

American Academy of Family Physicians
P.O. Box 11210
Shawnee Mission, KS 66207-1210
(800) 274-2237
http://www.aafp.org

American Academy of Neurology
1080 Montreal Avenue
Saint Paul, MN 55116
(651) 695-2717
(800) 879-1960
(651) 695-2791 (fax)
http://www.aan.com

American Academy of Pediatrics
141 Northwest Point Boulevard
Elk Grove Village, IL 60007
(847) 434-4000
http://www.aap.org

American Academy of Physician and Patient
16020 Swingley Ridge Road
Suite 300
Chesterfield, MO 63017
(636) 449-5080
(636) 449-5051 (fax)
http://www.physicianpatient.org

American Association for Geriatric Psychiatry
7910 Woodmont Avenue
Suite 1050
Bethesda, MD 20814-3004
(301) 654-7850
(301) 654-4137 (fax)
http://www.aagpgpa.org

American Association for the Advancement of Science
1200 New York Avenue, NW
Washington, DC 20005

(202) 326-6450
http://www.aaas.org

American Association for Social Psychiatry
Medical College of Wisconsin
Froedtert Behavioral Center
9200 West Wisconsin Avenue
Milwaukee, WI 53226
(414) 257-5070

American Association for the History of Medicine
Department of Medical Humanities
East Carolina University
School of Medicine
Greenville, NC 27834
http://www.histmed.org

American Association of Community Psychiatrists
AACP c/o Frances M. Roton
P.O. Box 570218
Dallas, TX 75228-0218
(972) 613-0985
(972) 613-5532 (fax)
http://www.comm.psych.pitt.edu

American Association of General Hospital Psychiatrists
Mt. Auburn Hospital
Wyman 2
Cambridge, MA 02238
(617) 499-5008

American Association of Neuropathologists
Department of Pathology
Case Western Reserve University
2103 Cornell Road, WRB, 5-101
Cleveland, OH 44106-7288
(216) 368-2488
(216) 368-8964 (fax)
http://www.aanp-jnen.com

American Association of Psychiatric Administrators
P.O. Box 570218
Dallas, TX 75357-0218
(800) 650-5888
(972) 613-5532 (fax)
http://www.psychiatricadministrators.org

American Association on Mental Retardation
444 North Capitol Street, NW
Suite 846
Washington, DC 20001-1512
(800) 424-3688 or (202) 387-1968
(202) 387-2193 (fax)
http://www.aamr.org

American Board of Medical Specialties
1007 Church Street
Suite 404
Evanston, IL 60201-5913
(847) 491-9091
(847) 328-3596 (fax)
http://www.abms.org

American Board of Psychiatry and Neurology
500 Lake Cook Road
Suite 335
Deerfield, IL 60015
(847) 945-7900
http://www.abpn.com

American College of Mental Health Administration
7804 Loma del Norte Road, NE
Albuquerque, NM 87109-5419
(505) 822-5038
http://www.acmha.org

American College of Neuropsychopharmacology
545 Mainstream Drive
Suite 110
Nashville, TN 37228
(615) 324-2360
(615) 324-2361 (fax)
http://www.acnp.org

American College of Psychiatrists
732 Addison Street
Suite C
Berkeley, CA 94710
(510) 704-8020
(510) 704-0113 (fax)
http://www.acpsych.org

American Hospital Association
One North Franklin
Chicago, IL 60606

(312) 422-3000
http://www.hospitalconnect.com

American Managed Behavioral Healthcare Association
AMBHA
1101 Pennsylvania Avenue, NW
Sixth Floor
Washington, DC 20004
(202) 756-7308 (fax)
http://www.ambha.org

American Medical Association
515 North State Street
Chicago, IL 60616
(312) 464-5000
http://www.ama.org

American Neurological Association
5841 Cedar Lake Road
Suite 204
Minneapolis, MN 55416
(952) 545-6284
(952) 545-6073 (fax)
http://www.aneuroa.org

American Neuropsychiatric Association
700 Ackerman Road
Suite 625
Columbus, OH 43202
(614) 447-2077
http://www.anpaonline.org

American Nurses Association
8515 Georgia Avenue
Suite 400
Silver Spring, MD 20910
(800) 274-4ANA
http://www.nursingworld.org

American Orthopsychiatric Association
Department of Psychology, Box 1104
Arizona State University
Tempe, AZ 85287-1104
(480) 727-7518
(480) 965-8544 (fax)
http://www.amerortho.org

American Pediatric Society
3400 Research Forest Drive
Suite B-7
The Woodlands, TX 77381
(281) 419-0052
(281)419-0082
http://www.aps-spr.org

American Psychiatric Association
1000 Wilson Boulevard
Suite 1825
Arlington, VA 22209-3901
(703) 907-7300
http://www.psych.org

American Psychiatric Nurses Association
1555 Wilson Boulevard
Suite 515
Arlington, VA 22209
(703) 243-2443
http:llwww.apna.org

American Psychological Association
750 First Street, NE
Washington, DC 20002-4242
(202) 336-5500
(800) 374-2721
http://www.apa.org

American Psychosomatic Society
6728 Old McLean Village Drive
McLean, VA 22101-3906
(703) 556-9222
(703) 556-8729 (fax)
http://www.psychosomatic.org

American Society for Adolescent Psychiatry
P.O. Box 570218
Dallas, TX 75357-02 18
(972) 686-6166
http://www.adolpsych.org

American Society of Addiction Medicine
4601 North Park Avenue
Upper Arcade #101
Chevy Chase, MD 20815
(301) 656-3920
(301) 656-3815 (fax)
http://www.asam.org

American Society of Clinical Hypnosis
140 North Bloomingdale Road
Bloomingdale, IL 60108-1017
(630) 980-4740
http://www.asch.net

American Society of Clinical Psychopharmacology
P.O. Box 40395
Glen Oaks, NY 11004
(718) 470-4007
http://www.ascpp.org

American Society of Law, Medicine and Ethics
765 Commonwealth Avenue
Suite 1634
Boston, MA 02215
(617) 262-4990
(617) 437-7596 (fax)
http://www.aslme.org

Association for Academic Psychiatry
AAP Executive Office
464 Common Street, #147
Belmont, MA 02478
(617) 393-3935
(617) 393-1808 (fax)
http://www.hsc.wvu.edu/aapl

Association for Ambulatory Behavioral Healthcare
247 Douglas Avenue
Portsmouth, VA 23707
(757) 673-3741
http:llwww.aabh.org

Association for Psychological Science
1010 Vermont Avenue, NW, 11th Floor
Washington, DC 20005-4918
(202) 783-2077
(202) 783-2083 (fax)
http://www.psychologicalscience.org

Association for the Advancement of Philosophy and Psychiatry
Department of Psychiatry
UT Southwestern Medical Center at Dallas
5323 Harry Hines Boulevard
Dallas, TX 75390-9070
http://www3.utsouthwestern.edu/aapp/

Association of American Indian Physicians
1225 Sovereign Row
Suite 103
Oklahoma City, OK 73108
(405) 946-7072
(405) 946-7651 (fax)
http://www.aaip.org

Association of Behavioral Healthcare Management
12300 Twinbrook Parkway
Suite 320
Rockville, MD 20852
(301) 984-6200
(301) 881-7159 (fax)
http://www.nccbh.org/abhm/

Association of Directors of Medical Student Education in Psychiatry
Department of Psychiatry & Behavioral Sciences
University of Louisville School of Medicine
501 East Broadway
Suite 340
Louisville, KY 40202
(502) 852-5431
(502) 852-3971 (fax)
http://www.admsep.org

Association of Gay and Lesbian Psychiatrists
4514 Chester Avenue
Philadelphia, PA 19143-3707
(215) 222-2800
http://www.aglp.org

Bazelon Center for Mental Health Law
Judge David L. Bazelon Center for Mental Health Law
11011 5th Street, NW
Suite 1212
Washington, DC 20005
(202) 467-5730
(202) 223-0409 (fax)
http://www.bazelon.org

Black Psychiatrists of America
640 Temple 8th Floor
Detroit, MI 48201
(313) 833-2421
(313) 833-4281 (fax)

Canadian Medical Association
1867 Alta Vista Drive
Ottawa, ON K1G 3Y6
(800) 457-4205
http://www.cma.ca

Canadian Mental Health Association
Canadian Mental Health Association
8 King Street East
Suite 810
Toronto, ON M5C lBS
(416) 484-7750
http://www.cmha.ca

The Canadian Psychiatric Association
141 Laurier Avenue West
Suite 701
Ottawa, ON K1P 5J3
(613) 234-2815
http://www.cpa-apc.ca

The Center for Behavioral Health, Justice, and Public Policy
8490 Dorsey Run Road
Jessup, MD 20794
(410) 724-5007
http://www.umaryland.edu/behavioraljustice

Center for Mental Health Services
P.O. Box 42557
Washington, DC 20015
(800) 789-2647
http://www.mentalhealth.samhsa.gov/aboutken/contact.asp

Center for Psychiatric Rehabilitation
Boston University
940 Commonwealth Avenue West
Boston, MA 02215
(617) 353-3549
(617) 353-7700 (fax)
http://www.bu.edu/cpr

Criminal Justice/Mental Health Consensus Project
Project Coordinator:
Council of State Governments / Eastern Regional Conference
40 Broad Street
Suite 2050
New York, NY 10004
(212) 482-2320
(212) 482-2344 (fax)
http://www.csgeast.org

Epilepsy Foundation
4351 Garden City Drive
Landover, MD 20785-7223
(800) 332-1000
http://www.efa.org

Federation of Families for Children's Mental Health
9605 Medical Center Drive
Suite 280
Rockville, MD 20850
(240) 403-1901
(240) 403-1909 (fax)
http://www.ffcmh.org

Frontier Mental Health Services Resource Network
Western Interstate Commission for Higher Education
Mental Health
P.O. Box 9752
Boulder, CO 80301
(303) 541-0256
(303) 541-0291 (fax)
http://www.wiche.edu/Mentalhealth/Frontier/frontier.asp

Group for the Advancement of Psychiatry
P.O. Box 570218
Dallas, TX 75357-02 18
(972) 613-3044
http://www.groupadpsych.org

HSRI–The Evaluation Center
The Evaluation Center @HSRI
2269 Massachusetts Avenue
Cambridge, MA 02140
(617) 876-0426, Ext. 4
http://www.tecathsri.org/contact.asp?frm=gen

Indo-American Psychiatric Association
107 Chesley Drive
Unit #4
Media, PA 19063
(610) 891-9024, ext. 115
http://www.myiapa.org

Institute of Medicine–National Academy of Sciences
500 Fifth Street, NW
Washington, DC 20005

(202) 334-2352
http://www.iom.edu

International Academy of Law and Mental Health
Académie internationale de droit et de santé mentale
c/o Chaire de psychiatrie légale et d'éthique biomédicale Philippe Pinel
Faculté de médecine, Université de Montréal
C.P. 6128, Succ. Centre-Ville,
Montréal, QC, H3C 3J7
Canada
+1(514) 343-5938
+1(514) 343-2452 (fax)
http://www.ialmh.org

International Society for the Study of Bipolar Disorders
P.O. Box 7168
Pittsburgh, PA 15213
(412) 605-1412
http://www.isbd.org

International Society for the Study of Dissociation
60 Revere Drive
Suite 500
Northbrook, IL 60062
(847) 480-0899
(847) 480-9282 (fax)
http://www.issd.org

Mental Health Liaison Group (MHLG)
http://www.mhlg.org

Mental Health Part D
http://www.mentalhealthpartd.org/

Mental Health Statistics Improvement Program Online
http://www.mhsip.org

NAMI/National Alliance on Mental Illness
Colonial Place Three
2107 Wilson Boulevard
Suite 300
Arlington, VA 22201-3042
(703) 524-7600
(703) 524-9094 (fax)
http://www.nami.org

NARSAD, The Mental Health Research Association
60 Cutter Mill Road
Suite 404
Great Neck, NY 11021
(516) 829-0091
(800) 829-8289
http://www.narsad.org

Nathan S. Kline Institute for Psychiatric Research
140 Old Orangeburg Road
Orangeburg, NY 10962
(845) 398-5500
(845) 398-5510 (fax)
http://www.rfmh.org/nkil

National Alliance of Multi-Ethnic Behavioral Health Associations
1875 I Street, NW
Suite 5009
Washington, DC 20006
(202) 429-5520
(202) 429-9574 (fax)
http://www.nambha.org

National Asian American Pacific Islander Mental Health Association (NAAPIMHA)
1215 19th Street
Suite A
Denver, CO 80202
http://www.naapimha.org

National Association of Psychiatric Health Systems (NAPHS)
701 13th Street, NW
Suite 950
Washington, DC 20005-3903
(202) 393-6700
http://www.naphs.org

National Association of Social Workers
750 First Street, SW
Suite 700
Washington, DC 20002-424 1
(202) 408-8600
http://www.naswdc.org

National Association of State Mental Health Program Directors
66 Canal Center Plaza
Suite 302
Alexandria, VA 22314

(703) 739-9333
http://www.nasmhpd.org

National Empowerment Center
599 Canal Street
Lawrence, MA 01840
(800) 769-3728
(978) 681-6426 (fax)
http://www.power2u.org/contact.html

National Institute of Mental Health (NIMH)
6001 Executive Boulevard
Room 8184, MSC 9663
Bethesda, MD 20892-9663
(301) 443-4513
(866) 615-6464
(301) 443-4279 (fax)
http://www.nimh.nih.gov

National Latino Behavioral Health Association (NLBHA)
P.O. Box 387
506 Welch Street, Unit B
Berthoud, CO 80513
(970) 532-7210
(970) 532-7209 (fax)
http://nlbha.org

National Leadership Council on African American Behavioral Health, Inc.
http://www.nlcouncil.org

National Mental Health Association (NMHA)
2001 North Beauregard Street
12th Floor
Alexandria, VA 22311
(703) 684-7722
(703) 684-5968
http://www.nmha.org

National Mental Health Consumer's Self-Help Clearinghouse
1211 Chestnut Street
Suite 1207
Philadelphia, PA 19107
(800) 553-4539
http://www.mhselthelp.org

National Resource and Training Center on Homelessness and the Mentally Ill
(800) 444-7415
http://www.nrchmi.samhsa.gov

National Research and Training Center on Psychiatric Disability
104 South Michigan Avenue
Suite 900
Chicago, IL 60603
(312) 422-8180
(312) 422-0740 (fax)
(312) 422-0706 (TDD)
http://www.psych.uic.edu/uicnrtc

Network of Care for Mental Health
Trilogy Integrated Resources LLC
1101 Fifth Avenue
Suite 250
San Rafael, CA 94901
(415) 256-9036 (fax)
http://networkofcare.org

Schizophrenia International Research Society
P.O. Box 212
Piermont, NY 10968
http://www.schizophreniasirs.org

Society of Behavioral Medicine
555 East Wells Street
Suite 1100
Milwaukee, WI 53202-3823
(414) 918-3156
http://www.sbm.org

Society of Biological Psychiatry
c/o Mayo Clinic Jacksonville
Research—Birdsall 310
4500 San Pablo Road
Jacksonville, FL 32224
(904) 953-2842
953-7117 (fax)
http://www.sobp.org

Society for Neuroscience
11 Dupont Circle, NW
Suite 500
Washington, DC 20036
(202) 462-6688
(202) 462-9740 (fax)
http://web.sfn.org

Southern Psychiatric Association
35 Lakeshore Drive
Birmingham, AL 35209

(205) 945-1840
(800) 423-4992
http://www.smaservicesinc.com

Treatment Advocacy Center
The Treatment Advocacy Center
200 North Glebe Road
Suite 730
Arlington, VA 22203
(703) 294-6001 or 6002
(703) 294-6010 (fax)
http://www.psychlaws.org

World Federation for Mental Health
P.O. Box 16810
Alexandria, VA 22302-0810
(703) 519-7648
http://www.wfmh.com

World Health Organization
20 Avenue Appia
CH-1211 Geneva 27
Switzerland
http://www.who.int/en

World Psychiatric Association
WPA Secretariat
Psychiatric Hospital
2, ch. du Petit-Bel-Air
1225 Chêne-Bourg
Switzerland
+41 22 305 57 30
http://www.wpanet.org

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ABOUT THE AUTHOR

Richard Noll, Ph.D., is a clinical psychologist, a historian of science, and an award-winning author. From 1994 to 1998 he was a postdoctoral fellow and lecturer in the history of science at Harvard University. He is a former Resident Fellow of the Dibner Institute for the History of Science and Technology as well as Visiting Scholar at the Massachusetts Institute of Technology. Noll is the author of dozens of scholarly articles and seven books on the history of psychiatry, unusual psychiatric syndromes, and anthropology. His book *The Jung Cult: Origins of a Charismatic Movement* (Princeton University Press, 1994) was chosen by the Association of American Publishers as the Best Book in Psychology published that year, and Princeton University Press submitted it as one of its entries for the Pulitzer Prize competition. Noll's scholarship has been translated into 13 foreign languages, and he has taught courses or delivered invited lectures in 14 foreign countries on five continents.

Currently, Noll is associate professor of psychology at DeSales University in Center Valley, Pennsylvania.