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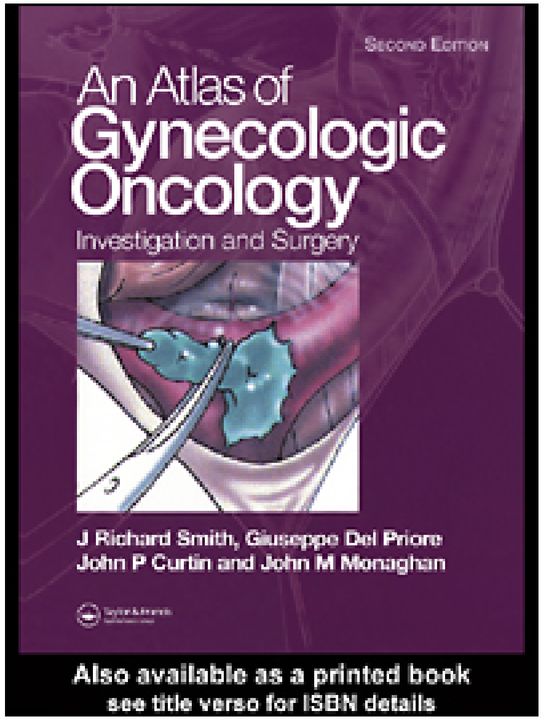

Second Edition
An Atlas of
Gynecologic
Oncology
Investigation and Surgery
J Richard Smith, Giuseppe Del Priore
John P Curtin and John M Monaghan
Also available as a printed book
see title verso for ISBN details

Atlas of **Gynecologic Oncology**

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Second Edition
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Taylor & Francis
Taylor & Francis Group
LONDON AND NEW YORK

First published in the United Kingdom in 2001 by
Taylor & Francis, an imprint of the Taylor & Francis Group,
2 Park Square, Milton Park, Abingdon, Oxfordshire, OX14 4RN.
Tel: +44 (0) 20 7017 6000
Fax.: +44 (0) 20 7017 6699
E-mail: info.medicine@tandf.co.uk
Website: http://www.tandf.co.uk/medicine
This edition published in the Taylor & Francis e-Library, 2005.

A CIP record for this book is available from the British Library.

Library of Congress Cataloging-in-Publication Data

Data available on application

ISBN 0-203-30851-4 Master e-book ISBN

ISBN 1 84184 368 7 (Print Edition)

Distributed in North and South America by
Taylor & Francis
2000 NW Corporate Blvd
Boca Raton, FL 33431, USA
Within Continental USA
Tel: 800 272 7737; Fax: 800 374 3401
Outside Continental USA
Tel: 561 994 0555; Fax: 561 361 6018
E-mail orders@crcpress.com
Distributed in the rest of the world by
Thomson Publishing Services
Cheriton House
North Way
Andover, Hampshire SP10 5BE, UK
Tel.: +44 (0) 1264 332424
E-mail: salesorder.tandf@thomsonpublishingservices.co.uk

To Mr Tom Lewis and Dr Bruce A Barron, whose friendship was responsible for bringing the editors together. Also to my wife Deborah, for her patience, support and tolerance of this and many another project.

JRS

To my family—from the smallest latest joyous addition, to the oldest and wisest, some departed, and in the center of them all, my wife, Men-Jean Lee.

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Preface to the Second Edition

We, the editors, are pleased to introduce you to an updated second edition. We believe that in the mould of the first edition we have included the standard repertoire of the gynecologic oncologist plus all that is new and leading edge. All chapters have been reviewed by both the editors and their authors, some chapters have been replaced and we have added some new chapters. Amongst the new chapters there are included surgical simulation with its impact on training, palliative care, ovarian tissue preservation/ transplantation and sentinel lymph node biopsy. The superb artwork of Dee McLean and Joanna Cameron is continued and we believe allows easy step-by-step breakdown of each procedure. This book follows the 'cookbook' formula of the first edition, that is, nobody is telling you which operation to do, but rather telling you how to do the operation you have decided upon. Many of our contributors have developed/improved the operations they describe. It has once again been a privilege and a pleasure to collect together and edit this selection of contributions which we hope covers all the mainline procedures currently in use in gynecolgic oncology, not to say a few which we believe may become important.

J Richard Smith

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Acknowledgments

Mr Smith would like to thank Mrs Christine Pietraszewska, Dr Charles J Lockwood, Chief of Obstetrics and Gynecology at Yale University and Professor PJ Steer, Professor of Obstetrics, Imperial College School of Medicine, at Chelsea and Westminster Hospital. He would also like to thank Dr JA Davis, Stobhill Hospital, Glasgow and Mr BV Lewis of Watford General Hospital, for their surgical teaching and stimulus ‘to go and see new things’.

Dr. Del Priore would like to thank his students, residents and colleagues for inspiring him to pursue this work, and all his academic activities, through their constant questioning concerning the women we all care for.

1
Introduction

J Richard Smith
Giuseppe Del Priore

This chapter reviews three specific areas relevant to virtually all surgical procedures and surgeons, namely infection prophylaxis, deep venous thrombosis prophylaxis and universal precautions: the latter facilitate the protection both of surgeons and their assistants, both medical and nursing, and of patients.

Infection prophylaxis

Most gynecology units now routinely use antibiotic prophylaxis prior to major surgery. In the absence of such prophylaxis, abdominal hysterectomy is complicated by infection in up to 14% of patients, and following vaginal hysterectomy, infection rates of up to 38% have been reported (Sweet and Gibbs 1990). This results in much morbidity, increased length of hospital stay, increased prescribing of antibiotics and a large financial burden. The risk factors for postoperative infection are shown in Table 1. By its very nature, oncological surgery carries greater risks of infection than routine gynecological surgery, owing to the length of the procedures and increased blood loss.

It is difficult to compare many of the studies on prophylaxis, as diagnosis and antibiotic regimens are not standardized. However, there seems to be general agreement that approximately 50% of infections are prevented in this way and that the potential dangers of increased microbial resistance do not justify withholding prophylaxis. Prophylaxis is thought to work by reducing, but not eradicating, vaginal flora. The antibiotic used, its dose and the duration of therapy do not

Table 1 Rick factors for postoperative infection

1.	Hospital stay for more than 72 hours before surgery
2.	Prior exposure to antimicrobial agents in the immediate preoperative period
3.	Morbid obesity
4.	Chronic illness (e.g. hypertension, diabetes)
5.	History of repeated infection
6.	Prolonged operative procedure (>3 hours)
7.	Blood loss in excess of 1500 mL

appear to influence results. It is therefore suggested that short courses of antibiotics should be used, involving a maximum of three doses. First-generation cephalosporins, broad-spectrum penicillins and/or metronidazole are all reasonable choices on grounds of efficacy and cost. Antibiotic prophylaxis should not detract from good surgical technique, with an emphasis on strict asepsis, limitation of trauma and good hemostasis. This should be coupled with adequate drainage of body cavities, where particularly blood and also lymph are likely to pool postoperatively

Prevention and treatment of thromboembolic disease

Thromboembolic disease (TED) is a significant cause of morbidity and mortality in gynecologic oncology patients. If sensitive methods of detection are employed and no preventive measures taken, at least 20% and as many as 80% of gynecologic cancer patients may have some evidence of thrombosis after cancer surgery. In certain situations, such as with a long-term in-dwelling venous catheter of the upper extremity, nearly all patients will have some degree of TED though it may not be as clinically significant as lower-extremity TED. Below the knee venous thromboses may spread to the upper leg in approximately 10–30% of cases or resolve spontaneously in approximately 30%. Once in the proximal leg, the risk of pulmonary embolism (PE) increases from less than 5% for isolated, below-the-knee TED, to up to 50% for proximal TED. The mortality rate for an undiagnosed PE is high. Up to two thirds of patients who die from pulmonary embolism do so in the first 30 minutes after diagnosis. Early recognition and effective treatment can reduce this mortality. Even employing the current best efforts, postoperative TED is still a leading cause of death in gynecologic oncology patients. It is especially disappointing that despite the considerable data on the consequences of TED, only one third of hospitalized high-risk patients receive appropriate prophylaxis.

Prevention and risk assessment

Patients may be considered candidates for preventive treatment of TED based on their clinical risk category. Laboratory tests such as euglobulin lysis time do correlate with the risk of TED but are not any more helpful than clinical risk assessment in selecting patients for prophylaxis. Low-risk patients are young (less than 40), undergoing short operative procedures (less than one hour), and do not have co-morbid conditions, such as a malignancy or obesity, that would elevate the risk of TED. Moderate-risk patients include those undergoing longer procedures, older or obese patients, and patients having pelvic surgery. High-risk patients are composed of moderate-risk patients with cancer and those with a previous history of TED. An even more accurate risk assessment can be done using lab tests (e.g. D-Dimer) and other clinical factors (e.g. positioning for vaginal surgery, use of regional anesthesia) but these more complicated algorithms have not been able to significantly reduce TED complications.

All patients should have some form of TED prevention. Low-risk patients, with a 3% approximate incidence of TED, may be adequately prophylaxed with early ambulation, elevation of the foot of the bed, and graduated compression stockings. Early ambulation has been defined by some investigators as walking around the nursing station at least three times within the first 24 hours post-operation. Graduated compression stockings are readily available, however ensuring their proper application and size can be more difficult. Obese patients may suffer from a tourniquet-like effect if the stocking rolls off the thigh. This may actually increase the risk of TED, not prevent it. Moderate-risk patients include the majority of general gynecology patients and have an approximate 10–40% chance of developing TED. These patients should receive the same measures as low-risk patients with the addition of low-dose unfractionated heparin, 5000 IU subcutaneously twice a day. Easier once daily low-molecularweight heparin is as effective, requires less nursing time but is more expensive. Intermittent pneumatic compression devices applied to the lower extremity are an alternative to heparin. High-risk category patients require even more measures due to the estimated 40–80% risk of TED in patients receiving no prophylaxis.

Most gynecologic oncology cases will fall into the high-risk category. Standard unfractionated heparin (UH) is ineffective in low doses, i.e. 5000 units b.i.d., in high-risk cancer cases. If given three times daily, UH is effective but no better than pneumatic calf compression. Unfortunately, this more frequent dosing is associated with significantly more wound hematoma formation and blood transfusions. It also requires additional nursing and pharmacy personnel time, and is more uncomfortable for the patient. Unfortunately, though compression devices are effective in gynecologic oncology patients, the devices are somewhat cumbersome leading to patient and nursing resistance and non-compliance. In fact, improper application of the devices occurs in approximately 50% of patients on routine in-patient nursing stations. Compression devices are also contraindicated in patients with significant peripheral vascular disease.

Low-molecular-weight heparins (LMWH) have many potential advantages over the previously cited alternatives. These include excellent bioavailability allowing for single daily dosing. This reduces nursing effort, and therefore labor cost, and may be better accepted by the patient owing to its once-a-day schedule. It is also associated with less thrombocytopenia and postoperative bleeding than UH t.i.d. Patients with UH associated thrombocytopenia will usually tolerate LMWH without difficulty. In summary, in extremely high-risk patients, i.e. gynecologic oncology patients, LMWH may be more efficacious, more cost effective and less toxic, than the other alternatives. Combination prophylaxis with LMWH and pneumatic compression devices are even more effective in other high-risk patients (neurosurgery) and are being investigated. Many other agents have been tried given the imperfect options that exist to date. All have their limitations and are not currently used routinely, however all are effective to some degree and may be appropriate in highly selected patients. Some of these agents include aspirin, coumadin/warfarin and high-molecular-weight dextran. Aspirin has been compared to LMWH directly. Depending on the dose and duration, aspirin, while somewhat effective, is associated with more bleeding complications and is less effective than the heparin in preventing TED. Coumadin/warfarin is similar to aspirin in that it is effective in preventing TED but again it is associated with a higher risk of complications and requires more intensive monitoring. Dextrans are also effective but have been associated with rare cases of allergic reactions. Other complications reported include fluid overload and nephrotoxicity. Further research to avoid some of these limitations may improve the therapeutic value of these alternatives in the future. Alternatives to heparins altogether are also becoming more available including hirudin, ximelagatran and others.

The duration of prophylaxis has traditionally been limited to the duration of the in-patient stay. In many older studies, before the era of for-profit health care corporations, this may have been several days to weeks. Currently, lengths of stay are much shorter and as a result, so is the duration of TED preventive measures. Even before this forced change in clinical practice, it was recognized that a significant minority of TEDs either developed or were diagnosed long after discharge from the hospital. The optimal duration of prophylaxis is still not known and depends on the method used. For instance patients should be instructed to ambulate daily at home once discharged from the hospital. Similarly, graduated compression stockings may be continued after surgery until discharge with little risk and possibly some benefit. However pharmacologic therapies have side effects, may require some training, i.e. self or nurse injections, and are associated with considerable cost in both monitoring and potential toxicity. For these reason, the optimal method and duration of post-discharge TED prophylaxis has not been determined but is probably longer than 3 months and in cancer patients, may extend for up to a year after surgery.

The preceding agents are all designed to prevent TED and thereby reduce the risk of developing a clinically significant pulmonary embolism. When used properly, most patients will not develop TED and therefore will be at low risk for a pulmonary embolism. However it is not uncommon for a gynecologic oncology patient to present with TED as the first manifestation of their underlying malignancy. Trousseau’s sign, i.e. venous thrombosis due to malignancy, may be the presenting symptom in up to 10% of ovarian cancer patients. In these patients, and in those who despite appropriate prophylaxis, have or develop TED, something must be done to prevent the progression to a potentially fatal pulmonary embolism. This becomes an especially difficult situation if the patient requires surgery for the treatment of the etiologic malignancy.

One common management technique for these difficult situations is mechanical inferior vena cava interruption either temporarily or irreversibly. This can be accomplished preoperatively with peripheral venous access and interventional radiology techniques. Care must be taken to delineate the extent of the clot so that no attempt is made to pass the device through an occluded vein. If peripheral caval interruption is not possible, intraoperative vena caval clip may be applied. However, large pelvic masses, not uncommon in gynecologic cancer patients, may prevent access. Additional problems with vena caval interruption include migration of the device, complete occlusion of the cava, perforation and infection. In preoperative cases that can not have a filter or clip placed, one option includes the discontinuation of intravenous UH one hour before the perioperative period with its resumption approximately 6 hours after completion of the surgery. Most patients will do well with this technique, however the patient is still vulnerable to intraoperative pulmonary embolisms. Another pharmacologic option may include the preoperative lysis of the thrombus with thrombolytic agents such as urokinase followed by resumption of standard prophylactic measures. Oral anticoagulation is used after caval interruption, if not contraindicated, to prevent post-thrombotic venous stasis of the lower extremity. Therefore, mechanical devices, while reducing perioperative pulmonary emboli, do not obviate the need for long-term anticoagulation.

Diagnosis

Given the imperfection of prophylaxis and the high risk of TED in gynecologic oncology patients, all physicians caring for these women should be familiar with the treatment and diagnosis of TED including pulmonary embolism. Fewer that one third of patients with TED of the lower extremity will present with the classic symptoms of unilateral edema, pain and venous distension. Homan's sign, i.e. calf pain with dorsiflexion of the foot, is also unreliable and present in less than half of patients with TED. Calf TED occurs bilaterally in approximately 40% of cases and is more common on the left (40%) than on the right (20%). Only a high index of suspicion and objective testing can correctly identify patients with TED.

In high-risk patients with a high baseline prevalence, sensitive but non-specific tests are useful due to their high positive predictive value. By the same token, with a high pretest probability, repeat testing on subsequent days or more sensitive techniques are needed to exclude disease in these same high-risk patients. Non-invasive diagnostic testing should always be considered before interventional techniques including venography and arteriography D-Dimer is a good example of a sensitive non-invasive test that can be used to exclude TED in high-risk patients. Lower-extremity Doppler and real-time two-dimensional sonography are fairly sensitive (85%) and specific (>95%) for TED. If positive in a high-risk population, including patients with symptoms suggestive of a pulmonary embolism, no further testing is indicated and therapy may be initiated. Ventilation perfusion scans may be used similarly in patients with a high suspicion for pulmonary embolism. If the scan is intermediate or high probability, treatment is usually indicated. In patients at higher risk for hemorrhagic complications, such as the recent postoperative period with residual tumor, confirmatory tests may be indicated before therapy. Pulmonary arteriography may be indicated in this setting. CT or magnetic resonance pulmonary artery imaging is as accurate, less invasive and safer that arteriography and should be available in most centers.

Treatment

If there is no contraindication to anticoagulation, therapy should be started as soon as the diagnosis of TED is made. In certain circumstances, e.g. high clinical suspicion but a delay in definitive testing, empiric anticoagulation may be indicated. Outcomes are correlated with the time it takes to achieve therapeutic anticoagulation. Therefore the fastest means available should be employed. Low-molecular-weight heparin (LMWH) has an advantage over UH in that a single daily dose of approximately 175 IU/kg (factor Xa inhibitory units) subcutaneously will be therapeutic almost immediately (1–4 hours). Unfractionated heparin may require approximately 24 hours and repeated blood testing before becoming therapeutic. Coumadin can be started once the anticoagulation effect of either heparin is realized. With UH, this may be as early as day one, although 2 or 3 days of therapy may be needed before anticoagulation is achieved. With LMWH, coumadin can be started within a few hours and definitely on the same day. Either heparin should be continued until the coumadin has achieved an International Normalized Ration (INR) of 2–3. Anticoagulation should continue with coumadin for at least 3 to 12 months. Patients with recurrent TED or persistent precipitating events, e.g. vessel compression by tumor, may need indefinite anticoagulation.

Disseminated cancer and chemotherapy will unavoidably increase the risk of complications from anticoagulation. Cancer patients who have nutritional deficits, organ damage and unknown metastatic sites are particularly vulnerable because of altered liver and renal function making dosing more difficult. Chemotherapy may also share similar toxicities with anticoagulants and thereby worsen hemorrhagic complications from thrombocytopenia and anemia. For these reasons, treatment of TED may not be desired by the patient nor recommended by her physician in all situations. TED restricted to the calf may be followed with frequent sonograms in these situations and the decision to treat reconsidered if there is TED progression. Although these guidelines may be appropriate for most cancer patients, the care of individual gynecologic oncology patient demands personalized treatments.

Infection control*

There is increasing awareness of the risks of transmission of blood-borne pathogens from surgeon to patient and vice versa during surgical practice. These risks have been highlighted by the publicity surrounding human immunodeficiency virus (HIV), but are generally greater from other pathogens including hepatitis B virus (HBV). Infection with hepatitis C virus (HCV) also poses a risk of transmission from patient to surgeon. The prevalence of these viral infections varies

* This section is adapted and updated from *Br J Gynaecol Obstet* (1995) **102**:439–41 (with permission).

widely with different populations, and this exerts an influence on the surgeon's risk, as does the number of needlestick (or sharps) injuries sustained and the surgeon's immune status. The risks of transmission of these viruses and their subsequent pathogenicity are discussed below. The necessity for universal precautions in surgical practice need not affect overmuch operator acceptability or cost.

Antenatal anonymous surveys have shown a seroprevalence of HIV in metropolitan areas of the UK to be as high as 0.26% (Goldberg et al. 1992). More recently a survey published in 2002 showed that there are 49 500 adults infected with HIV in the UK, a third of whom are unaware of their diagnosis. In 2002 there were 686 births to women infected with HIV, this translating into a 0.38% seroprevalence in London and 0.06% in the rest of the UK (Health Protection Agency). Seroprevalence data of women undergoing gynecological or general surgical procedures are not currently available, but an unlinked anonymous survey of 32 796 London hospital in-patients aged 16–49 years from specialties not usually dealing with illness related to HIV infection has found a seroprevalence of 0.2% (Newton and Hall 1993).

The risk of acquiring HIV from a single needlestick injury from an infected patient is in the region of 0.10% to 0.36% (Shanson 1992, Ippolito et al. 1993). However, using mathematical models to predict lifetime risks of acquiring the infection in a population with a low HIV seroprevalence (0.35%), it has been suggested that 0.26% of surgeons would seroconvert during their working lives (Howard 1990). If the seroprevalence of HIV infection in surgical patients were as high as 5%, then the estimated 30-year risk of HIV seroconversion for the surgeon might be as high as 6%, depending on the number and type of injuries sustained (Lowenfels et al. 1989). At December 2001 57 health care workers in the USA had seroconverted to HIV as a result of occupational exposure (www.cdc.gov). This website is a valuable resource particularly with respect to new and ever-changing drug regimens currently in use in the management of blood-borne pathogens.

Intact skin and mucous membranes are thought to be effective barriers against HIV Only a very few cases of transmission via skin contamination are known to have occurred, and these health care workers had severe dermatitis and did not observe barrier precautions when exposed to HIV-infected blood (Centers for Disease Control 1987). Aerosol transmission of HIV is not known to occur, and the principal risks are related to injuries sustained from hollow-bore needles, suture needles and lacerations from other sharp instruments. Infectivity is determined by the volume of the inoculum and the viral load within it: thus a hollow-bore needlestick injury carries greater risk than injury from a suture needle. Prior to highly active antiretroviral therapy, infection with HIV results in the acquired immune deficiency syndrome (AIDS) in 50% of patients over a 12-year period and has a long-term mortality approaching 100%. For HIV-seropositive surgeons, further operative practice involving insertion of the fingers into the body cavity is precluded owing to the potential risk of doctor-to-patient transmission: for gynecological surgeons, this encompasses virtually their entire surgical practice, with the exception of simple laparoscopic and hysteroscopic procedures. At present there is no vaccine available to prevent infection with HIV Should needlestick injury occur, the injured area should be squeezed in an attempt to expel any inoculum, and the hands should be thoroughly washed. There is good evidence that after exposure prophylactic zidovudine (azidothymidine, AZT) reduces transmission by 79% (Centers for Disease Control 1996). Most occupational health departments now advise their health care workers to commence treatment within 1 hour of injury with multiple therapy which depending on the risk of HIV exposure should either be two-drug regimen for 4 weeks or for those at higher risk a three-drug regimen. These usually include zidovudine (AZT), lamivudine (3TC), although these may be modified in event of known drug resistance in the index case. This type of regimen may well reduce the risks of seroconversion further. A further study suggested a reduced risk from multiple therapy of 81% (95%CI 43–94%) (Cardo et al. 1997).

Intraoperative transmission of HBV occurs more readily than with HIV, and exposure of skin or mucous membrane to blood from a hepatitis Be antigen (HBeAg) carrier involves a highly significant risk of transmission for those who are not immune. The risk of seroconversion following an accidental inoculation with blood from an HBeAg carrier, in the absence of immunity, is in the order of 35% (Bradbeer 1986). Hepatitis B surface antigen (HBsAg) is found in 0.5–1% of patients in inner cities and in 0.1% of patients in rural areas and blood donors. Given a needlestick rate of 5% per operation, the risk of acquiring the virus in a surgical lifetime is potentially high. Prior to the introduction of HBV vaccination an estimated 40% of American surgeons became infected at some point in their careers, with 4% becoming carriers. Acute infection with HBV is associated with the development of fulminant hepatitis in approximately 1% of individuals. Carriers may go on to develop chronic liver damage,

cirrhosis or hepatocellular carcinoma, carrying an overall mortality of approximately 40%.
Transmission of HBV from infected health care workers to patients is rare but well documented. Welch et al. (1989) reported a case of an infected gynecologist who transmitted HBV to 20 of his patients; the operations carrying greatest risk of infection were hysterectomy (10/42) and cesarean section (10/51). In view of this risk government guidelines in most countries stipulate that surgeons should be immune to HBV, either through natural immunity or vaccination, the exceptions being staff who fail to respond to the vaccine (5–10%) and those who are found to be HBsAg positive in the absence of 'e' anti-genemia ([UK] Advisory Group on Hepatitis 1993). In the UK, the USA and other countries this is a statutory obligation. Those who fail to respond to vaccination should receive hepatitis B immunoglobulin following needlestick injury where the patient is HBV positive.

Hepatitis C virus, the commonest cause of non-A non-B hepatitis in the developed world, is also known to be spread by blood contamination. Routine screening for antibodies amongst blood donors in the UK has shown that 0.05% were seropositive in 1991; many of these were seemingly healthy asymptomatic carriers. However, as many as 85% of injecting drug users may be seropositive. Antibodies to HCV were detected in 4.3% of 599 pregnant women screened anonymously in a North American inner city (Silverman et al. 1993). In the UK, infection with HCV is second only to alcohol as a cause of cirrhosis, chronic liver disease and hepatocellular carcinoma, although the clinical course in seemingly healthy individuals is unclear. Recent data suggest that there are 250 000 people infected with HCV in England alone (HCV Clinical Bulletin).

An anonymous seroprevalence study of staff at an inner London teaching hospital reported that infection with HCV was no higher than that previously seen in blood donors. The seroprevalence was no different for workers involved with direct clinical exposure (medical and nursing staff) compared with those at risk of indirect clinical exposure (laboratory and ancillary staff) (Zuckerman et al. 1994). However, these findings should not lead to complacency. From epidemiological data, it would appear that HCV infection is less contagious than HBV, but more so than HIV The currently quoted risk of transmission from patient to health care worker following needlestick injury is 1.8% (range 0–7%) (Puro et al. 1995). It would however appear that transmission is very rare with solid-bore needles, i.e. almost exclusively following innoculation with hollow-bore needles. Transmission has rarely followed mucous membrane exposure and never via non-intact or intact skin. The possibility of HCV infection should be considered in the event of needlestick injury. Immunization and postexposure prophylaxis are not available for those exposed to HCV In the UK recently for those health care workers infected with hepatitis C, the same restrictions with respect to HIV i.e. preclusion from performing exposure-prone procedures (EPPs) has been introduced; this is not the case in any other country.

In the UK health care workers found to be infected with blood-borne pathogens will be precluded from performing exposure-prone procedures. In the USA these restrictions apply to infection with HIV and HBV, but not HCV EPPs are defined as procedures where a digit is present within a body cavity in the presence of a sharp object. For the purposes of lookback a lot of work has been going on in the UK recently to subdivide EPPs into: no risk, i.e. not an EPP; low risk; medium risk; and high risk. Examples in each group would be venesection, repair of an episiotomy, a cold knife cone biopsy and cesarean section, respectively. This exercise is to allow fine tuning of any potential lookback exercises. It is not designed to determine what procedures the infected surgeon might perform.

Prevention of blood-borne infection

Some surgeons have advocated preoperative screening of patients for HIV infection. They argue that patients shown to be infected should be treated as high-risk, while the remaining patients would be labelled as low-risk, with the consequent development of a two-tier infection control policy. However, such an approach is fraught with political, ethical, logistical and financial implications and, furthermore, wrongly assumes that infected patients can always be identified by serological testing. The universal precautions suggested below are practicable, and effectively minimize the intraoperative infection risk of both surgeon and patient. These precautions are based on the procedure rather than the perceived risk status of the patient. As discussed above, the greatest risk of contracting a blood-borne pathogen is from needlestick injury. Vaginal hysterectomy has been shown to have the highest rate (10%) of needlestick injury of any surgical procedure (Tokars et al. 1991). A further study by Tokars showed that in a group of orthopedic surgeons surveyed 49% of UK surgeons and 39% of US surgeons had sustained a needlestick in the preceding month (www.aidsmap.com). Glove puncture has been used luntas a measure of skin contamination and a reflection of needlestick injury; the highest rate of glove puncture reported in any surgical procedure was 55% at cesarean section (Smith and Grant 1990). Double gloving has shown a 6-fold diminution in inner glove puncture rate, and anecdotally appears to result in a reduction in needlestick injury, but it is uncomfortable, particularly during protracted procedures, making it unsuitable for many gynecologic oncological operations. Blunt-tipped needles, such as the Protec Point (Davis & Geck, Gosport, UK) and Ethiguard (Ethicon, Edinburgh, UK), appear to reduce the rate of glove puncture, and one of the authors (JRS) has never sustained a needlestick injury in 8 years of continuously using these needles. The newer needles are capable of penetrating the majority of tissues including uterine muscle, vaginal vault, cervix, peritoneum and rectus sheath. They are unsuitable for bowel and bladder surgery and do not penetrate skin, but they have been used subcutaneously for abdominal wound closure. Abdominal skin closure can also be safely undertaken with the use of staples. This is particularly important since it has been shown that 5% of glove punctures occurred during this stage of the procedure (Smith and Grant 1990). Just under half of punctures occur in the right hand (Smith and Grant 1990)—a surprising finding considering that most surgeons are right-handed and therefore grasp the needleholder with the dominant hand. Injury appears to occur during knot tying, and a safety needleholder with provision for guarding the needle tip at this stage and when returning the needle to the scrub nurse is now available

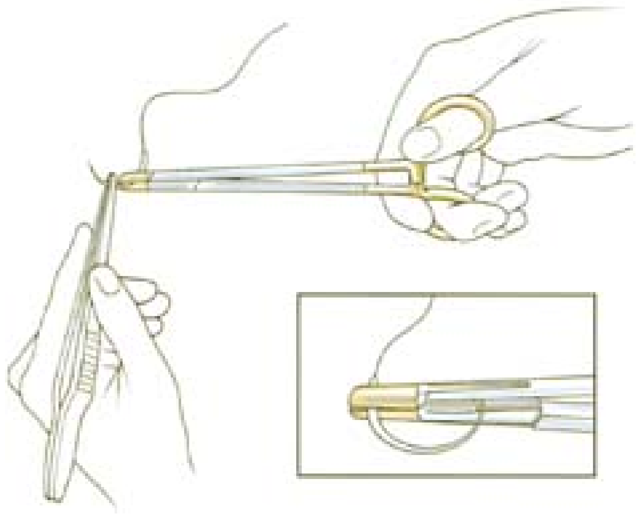

Figure 1

Safety needleholder

(Thomas et al. 1995) (Figure 1). The use of a kidney dish for passing scalpels between staff should also be encouraged, as should safe needle and blade disposal in hands-free surgical sharps boxes. Blades or needles that have fallen on the floor should be retrieved with a magnet prior to disposal. Blunt towel clips are also available to prevent injury while draping. Reusable self-adhesive drapes are available, as are disposable self-adhesive drapes with a surrounding bag to prevent gross contamination.

Skin and mucous membrane contamination should be avoided by the use of masks and waterproof gowns. Spectacles or other protective eyewear should be worn to prevent contamination by facial splashes of blood and other body fluids.

The risks and safety measures discussed above are summarized in Tables 2 and 3. Table 2 demonstrates that oncological surgery carries the greatest risk

Table 2 Risk factors for transmission of bloodborne pathogens during surgical practice

1.	Prolonged surgical procedure
2.	Heavy blood loss
3.	Operating within a confined space (e.g. pelvis or vagina)
4.	Poor lighting
5.	Guiding the needle by feel

Table 3 Simple precautions available to reduce needlestick injury

1. Blunt-tipped needles: available from Davis & Geck (Protec Point) and Ethicon (Ethiguard needle)
2. Staple guns for skin closure: available from Autosuture and Ethicon Endosurgery
3. Staples for bowel anastomosis: available from Autosuture and Ethicon Endosurgery
4. Safety needleholders: available from JRS Surgical (London, UK)
5. Spectacles/protective eyewear
6. Magnet for picking up sharps
7. Hands-free disposable sharps boxes for needles and blades
8. Blunt towel clips
9. Self-adhesive drapes

These measures are summarized in an educational video produced by the TV Unit at Imperial College School of Medicine, Charing Cross Hospital, St Dunstan's Road, London W6 8RP, UK.

within gynecological practice. However, the simple and relatively cheap procedures and precautions suggested in Table 3 can reduce the risk for both surgeon and patient to extremely low levels.

References

Advisory Group on Hepatitis (1993) *Protecting health care workers and patients from hepatitis B.* HMSO: London.

Bradbeer C (1986) AIDS—epidemiology and screening. *Med Internat* **2**:1241–6.

Cardo DM, Culver DH, Ciesielski CA et al. (1997) A case control study of HIV seroconversion in health care workers after percutaneous exposure. *N Engl J Med* **337**:1485–90.

Centers for Disease Control (1987) Update: human immuno deficiency virus infection in health care workers exposed to blood of infected patients. *MMWR* **36**:285–9.

Goldberg DJ, MacKinnon H, Smith R et al. (1992) Prevalence of HIV among childbearing women and women having termination of pregnancy: multidisciplinary steering group study. *Br Med J* **304**:1082–5.

HCV Clinical Bulletin. National Register, Sept 2002. Available at www.hpa.org.uk/infections/topics_az/hepatitis_c/pdf/bulletin0902.pdf. (accessed 28 April 2005)

Health Protection Agency: HIV and Sexually Transmitted Infections. Reviewed on 24 November 2003. Annual Report 1 November 2003. (www.hpa.org.uk). (accessed 9 March 2005)

Howard RJ (1990) Human immunodeficiency virus testing and the risk to the surgeon of acquiring HIV. *Surg Gynaecol Obstet* **171**:22–6.

Ippolito G, Puro V, De Carli G (1993) The risk of occupational human immunodeficiency virus infection in health care workers: The Italian Study Group on occupational risk of HIV infection. *Arch Intern Med* **153**:1451–8.

Lowenfels AB, Worsmer GP, Jain R (1989) Frequency of puncture injuries in surgeons and estimated risk of HIV infection. *Arch Surg* **124**:1284–6.

Newton L, Hall SM (1993) Unlinked anonymous monitoring of HIV prevalence in England and Wales: 1990–1992. *Common Dis Rep* **3**:1–16.

Puro V, Petrosilla N, Ippolito G (1995) Italian Study Group on Occupational Risk of HIV and Other Bloodborne Infections. Risk of hepatitis C seroconversion after occupational exposure in health care workers. *Am J Infect Contr* **23**:273–7.

Shanson DC (1992) Risk to surgeons and patients from HIV and hepatitis: guidelines on precautions and management of exposure to blood or body fluids. (Joint Working Party of the Hospital Infection Society and the Surgical Infection Study Group). *Br Med J* **305**:1337–43.

Silverman NS, Jenkin BK, Wu C et al. (1993) Hepatitis C virus in pregnancy: seroprevalence and risk factors for infection. *Am J Obstet Gynecol* **169**:583–7.

Smith JR, Grant JM (1990) The incidence of glove puncture during caesarean section. *J Obstet Gynaecol* **10**:317–18.

Sweet RL, Gibbs RS (1990) *Infectious Diseases of the Female Genital Tract,* 2nd edn. Williams & Wilkins: Baltimore.

Thomas PB, Falder S, Jolly M et al. (1995) The role of blunt-tipped needles and a new needle-holder in reducing needlestick injury. *J Obstet Gynaecol* **15**:336–8.

Tokars J, Bell D, Marcus R et al. (1991) Percutaneous injuries during surgical procedures (Abstract). *VII International Conference on AIDS,* Florence, Italy.

Welch J, Webster M, Tilzey AJ et al. (1989) Hepatitis B infections after gynaecological surgery. *Lancet* **i**:205–7.

West DJ (1984) The risk of hepatitis B among health care professionals in the United States: a review. *Am J Sci* **287**:26–33. www.aidsmap.com—25.6.04.

Zuckerman J, Clewley G, Griffiths P, Cockroft A (1994) Prevalence of hepatitis C antibodies in clinical health-care workers. *Lancet* **343**:1618–20.

2
Anatomy

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Introduction

Surgical anatomy is the synthesis of topographic and functional anatomy and surgical techniques. Surgical anatomy presents much more than the systematic description of organs and anatomic structures with particular emphasis on the relationships of the parts to each other. The tumor biology and tumor spread will also be taken into account with the different surgical techniques. To achieve the primary goal of cancer treatment to extirpate the tumor masses completely and to preserve important relevant anatomic structures a detailed knowledge of the anatomy of the pelvis and abdomen is essential. This skill will also influence the complication rate (morbidity) and the optimal debulking rates (survival) of patients with gynecologic tumors directly. Studies have shown that the strongest clinician-driven predictor of survival is the optimal surgical outcome (Nguyen et al. 1993, Lichtenegger et al. 1998, Bristow et al. 2000).

In a national survey on 12 316 patients with ovarian carcinoma from 904 American hospitals, Nguyen and coworkers have demonstrated that gynecologic oncologists frequently performed more hysterectomies, oophorectomies, omentectomies, lymph node and peritoneal biopsies and yielded higher debulking rates than other specialists. With the exception of patients with Stage I disease, patients treated by general surgeons had significantly reduced survival than those treated by gynecologic oncologists (p<0.004).

To optimize clinical management, systematic and continual teaching in anatomy is required for all physicians who are involved in the surgical treatment of patients with gynecologic malignancies.

Pelvic fascia and pelvic spaces

Within the space lined by the pelvic fascia lies a mass of subserous tissue which as a whole is termed the *tela urogenitalis* (Figure 1). The tissue has various functions. It forms the fascia of the pelvic viscera as well as denser tissues conducting blood vessels and nerves from the pelvic wall. Between the pelvic wall, the uterus and the denser tissue, lie spaces filled with loose connective tissues. These spaces can be easily opened during surgery. The anatomic nomenclature includes many different interpretations and synonyma of the connective tissue structures in the pelvis. These terms include endopelvic fascia, intrapelvic fascia and connective tissue body, neurovascular plate, corpus intrapelvinum, paratissue (Stoeckel) parametrium, parangium hypogastricum (Pernkopf), transverse ligament of the collum (Mackenrodt), cardinal ligament (Kocks), web (Meigs), broad ligament and hypogastric sheets. The mass of the connective tissue body originates at the pelvic wall and runs in a transverse direction to the uterus and the vagina. Before reaching it, it provides one connective tissue sheet to the rectum and one to the bladder. These structures can be distinguished as the uterovaginal pillar, the bladder pillar and the rectal pillar. In a transverse section of the pelvis it resembles a horizontal letter Y, the base of which originates at the pelvic wall and which follows the pelvic axis. The body of the corpus intrapelvinum can originate only from the posterior ascending field of the arcus. Pernkopf took this into account in describing what he called the *frontal dissepiment* as meaning the pelvic wall at the posterior part of the arcus (Figure 2).

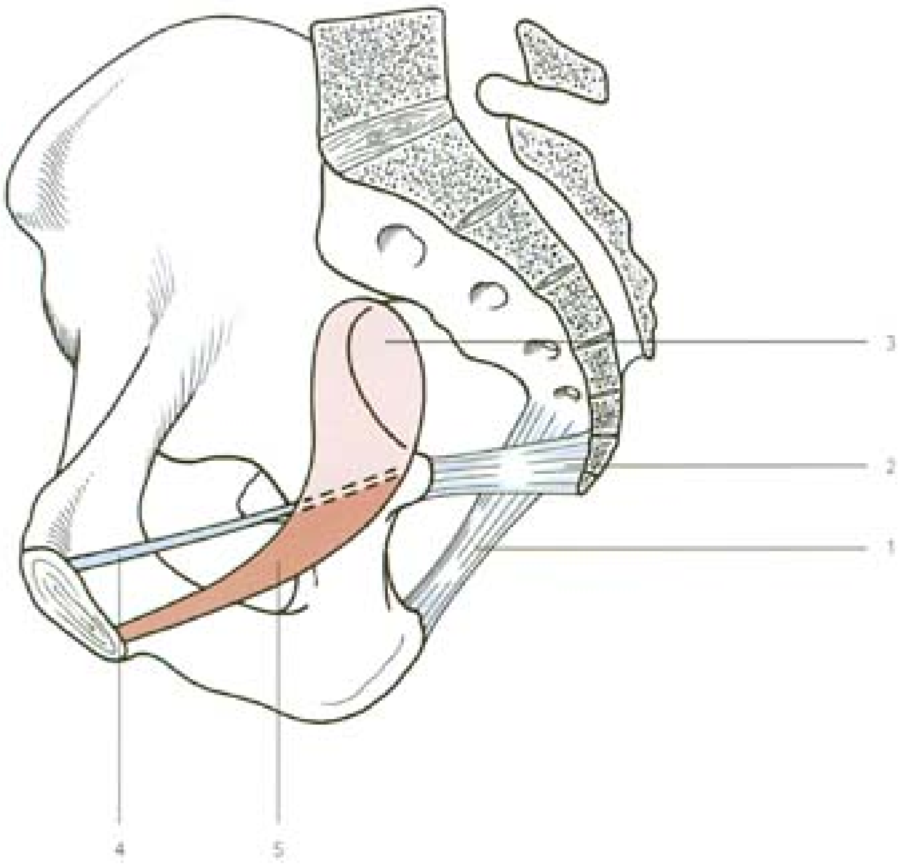

Figure 1

1 Ischiosacral ligament
2 Sacrospinous ligament
3 Origin of corpus intrapelvicum at lateral pelvic side-wall
4 Arcus tendineus levatoris ani
5 Arcus tendineus fasciae pelvis

A confluence of this connective tissue from the sidewall to the uterus is called the *cardinal ligament* (Figure 3). This is the strongest thickening of the pelvic fascia between the pelvic wall and the uterus. It emits the rectal pillar and the bladder pillar. Only the para-metrium actually reaches the supravaginal part of the cervix and therefore the uterus. The paracolpium, the part of the uterovaginal pillar below the level of the ureter, reaches the vagina and the cervix at the level of the vaginal fornix.
The bladder pillar from the abdominal view stretches from the body of the corpus intrapelvinum to the bladder. Viewed from the vagina, the distal pillar, which also lies in a sagittal plane, rises to the bladder. The sagittal bladder pillar is also called the *vesicouterine ligament*. The part of the ligament covering the ureter (the ureteral roof) forms the upper limit of the para-cystium. Loose connective tissue lies between the uterus and the wall of the canal of the ureter. This tissue contains the blood supply for the ureter and has been called the *mesoureter*.
The rectal pillar (uterosacral) spans the distance from the dorsal of the cardinal ligament to the sacrum. The upper portion represents the sagittal rectal pillar. The sagittal rectal pillar does not lie in a sagittal plane, but deviates far laterally to accommodate the pouch of Douglas. This brings it very close to the pelvic wall. The rectouterine ligament splits into an anterior leaf that emits the rectal fascia and a posterior leaf, which reaches the sacrum at the level of anterior sacral foramina II–IV. The insertion at the sacrum can extend upward beyond the sacral promontory (Figures 3 and 4).
The paravesical space is limited medially by the vesical fascia and the bladder pillar that enters it. Laterally, it reaches the parietal pelvic fascia and medially and anteriorly, it merges into the prevesical space. The major pelvic vessels lie in the lateral margin. Posteriorly it is limited by the body of the corpus intrapelvinum and the uterine artery in the cardinal ligament. The roof of the paravesical and prevesical space is formed by the vesicoumbilical fascia, which forms a vertical plane at the anterior abdominal wall at the horizontal plane in the pelvis.
The pararectal space is limited medially by the rectal fascia and the rectal pillar and laterally by the parietal pelvic fascia. After being opened from the abdomen, the pararectal space is narrow, because the rectal pillar lies close to the pelvic wall. The space is

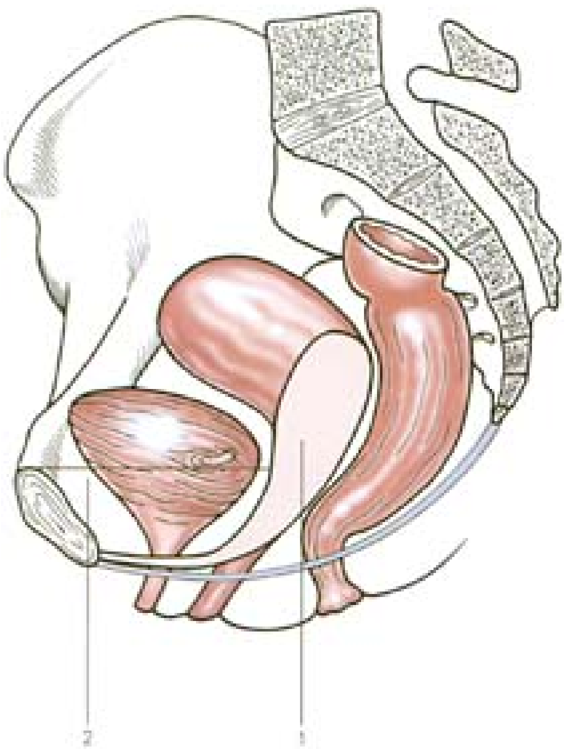

Figure 2

1 Corpus intrapelvicum
2 Arcus tendineus levatoris ani

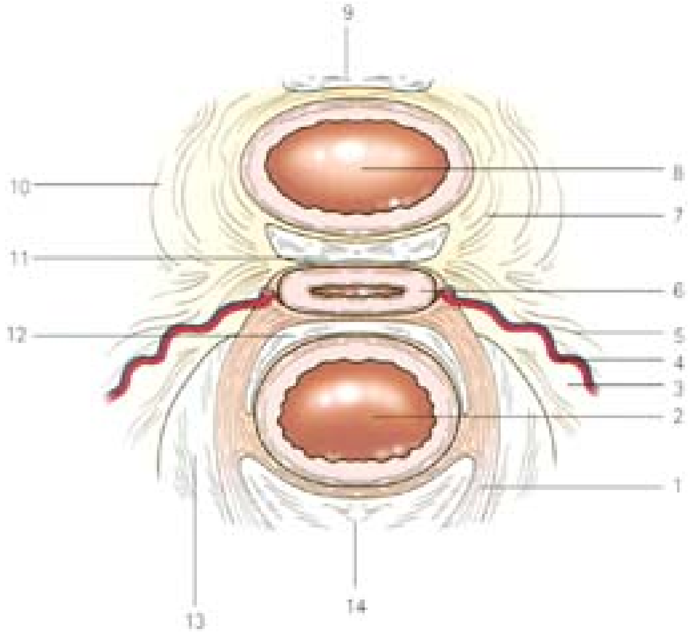

Figure 3

1 Uterosacral ligament
2 Rectum
3 Adventitia
4 Vessels
5 Cardinal ligament
6 Vagina
7 Bladder pillar
8 Urinary bladder
9 Prevesical space
10 Paravesical space
11 Vesicovaginal space
12 Rectovaginal space
13 Pararectal space
14 Retrorectal space

best demonstrated by pulling the uterus anteriorly so that the rectal pillar is lifted off the pelvic wall. The retrorectal/presacral space lies behind the rectum and is limited by rectal fascia and the parietal pelvic fascia. The retrorectal space is separated from the pararectal spaces by the part of the rectal pillar that joins the pelvic sacral foramina II–IV.

Between the vaginal and rectal fascia lies the recto-vaginal space. It reaches caudally to the centrum tendinum. Superiorly it is limited by the peritoneum of the pouch of Douglas. Laterally, the space is limited by the rectal pillars.

The vesicocervical and vaginal spaces are limited by the vesical fascia and the cervix. They reach the peritoneum and are inferiorly separated by the supravaginal septum. The vesicovaginal space reaches caudally the origin of the urethra and lies between the bladder pillars.

Upper part of the abdomen

Although in most patients with primary gynecologic cancers the highest tumor mass is concentrated in the pelvis, the upper quadrants of the abdomen are predominantly involved by metastasis in patients with recurrence (‘change of level’).

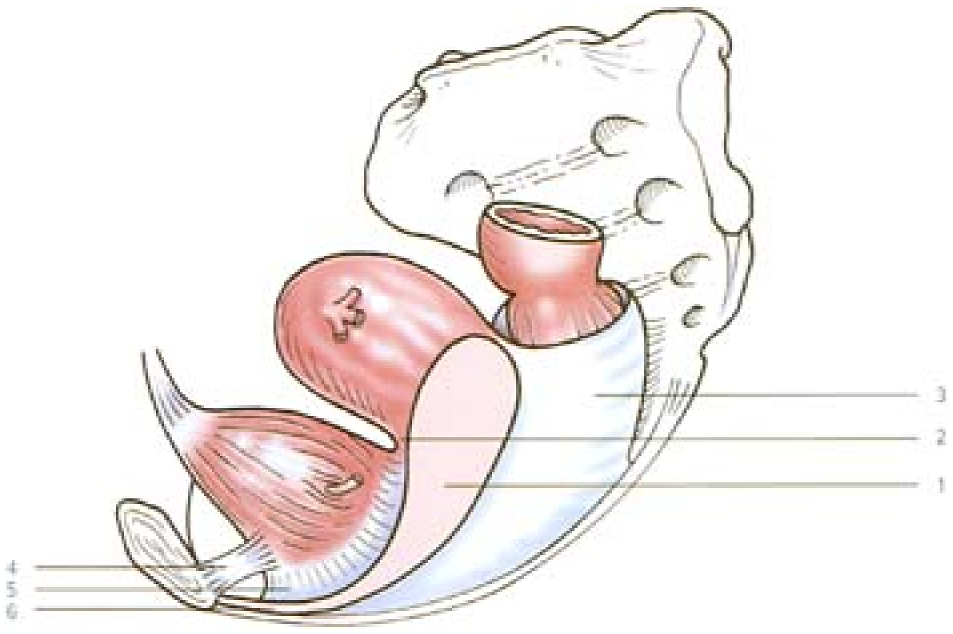

Figure 4

1 Origin of connective tissue, detached at lateral pelvic wall
2 Cardinal ligament
3 Uterosacral ligament
4 Pubovesical ligament
5 Laterovesical ligament
6 Arcus tendineus fasciae pelvis

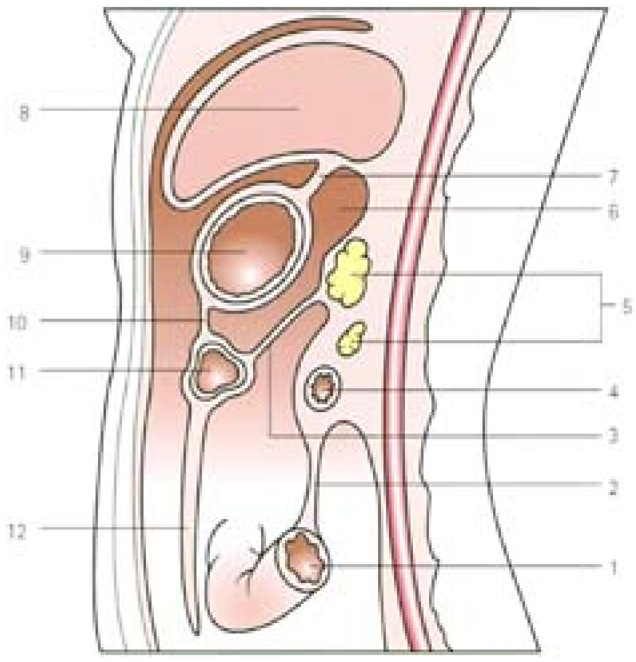

Figure 5

1 Small intestine
2 Mesentery
3 Transverse mesocolon
4 Duodenum
5 Pancreas
6 Omental bursa
7 Lesser omentum
8 Liver
9 Stomach
10 Gastrocolic ligament
11 Transverse colon
12 Greater omentum

The omental bursa is limited ventrally by: stomach, lesser omentum, and gastrocolic ligament; dorsally by: peritoneum (ceiling), pancreas, duodenum (middle) and greater omentum; posterior lamina (bottom) cranially by: caudate lobe of liver, left diaphragmatic vault; caudally by: transverse colon, transverse mesocolon, greater omentum (with inferior recession). To the left this space is limited by the following structures and organs: spleen, gastrophrenic ligament, gastrolienal ligament, splenorenal ligament, phrenico-splenal ligament and splenocolic ligament (Figure 5). The omental bursa communicates with the peritoneal cavity via the epiploic foramen (foramen of Winslow). This foramen is located below the free right margin of the hepaticoduodenal ligament and is limited cranially by the caudate lobe of the liver and distally by the superior duodenal flexure. The best way to explore the omental bursa is to prepare the space between the gastrocolic ligament and the transverse colon. During primary surgery of ovarian cancer the greater omentum is often resected incompletely. As a consequence, residuals of the omentum will be detected during surgery in relapse, frequently. In case of an acute pancreatitis, necrosis or effusion can also affect this pouch.
Peritonectomy is often applied in diffuse peritoneal carcinomatosis. This can also be performed in case of infection of the right diaphragm. Therefore, the falciform ligament of the liver should be cut in order to inspect the diaphragm completely. The falciform ligament is a wide, sickle-shaped fold of the peritoneum and attached to the lower surface of the diaphragm,

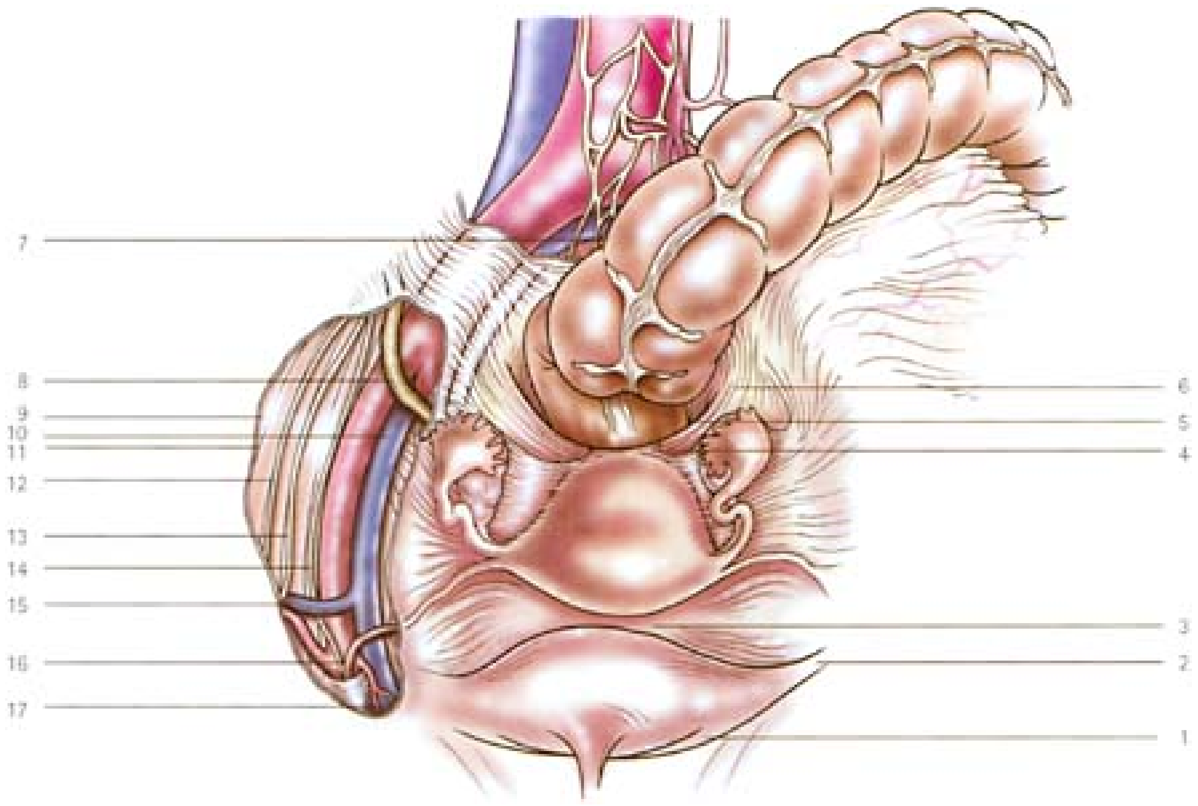

Figure 6

1 Paravesical fossa
2 Transverse vesical fold
3 Uterovesical pouch
4 Rectovesical pouch
5 Sacrogenital fold of uterosacral ligament
6 Pararectal fossa
7 Superior hypogastric plexus
8 Ureter
9 Psoas muscle
10 Internal iliac artery
11 Iliohypogastric nerve
12 Ilioinguinal nerve
13 Lateral femoral cutaneous nerve
14 Genitofemoral nerve
15 Circumflex iliac artery
16 Round ligament inserting into internal inguinal ring
17 Inferior epigastric artery

internal surface of the right rectus abdominis muscle and the surface of the liver.
The duodenum is about 25 cm long, C-shaped and begins at the pyloric sphincter. It is entirely retro-peritoneal and is the most fixed part of the small intestine. The duodenum has four parts: (1) superior, (2) descending, (3) horizontal, (4) ascending.
The fourth part of the duodenum terminates at the duodenojejunal flexure with the jejunum. The ligament of Treitz is a musculofibrous band (suspensory muscle) that extends from the upper aspect of the ascending part of the duodenum to the right crus of the diaphragm and tissue around the celiac artery.

Vascular supply

Most vessels encountered during oncologic procedures can be interrupted without ill effect because of the rich collateral circulation (Figures 6–8). These anastomoses prevent ischemia unless more than one of the major vessels is occluded. However, patchy ischemia, especially induced by atherosclerosis, fibrosis or irradiation, can occur since the small vessels that enter the gut wall are essentially terminal arteries. Obstruction of these vessels results in segmental ischemia.
However, whenever possible, vessels should be spared in order to promote healing and optimize chemotherapy and radiotherapy. Certain vessels, such as the superior mesenteric artery, can never be interrupted without reanastomosis. Care must be exercised around these structures, as blood vessels are not entirely consistent in their course or points of origin.

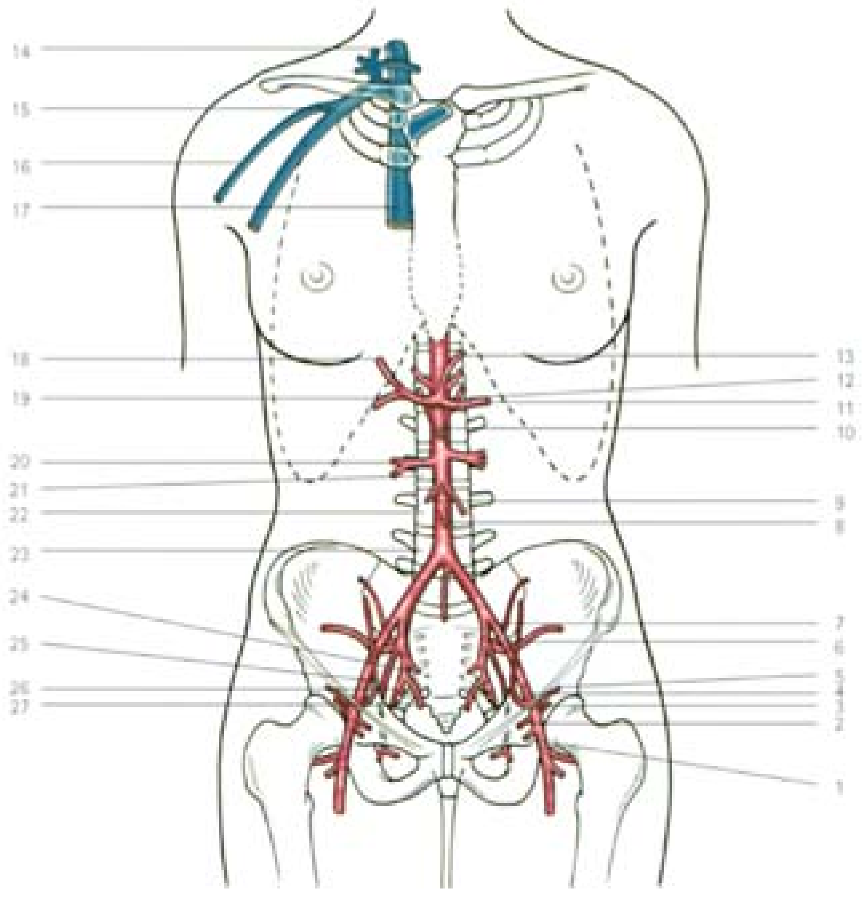

Figure 7A

1 External pudendal artery
2 Superficial epigastric artery
3 Superficial circumflex iliac artery
4 Inferior epigastric artery
5 Deep circumflex iliac artery
6 Internal iliac artery
7 External iliac artery
8 Inferior mesenteric artery
9 Gonadal artery
10 Superior mesenteric artery
11 Splenic artery
12 Celiac trunk
13 Left gastric artery
14 Internal jugular vein
15 Subclavian vein
16 Cephalic vein
17 SVC
18 Hepatic artery
19 Gastroduodenal artery
20 Renal artery
21 L2
22 L3
23 L4
24 Inferior rectal artery
25 Obturator artery
26 Internal pudendal artery
27 Uterine artery

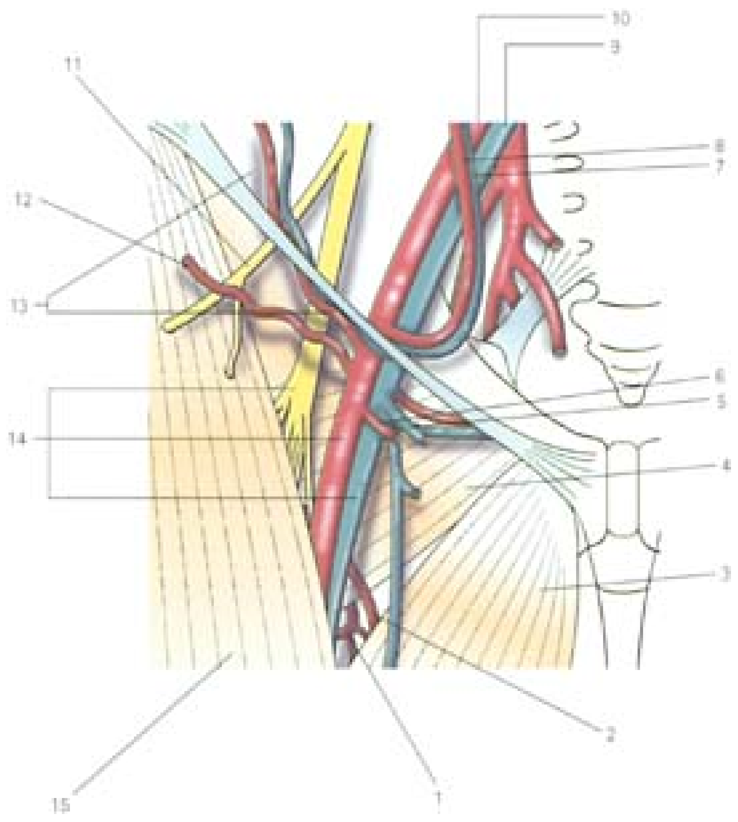

Figure 7B

1 1st pertorating artery
2 Femoral pudendis artery
3 Adductor longus muscle
4 Pectinius muscle
5 External pudendal vein
6 External pudendal artery
7 Inferior epigastric vein
8 Inferior epigastric artery
9 External iliac vein
10 External iliac artery
11 Lateral femoral cutaneous nerve
12 Superficial circumflex iliac artery
13 Deep circumflex iliac artery +vein
14 Femoral nerve, artery+vein
15 Sartorius

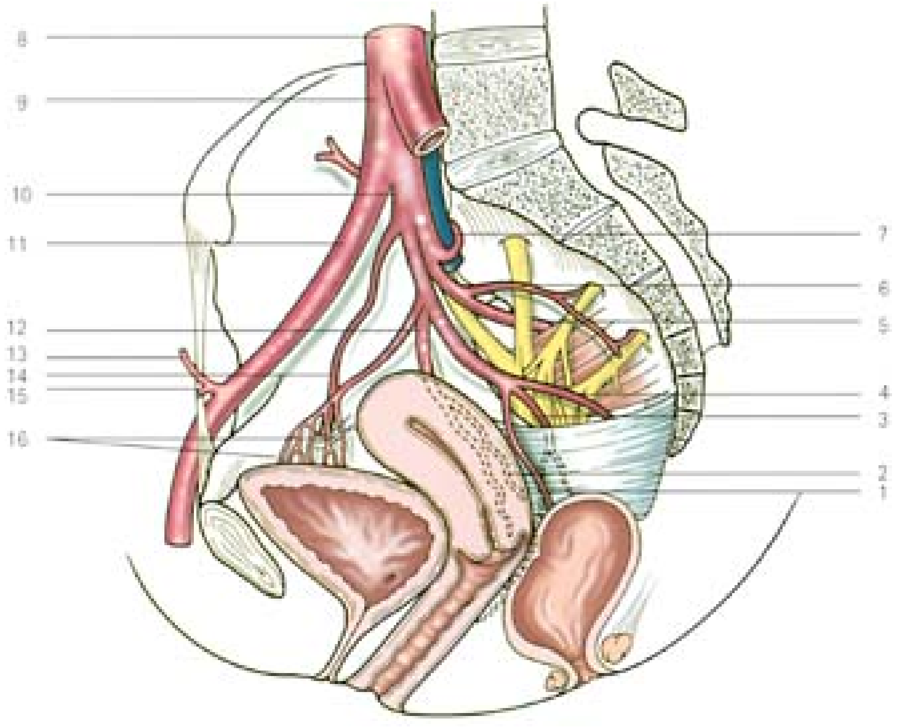

Figure 8

1 Middle rectal artery
2 Descending cervical of uterine artery
3 Internal pudendal artery
4 Inferior gluteal artery
5 Superior gluteal artery
6 Lateral sacral artery
7 Iliolumbar artery
8 Aorta
9 Common iliac artery
10 Internal iliac artery
11 External iliac artery
12 Uterine artery
13 Circumflex iliac artery
14 Obturator artery
15 Inferior epigastric artery
16 Superior vesical

Some helpful guidelines for locating these vessels include the bony, cutaneous and muscle relationships. For instance, the aortic bifurcation often occurs over the fourth lumbar vertebra which, in thin individuals, is at the level of the umbilicus. The renal vessels originate around the second lumbar vertebra. The ovary arteries arise just inferiorly to these at the third lumbar vertebra, around the level of the third part of the duodenum. The duodenum is also helpful in identifying the superior mesenteric artery, which leaves the aorta immediately cephalad to the third part, and the inferior mesenteric artery, which leaves the aorta just caudad to this same duodenal section. The ovary veins, on the other hand, are asymmetric, with the left vein emptying into the left renal vein, and are accompanied by many lymph vessels.

The umbilical artery originates where the uterine artery originates, at the termination of the internal iliac vessel. The distal region of this artery runs as the obliterated medial umbilical ligament and the proximal region is the origin of the superior vesical artery. The identification of the umbilical ligament is very helpful by the preparation of the parametrium; during radical hysterectomy, in the case of cervical cancer.

The external iliac artery and vein are additional important anatomic landmarks of the pelvis and can be easily palpated during surgery. The external iliac artery has two branches to the pelvic region: the deep circumflex iliac artery and the inferior epigastric artery. The external iliac artery continues as the femoral artery after crossing under the inguinal ligament through the lacuna vasorum. The lacuna vasorum is the anatomic space for the passage of the femoral vessels to the thigh. The femoralis vein, the femoral ramus of the genitofemoral nerve and the superior lymph node (‘node of Rosenmüller’) of the deep inguinal nodes are also located in the lacuna vasorum. The femoral nerve (L1–L2) is located between the psoas muscle and iliac muscle and passes laterally from the femoral artery with the lateral cutaneous femoral nerve and the lacuna musculorum.

In advanced cancer, regions of the intestinum are frequently involved. Knowledge of the blood supply of the mesenteric arteries is required to determine the area of intestinal resection in order to obtain maximal debulking. The superior mesenteric artery has branches to the stomach, inferior part of the duodenum, jejunum, ileum, cecum, ascending and transverse colon, ending at the left flexura. The inferior mesenteric artery gives branches to the descending and sigmoid colon and the rectum. The lower mesenteric vein carries blood from the descending colon, sigmoid colon and rectal vein plexus into the portal vein. The superior mesenteric vein takes blood from the jejunum, ileum, cecum, ascending colon and the transverse colon into the portal vein and receives additional blood from veins of the duodenum and the pancreas.

The celiac artery is the first branch of the abdominal aorta and supplies the stomach, liver, spleen, duo-

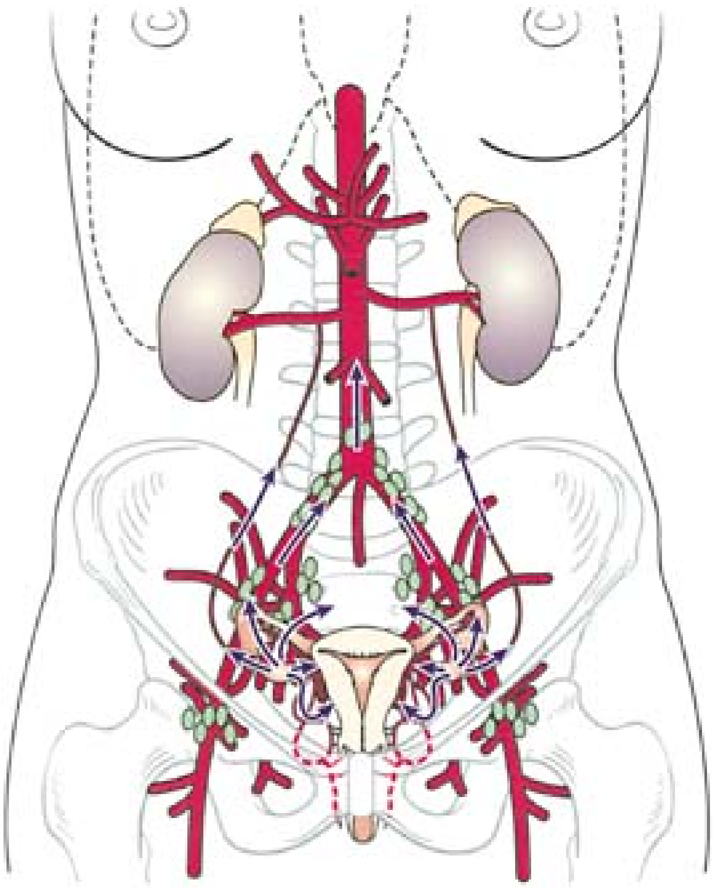

Figure 9

Lymphatic spread in ovarian cancer

denum and pancreas. There are also various anasto-moses between the superior mesenteric artery and celiac trunk (pancreaticoduodenal artery) and the superior mesenteric artery and inferior mesenteric artery. The so-called Riolan’s arch is an inconstant artery which is parallel to a portion of the middle colic artery and can be identified in the area of the left flexura of the colon. When Riolan’s arch is not developed—narrowed by irradiation or artherosclerosis—a ligation of the inferior mesenteric artery can induce necrosis of the descending colon because arterial perfusion by the medial colic artery is interrupted.

Lymphatic drainage parallels the course of venous blood supply. However, drainage is not always as straightforward as the blood supply. Lymph node metastases can obstruct flow and lead to retrograde metastases, which appear to skip regional chains. For instance, some endometrial and ovarian cancers can have isolated para-aortic lymph node spread through the lymph vessels of the infundibulopelvic ligament and show a retograde lymphatic spread (Figure 9).

For performing a systematic pelvic lymphadenectomy and for extraperitoneal preparation in case of bulky disease it is advisable to distinguish the different anatomic spaces around the pelvic vessels and structures. For simplification, it is helpful to visualize four associated spaces.

1. *Lateral pelvic wall.* Entrance between the medial part of the psoas muscle and laterally from the external iliac artery
2. *Paravesical fossa.* Entrance between the posterior wall of the urinary bladder and the external pelvic vein
3. *Obturator fossa.* Entrance between external iliac vein and medial umbilical artery
4. *Prevesical (retropubical) space (space of Retzius).* Entrance between the lower portion of the abdomen (pubic bones) and urinary bladder.

Nerves

There are few procedures that require a complete dissection of nerves in gynecologic oncology. In particular, the nerves of the pelvis and abdomen show a wide spectrum of variation in topographic anatomy. Nevertheless, the general course and function of many nerves should be known in order to avoid their injury and minimize surgical complications (Figure 10). The larger nerves are sometimes used as landmarks during surgical dissections, for instance, the obturator (L1–L4) nerve may serve as the near-to-inferior border of the pelvic lymphadenectomy (obturator fossa) and the phrenic nerve as the posterior border of the scalene node dissection.

To avoid injury, at the very beginning of a surgical procedure, the anatomy of the nervous system should be kept in mind when positioning the patient. For instance, because laparoscopy requires the surgeon to be further cephalad than during the same procedure done by laparotomy, both arms should be tucked at the patient’s side to avoid excessive superior traction on the brachial plexus by the surgeon leaning on the extended arm. During vaginal procedures, an assistant unfamiliar with the course of the femoral nerve might rest an arm on the patient’s medial anterior thigh and compress the femoral nerve. This nerve may also be injured by an abdominal retractor placed too deeply over the psoas muscle. Finally, some of the smaller nerves, such as the genital femoral nerve, may be transected during the removal of suspicious lymph nodes.

Femoral nerve injury results in decreased hip flexion and leg extension due to the loss of the iliacus, rectus femoris, vastus lateralis, intermedius and medialis, and sartorius muscle function. Injury to the obturator nerve results in loss of leg adduction and pronation from loss of the adductor brevis, longus and magnus, as well as obturator externus and gracilis muscle innervation.

The obturator nerve is surrounded by soft tissue consisting of lymph nodes and vessels and can be easily seen at the lateral pelvic wall medially from the lumbosacral trunk and the obturator fossa. In 30% of cases, an accessory obturator vein runs across the fossa. The obturator nerve leaves the pelvic wall by traversing through the obturator canal of the hip bone and crossing the paravesical fossa. The obturator canal is an opening in the obturator membrane and located a distance of 2–4 cm directly under the upper part of the symphysis.

The sciatic nerve is located laterally to the internal iliac artery and is not usually injured during surgical procedures. The sciatic nerve leaves the pelvis together with the inferior gluteal vein through the sciatic fora-

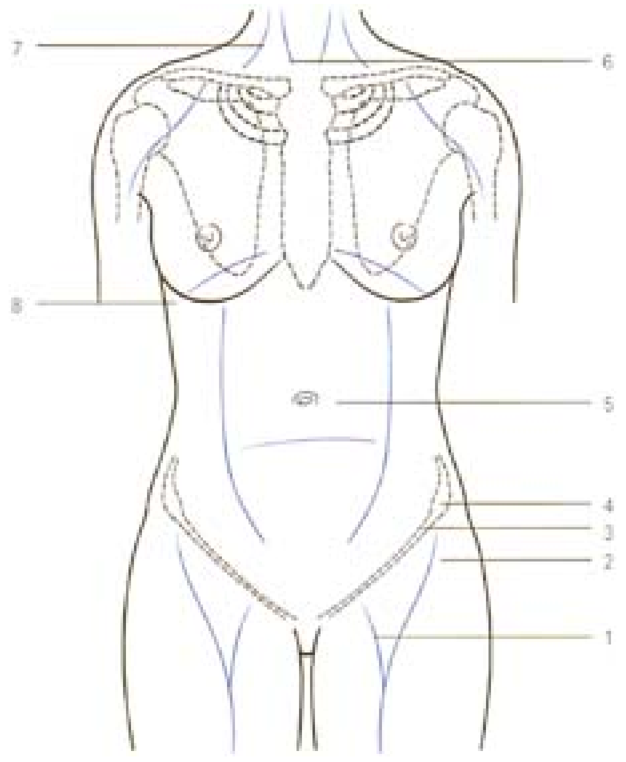

Figure 10

1 Adductor longus groove
2 Sartorius muscle groove
3 Inguinal ligament
4 Anterior superior iliac spine
5 Level of L4/L5 vertebral bodies
6 Sternal head sternocleidomastoid muscle
7 Clavicular head
8 Seventh rib

men. The sciatic nerve can be compromised by inadequate positioning during surgery and by advanced cancer (e.g. cervical cancer) spread to the lateral pelvic wall. Pain, secondary to cancer or postoperatively can be controlled in the pelvis by regional anesthetic blockade of the dorsal nerve roots of T10, T11 and T12 to the uterus tubes and ovary, and S2, S3 and S4 to the remaining genital structures (see Chapter 26).

The sympathetic trunk and the hypogastric nerves are responsible for the sympathetic innervation of the pelvis. Both lumbar trunks run across the medial origin of the iliopsoas muscle and ventrally to the lumbar veins. Injury to the sympathetic trunk can cause homolateral vasodilatation postoperatively: a feeling of hyperthermia in the lower extremity. The splanchnic nerves take the parasympathetic innervation of the pelvis and control micturition and defecation.

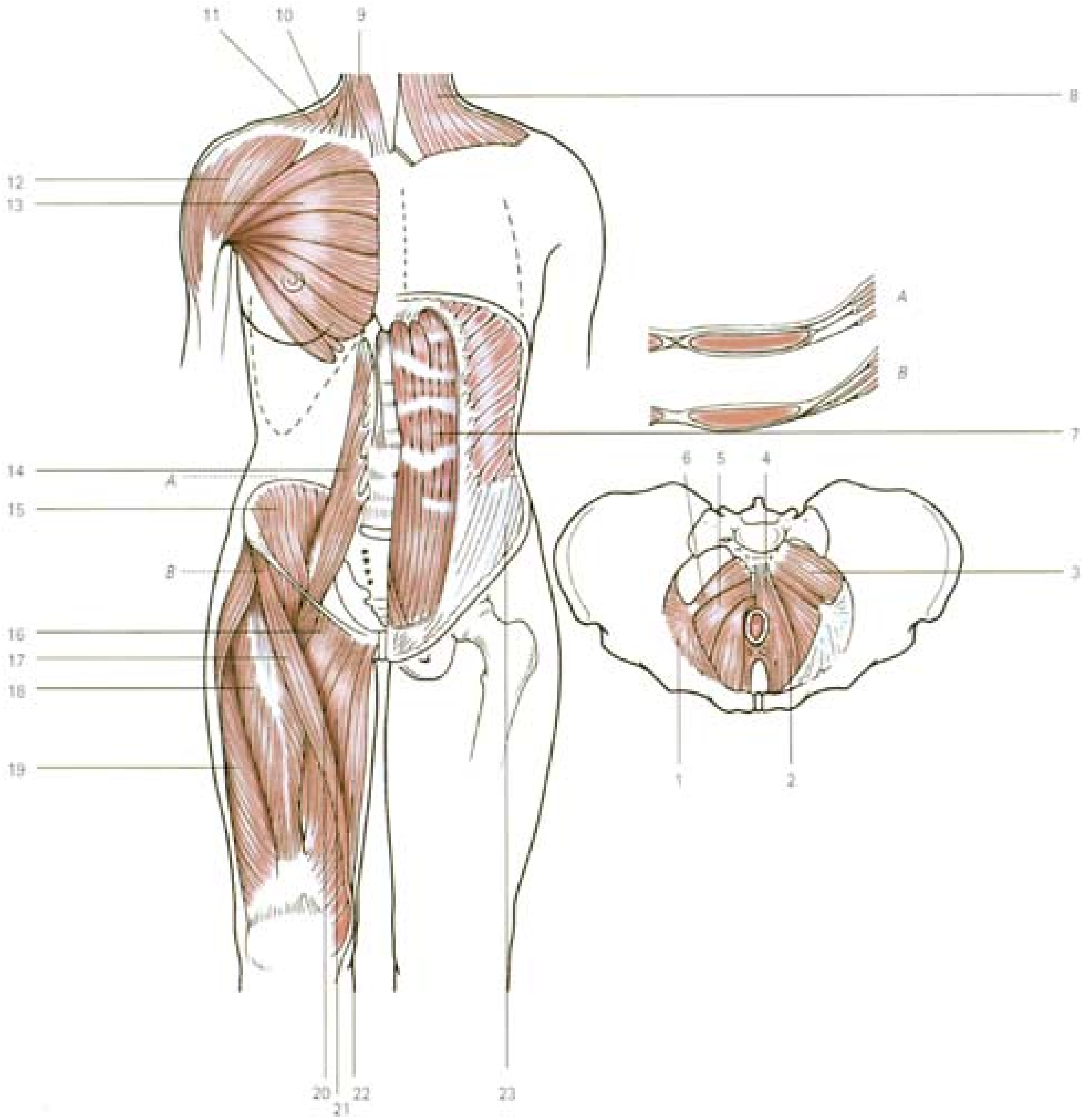

Figure 11

A Transverse level, umbilicus
B Transverse level, arcuate line
1 Obturator internus
2 Puborectalis
3 Piriformis
4 Pubococcygeal muscle
5 Iliococcygeal muscle
6 Coccygeus
7 Rectus abdominis
8 Platysmus
9 Sternocleidomastoid muscle
10 Anterior scalene muscle
11 Trapezius
12 Deltoid
13 Pectoralis major
14 Psoas
15 Iliacus
16 Pectineus
17 Sartorius
18 Rectus femoris
19 Adductor brevis
20 Adductor longus
21 Vastus lateralis
22 Gracilis
23 Anterior superior iliac spine

Muscles

Many of the cutaneous landmarks used in planning gynecologic surgery comprise borders of the superficial muscles (Figures 10 and 11). In some of the reconstructive techniques discussed in this book, the muscles are the primary focus of the procedure. For the most part, however, they are structures to be retracted or transected. Nevertheless, they are helpful in identifying related anatomical structures, and therefore should be familiar to the operating surgeon.

One useful relationship is that between the rectus abdominis muscle and the epigastric vessels. When performing laparoscopy, it is best to place the lateral trocars completely laterally to these muscles to ensure avoidance of epigastric vessels. This procedure facilitates surgery also by keeping the surgical instruments as far apart as possible. It is this relationship with the epigastrics that makes the rectus abdominis muscle an ideal vascular pedicle flap for reconstructive procedures. The gracilis muscle is also a suitable pedicle flap, but because it is more variable, the rectus is preferred for perineal reconstruction.

The muscles of the abdominal cavity are sometimes involved in either the disease process or surgical procedures in gynecologic oncology. However, they do serve as borders for lymph node dissections. For example, the middle of the psoas muscle marks the lateral extent of the pelvic lymphadenectomy and the internal obturator muscle does the same for the obturator space lymphadenectomy. The muscles of the proximal lower extremity are similarly used as landmarks in inguinofemoral dissection. During a scalene node biopsy, dissection is carried to the surface of the scalenus anterior muscle between the sternocleidomastoid and the trapezius muscles (Figures 11 and 12).

Bony and cutaneous landmarks

Bony and cutaneous landmarks are sometimes overlooked by junior surgeons in their eagerness to enter the abdomen (see Figure 11). However, more experienced surgical oncologists will recognize their value in planning successful gynecologic oncology procedures. For instance, gaining central venous access always begins with determination of the location of the distal third of the clavicle or the heads of the sternocleidomastoid muscle. Vascular access may also be achieved through a cephalic vein cut-down. This vein is identified by the cutaneous border of the deltoid and pectoralis major muscles (Mohrenheim’s space). These same landmarks are also useful in initiating a scalene node biopsy. An inguinal node dissection may be performed through different incisions provided that the operator recognizes the relationship of the nodes to the inguinal ligament. Tube thoracotomy and thoracocentesis require recognition of the location of the inferior scapula at the seventh and eighth rib. Finally, although the patient’s soft tissue dimensions are important, the truly limiting factor for most is the bony confine of the operative field. For instance, a large patient may have a wide and shallow pelvis, making her an acceptable candidate for a radical hysterectomy. This may be determined before the incision by noting the distance between the anterior iliac crests in relation to the distance from the crest to the ischial tubercle. Similarly, for vaginal procedures, emphasis should be placed on the distance between the ischial tubercles and the angle of the pubic arch. The best way to assess the patient preoperatively is by recognizing the significance of the bony and cutaneous landmarks of the operative field.

References

Amreich I (1958) Zusammenhänge zwischen normaler und chirurgischer Anatomic des Beckenbindegewebes der Frau. *Klin Med* **13**:443.

Bristow RE, Tomacruz RS, Armstrong DK, et al. (2002) Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol* **20**(5):1248–59.

Burghardt E, Girardi F, Lahoussen M, et al. (1991) Patterns of pelvic and para-aortic lymph node involvement in ovarian cancer. *Gynecol Oncol* **40**(2):103–6.

Lee Anne MR, Agur AMR (1999) *Grant’s Atlas of Anatomy*. Philadelphia: Lippincott Williams & Wilkins.

Lichtenegger W, Sehouli J, Buchmann E, et al. (1998) Operative results after primary and secondary debulking-operations in advanced ovarian cancer (AOC). *J Obstet Gynaecol Res* **24**(6):447–51.

Netter FH, (2003) *Atlas of Human Anatomy*, Icon Learning Systems: Whitehead, UK.

Nguyen HN, Averette HE, Hoskins W, et al. (1993) National Survey of Ovarian Carcinoma: V. The impact of physician’s specialty on patient’s survival. *Cancer* **72**:3663–70.

Pernkopf E (1943) *Topographische Anatomie des Menschen*, 2nd edn. Berlin: Urban & Schwarzenberg. AT Krouse IT ided
Possover M, Krause N, Drahonovsky J, (1998) Left-sided suprarenal retrocrural para-aortic lymphadenectomy in advanced cervical cancer by laparoscopy Gynecol Oncol **71** (2):219–22.
Richter K (1985) Spezielle Gynäkologie 1. In: Ober KG, Thomsen K, eds. *Gynäkologie und Gerburtshilfe*, Vol. III/1, 2nd edn. Stuttgart: Thieme.
Richter K, Frick H (1985) Die Anatomie des Fascia pelvis visceralis aus didaktischer Sicht. *Geburtshilfe Frauenheilkd* **45**:275.

3
Tumor markers

Usha Menon
Ian J Jacobs

Introduction

Since the description of Bence-Jones proteins well over a century ago, a variety of substances have been investigated as potential tumor markers. The advances in molecular biology continually add to the ever-expanding armamentarium. However, the term *tumor marker* remains ill-defined. Broadly, it can be taken to mean any change that indicates the presence of cancer. With the study of the human 'proteome' gaining momentum, evidence is rapidly accumulating to show that global non-directed screening strategies can produce novel tumor markers to complement those previously identified by candidate gene or antibody-based approaches. Currently in clinical practice, tumor markers are usually biological substances detectable in the circulation that are produced by or in response to malignant tumors. The focus of this chapter is limited to such markers that are detectable in the blood and are clinically relevant to female genital tract malignancies.

Tumor markers can be broadly classified into tumor-specific antigens and tumor-associated antigens. The idiotypes of immunoglobulins of B-cell tumors and certain neoantigens of virus-induced tumors are two examples of strictly tumor-specific antigens. The vast majority of tumor markers are in reality tumor-associated antigens. In many cases, they were initially described as highly tumor-specific but subsequent studies have revealed their presence in multiple cancers and in normal adult or fetal tissues. On the basis of size, tumor-associated antigens can be divided into low-molecular-weight tumour markers (approximately <1000 daltons) and macromolecular tumor antigens (Suresh 1996). The former includes some nucleosides, lipid-associated sialic acid, polyamines and other metabolites. However, it is the macromolecular tumor markers that form the largest subgroup and have been most useful in the clinical management of cancer. They are either enzymes, hormones, receptors, growth factors, biological response modifiers or glycoconjugates.

Ideally, tumor markers should be tumor-specific, should be produced in sufficient amounts to allow detection of minimal disease and should quantitatively reflect tumor burden. This would enable their use in screening, diagnosis, monitoring response to therapy and detecting recurrence during follow-up. For each use, the value of the marker depends heavily on two parameters—sensitivity and specificity. These must be well-established with regard to the intended clinical use of the marker before it is adopted into routine practice.

Although, there has been a large expansion in the number of proposed tumor markers investigated in the last few years, very few fulfill all of the above criteria, with the main limitation being lack of specificity. The result is that relatively few tumor markers are currently used clinically in gynecologic oncology and use is limited to monitoring response and follow-up, albeit with a few exceptions.

Ovarian and fallopian tube cancers

Epithelial ovarian cancers represent the bulk of the ovarian malignancies and numerous serum tumor markers have been investigated in the context of screening, prognosis and monitoring of response and recurrence. The best known among them is cancer antigen 125 (CA125).

Cancer antigen 125

Cancer antigen 125 (CA125) is an antigenic determinant on a high-molecular-weight glycoprotein recognized by the murine monoclonal antibody OC125 which was raised using an ovarian cancer cell line as an immunogen (Bast et al. 1981). It is expressed by amnion and celomic epithelia during fetal development. In the adult, it is found in structures derived from celomic epithelia (the mesothelial cells of the pleura, pericardium and peritoneum) and in tubal, endometrial and endocervical epithelia. Curiously, the surface epithelia of normal fetal and adult ovaries do not express the determinant, except in inclusion cysts, areas of metaplasia and papillary excrescence (Kabawat et al. 1983). More recently, expression has been identified outside the female genital tract in epithelial cells of the lung, breast, conjunctiva and glandular epithelia of the prostate gland (Nap 1998).
CA125 is still poorly characterized. Molecular analysis of the CA125 antigen has identified a mucin-type glycoprotein which is highly glycosylated with the protein moiety rich in serine, threonine and pro-line (Lloyd et al. 1997). After cross-inhibition experiments with 26 different monoclonal antibodies, it was concluded that the CA125 antigen carries two major antigenic domains classified as: A, the domain-binding monoclonal antibody OC125; and B, a domain-binding monoclonal antibody M11 (Nustad et al. 1996). Immunoassays for quantitation of serum CA125 levels are now usually based on a heterologous assay (CA125 II) with two different monoclonal antibodies (M11 and OC125), replacing the original homologous assay done with monoclonal antibody OC125 alone. The CA125 II assay is sensitive and reliable for measuring serum CA125, and fully retains the cut-off values of 35 and 65 units/mL that were defined with the original CA125 immunoradiometric assay (Kenemans et al. 1993).
The serum value of 35 U/mL, representing 1% of healthy female donors, is widely accepted as the upper limit of normal (Bast et al. 1983). It should be noted that this is an arbitrary cut-off which may not be ideal for some applications of CA125. For example, in postmenopausal women or in patients after hysterectomy CA125 levels tend to be lower than in the general population and lower cut-offs may be more appropriate; 20 U/mL and 26 U/mL have been suggested (Alagoz et al. 1994, Bon et al. 1996). Approximately 83% of patients with epithelial ovarian cancer will have CA125 levels >35 U/mL (Bast et al. 1983, Canney et al. 1984). In patients with stage I disease, 50% have elevated levels while raised levels are found in >90% of the women with more advanced stages (Fritsche and Bast 1998). Lower incidences of CA125 elevation are found in mucinous, clear cell and borderline tumors (Vergote et al. 1987, Jacobs and Bast 1989, Tamakoshi et al. 1996). Elevation of serum CA125 may also be associated with other malignancies (pancreatic, breast, colon, bladder, liver, lung), as well as benign disease (diverticulitis, uterine fibroids, endometriosis, benign ovarian cysts, tuboovarian abscess, hyperstimulation syndrome, ectopic pregnancy), and physiological conditions (pregnancy and menstruation) (Meden and Fattahi-Meibodi 1998, Sjovall et al. 2002) (Figure 1). Many of these non-malignant conditions are not found in postmenopausal women, thereby improving the diagnostic accuracy of an elevated level in this population.

Screening

The role of CA125 in screening for early-stage ovarian cancer continues to be investigated. Like ultrasound, CA125 does not have sufficient sensitivity or specificity to be a suitable screening test when used in isolation. However, there is good evidence that a multimodal strategy combining CA125 with pelvic ultrasound in postmenopausal women can achieve encouraging specificity (99.9%), positive predictive value (26.8%) and sensitivity (78.6%) (Jacobs et al. 1993, 1996). There is preliminary evidence that screening using such a strategy may impact on ovarian cancer survival rates. Median survival was significantly increased in women with ovarian cancer in the screened group (72.9 months) when compared to the control group (41.8 months) in a randomized control trial (Jacobs et al. 1999). Improvements to the sensitivity of CA125 in screening have been achieved by the development of an algorithm (Risk of Ovarian Cancer [ROC] Algorithm) that incorporates age-related incidence of ovarian cancer, the absolute CA125 level and the CA125 profile with time (Skates and Jacobs 2001, Skates et al. 2003). This approach forms part of the multimodal screening strategy in the recently completed pilot randomied control trial of ovarian cancer screening at Bart's London (personal communication) and is part of the ongoing UK Collaborative Trial of Ovarian Cancer Screening (www.ukctocs.org.uk) (Figure 2). The ROC algorithm is also being evaluated

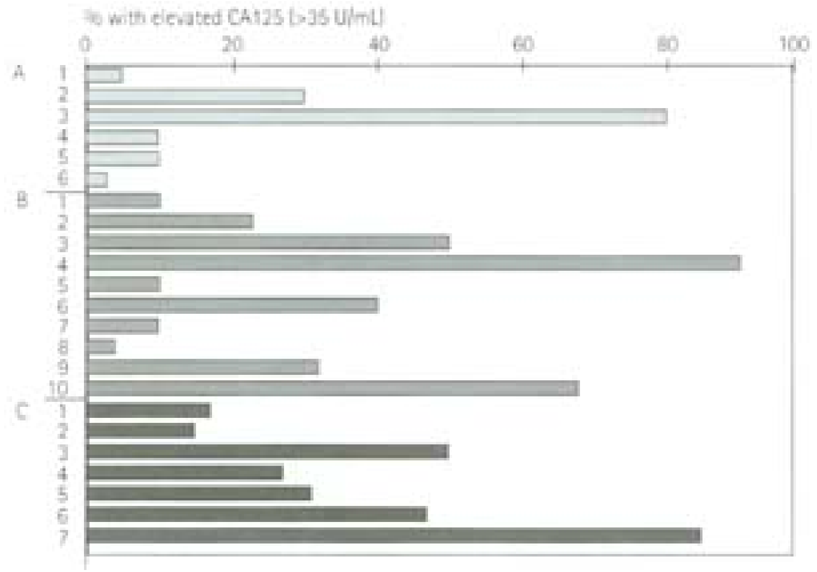

Figure 1

Causes of elevated serum levels of CA125. A, healthy: 1 premenopausal, 2 menstruation, 3 1st trimester of pregnancy, 4 2nd trimester, 5 3rd trimester, 6 postmenopausal. B, benign disease: 1 endometriosis grade 1, 2 grade II, 3 grade III, 4 grade IV, 5 benign cysts, 6 acute pelvic inflammatory disease, 7 fibroids, 8 chronic pancreatitis, 9 acute pancreatitis, 10 cirrhosis. C, malignant disease: 1 breast, 2 colon, 3 pancreas, 4 lung, 5 stomach, 6 liver, 7 ovary.

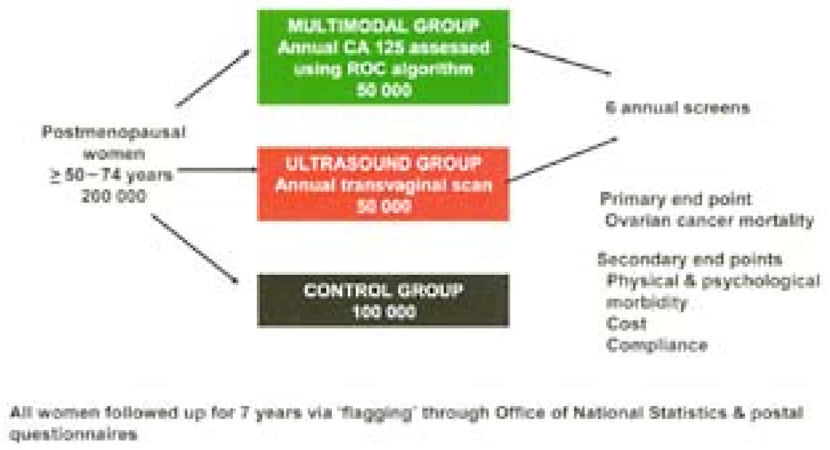

Figure 2 UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS)

prospectively in a pilot ovarian cancer screening trial in ‘high-risk’ women under the auspices of the Cancer Genetics Network in the United States.

In women with strong evidence of a hereditary predisposition to ovarian cancer, screening from the age of 35 is frequently advocated (Burke et al. 1997). This management has yet to be validated scientifically and can be problematic since this population often includes premenopausal women who are more likely than the postmenopausal population to have false positive CA125 or ultrasound abnormalities. There is a paucity of data in this population and the studies reported use a variety of screening protocols and criteria for interpreting the test results (Menon and Jacobs 2002). Only three studies have reported on interval cancers, which presented between 2 to 24 months following the last screen (Bourne et al. 1994, Dorum et al. 1999, Karlan et al. 1999). Multifocal peritoneal serous papillary carcinoma may be a phenotypic variant of familial ovarian cancer and screening strategies using ultrasonography and CA125 testing are not reliable in detecting this disease (Schorge et al. 1998, Karlan et al. 1999). Women in the high-risk population who request screening should be counseled about the current lack of evidence for the efficacy of both CA125 and ultrasound screening and the associated false-positive rates. Many still opt for screening despite understanding the risks and limitations. The other option for these women is risk-reducing salpingo-oopherectomy after completion of their families (Kauff et al. 2002, Rebbeck et al. 2002).

Differential diagnosis of an adnexal mass

Serum CA125 is of value in the differential diagnosis of benign and malignant adnexal masses, particularly in postmenopausal women. In 1986, Einhorn et al. measured CA125 preoperatively in women undergoing diagnostic laparotomy for adnexal masses (Einhorn et al. 1986). Using an upper limit of 35 U/mL, serum CA125 was found to have a sensitivity of 78%, specificity of 95% and positive predictive value of 82%. Since then, numerous tumor markers have been assessed with the view to improving preoperative diagnosis of benign from malignant pelvic masses. However, the additional discriminative value of these new markers in comparison to CA125 has been minor and they remain experimental. None are used routinely in clinical practice. Jacobs et al. (1990) combined serum CA125 values with ultrasound scan results and menopausal status to calculate a risk of malignancy index (RMI) (Jacobs et al. 1990). Patients with an elevated RMI score had, on average, 42 times the background risk of cancer (Jacobs et al. 1990). The RMI with refinements has subsequently been validated prospectively and retrospectively in both specialized and non-specialized gynecological departments (Davies et al. 1993, Tingulstad et al. 1996, Morgante et al. 1999, Aslam et al. 2000, Manjunath et al. 2001, Andersen et al. 2003, Ma et al. 2003). Although the method has limitations in borderline ovarian tumors, stage I invasive cancers, and non-epithelial tumors, it is simple and can be easily applied in the primary evaluation of patients with adnexal masses. It could provide a rationale for selection of patients for referral to specialized gynecological oncology centers (Timmerman et al. 1999, Tingulstad et al. 1999).

Prognosis

In ovarian malignancy, preoperative serum CA125 levels are related to histology, stage, grade and tumor load. However, the role of preoperative CA125 as a primary prognostic predictor is unclear. While some studies did not find preoperative CA125 to be an independent prognostic factor (Makar et al. 1992, Scholl et al. 1994, Venesmaa et al. 1994), others reported that it could identify poor prognostic subgroups, independent of stage (Parker et al. 1994, Nagele et al. 1995). Recent reports indicate that CA125 level is a weak predictor of optimal cytoreductive surgery in patients with advanced epithelial ovarian cancer (Memarzadeh et al. 2003). The current consensus is that the CA125 level should not be used as a primary predictor of the outcome of cytoreductive surgery but should be viewed in the context of all other preoperative features.

Postoperative CA125 levels and measurements taken during chemotherapy have been found to be significant prognostic indicators. It is important to state here that in the immediate postoperative period, CA125 levels can be elevated as a result of abdominal surgery (Yedema et al. 1993a) and measurements should be postponed for at least 4 weeks. With a half-life of 6 days, CA125 may take many weeks to return to normal. Residual disease should be suspected if levels plateau above the upper limit of normal or rise. Postoperative CA125 levels >35 U/mL in women with no residual disease and >65 U/mL in those with residual disease have been reported as independent prognostic factors (Makar et al. 1992). Several studies have investigated CA125 as a prognostic tool during initial chemotherapy. Initial small studies suggested that either serum CA125 half-life (van der Burg et al. 1988, Yedema et al. 1993b, Gadducci et al. 1995, Rosman et al. 1994) or regression pattern (Buller et al. 1996) or levels after one, two or three courses of chemotherapy (Lavin et al. 1987, Sevelda et al. 1989, Makar et al. 1993b, Gadducci et al. 1995) could be used to divide patients into better or worse prognostic groups. However, the prognostic information gained from CA125 alone is not sufficiently accurate to manage individual patients during chemotherapy (Peters-Engl et al. 1999, Meyer and Rustin 2000). At relapse, histologic type and serum CA125 level were found to be independent prognostic factors for survival (Makar et al. 1993a).

Monitoring response to treatment

Serum CA125 levels reflect progression or regression of disease in >90% of patients with ovarian cancer who have elevated preoperative levels (Bast et al. 1983, Hawkins et al. 1989b). This has led to wide application of CA125 measurements in monitoring response to chemotherapy and clinical course of the disease. From early studies on CA125 levels prior to second-look laparotomy, it is well established that the accuracy of an elevated CA125 is limited to 62–88% and values <35 U/mL do not exclude active disease (Jacobs and Bast 1989, Fioretti et al. 1992, Gallion et al. 1992). Thus, the general consensus that absolute values of CA125 should not be used as the sole criterion to determine clinical response and evaluate chemotherapeutic efficacy (Morgan et al. 1995).

With time, the pattern of CA125 may provide more useful information than an arbitrary cut-off level in the detection of residual tumor. Several definitions have been proposed: serum CA125 half-life of 20 days (Hawkins et al. 1989a), levels prior to the third course of chemotherapy (Payers et al. 1993, Makar et al. 1993b, Gadducci et al. 1995) but only the mathematical definition using strict CA125 criteria to evaluate

response has been validated (Rustin et al. 1996b). Definitions were derived from analysis of 277 patients in the North Thames Ovary Trial 3. Response to a specific treatment was defined as a 50% decrease in CA125 after two samples, confirmed by a fourth sample (50% response), or a serial decrease over three samples of greater than 75% (75% response). The final sample had to be at least 28 days after the previous sample (Rustin et al. 1996a). The definition was shown to reliably define response in 254 patients in the North Thames Ovary Trial 4 and 458 patients in the Gynaecologic Oncology Group protocol 97 receiving first-line chemotherapy (Rustin et al. 1996b). Subsequently, these CA125 response definitions have been validated in a large number of trials (Rustin et al. 1997, 2000, Bridgewater et al. 1999). The earlier concerns that CA125 levels may prove unreliable when specific drugs, such as paclitaxel, are used, has been proven unfounded (Bridgewater et al. 1999).
For the individual patient, caution is needed as the CA125 levels can undergo random fluctuations. The false-positive rate of a CA125 response is 3%, so radiological reassessment is probably not warranted. False-negative rates are however higher, in the region of 20%. This implies that stopping treatment based on CA125 response alone may result in under treatment and it may be best to continue treatment until there is progression based on radiological, clinical or CA125 criteria (Meyer and Rustin 2000).

Detecting relapse

Among patients with elevated antigen levels at diagnosis, relapse is often preceded by an elevation of serum CA125. A median lead time prior to clinical progression of 63–99 days was demonstrated between marker detection of disease progression and clinically apparent progressive disease (Cruickshank et al. 1991, Rustin et al. 1996a). However, the value of routinely measuring CA125 during follow-up is uncertain and practice varies. Any lead time gained depends ultimately on a patient’s remaining therapeutic options. It must be remembered that relapse after initial chemotherapy is usually incurable and any theoretical advantage must be balanced against anxiety, regular venepuncture and loss of treatment-free time as a result of such monitoring. The impact on survival and quality of life of therapeutic intervention based on pre-clinical relapse based on CA125 levels is currently being assessed in a UK multicenter randomized controlled Medical Research Council/European Organisation for Research and Treatment of Cancer (MRC/EORTC) trial. Until the results of this trial are known, the consensus is that CA125 should not be routinely monitored and its measurement should be reserved as an aid to diagnosis of relapse when clinically suspected (Meyer and Rustin 2000). There are various CA125 criteria used to define relapse. In the trial, it is defined as a confirmed rise of serum CA125 levels to more than twice the upper limit of normal. This has been shown to predict tumor relapse with a sensitivity of 84% and a false-positive rate of <2% (Rustin et al. 1996a).

Combination with other markers

Tumor-associated antigens other than CA125, such as CA19.9, CA15.3 and CA72.4, initially identified in gastrointestinal or breast malignancies, have also been detected in tissue and serum samples from patients with ovarian carcinoma. In particular, CA19.9 and CA72.4 are good supplements to CA125 in mucinous ovarian cancer which often fails to express CA125 (Stenman et al. 1995, Engelen et al. 2000). In patients with non-mucinous tumors, the addition of other serum markers to CA125 sometimes improves the diagnostic sensitivity but in general the effect is small (de Bruijn et al. 1997). Macophage colony-stimulating factor (M-CSF) and inhibin show promise of becoming useful supplements to CA125 in ovarian cancer in general. Serum CA125 correlates with the clinical course of disease better than the other antigens, and in patients with positive CA125 assay at diagnosis the concomitant evaluation of CA19.9 or CA72.4 or CA15.3 does not offer any additional benefit for monitoring ovarian carcinoma. Conversely, the serial measurements of these other antigens may represent an interesting biochemical tool for the management of patients with negative CA125 assay. Table 1 summarizes the current role of CA125 as a tumor marker in ovarian malignancy.

Carcinoembryonic antigen

Carcinoembryonic antigen (CEA) was detected in 1965 with heterosera from rabbits immunized with a colon carcinoma (Gold and Freedman 1965). It is an oncofetal antigen found in small amounts in adult colon. Elevated levels are associated with colon and pancreatic carcinoma. Levels are also raised in benign diseases of the liver, gastrointestinal tract and lung, and in smokers. In tissue studies on ovarian malignancies, it is expressed in most endometroid and Brenner tumors and in areas of intestinal differentiation in mucinous tumors. Unlike CA125, it is not expressed in normal and inflammatory conditions of the adnexa. Serum CEA levels are elevated in 25–50% of women

Table 1 Summary of the role of current tumor markers in ovarian cancer (2004)

Ovarian cancers	*Screening*	*Differential diagnosis*	*Prognostic indicator*	*Monitoring response to treatment*	*Detection of recurrence*
Epithelial cancers	CA125 General population research trials High-risk population screening with CA125 and ultrasound widely advocated but not yet validated	CA125 Significant contribution, especially in postmenopausal women As part of the risk of malignancy index a sensitivity of 70–85 % with a specificity of 96–97% CA19.9 and CA72.4 are good supplements to CA125 in mutinous ovarian cancer CEA *nonspecific assays that recognize all molecular forms of inhibin *Kallikreins *LPA *protein signature patterns *prostasin *osteopontin	CA125 Preoperative levels: conflicting evidence Should be viewed in the context of all other results Postsurgery levels: independent prognostic indicator Residual disease should be suspected if levels plateau above the upper limit of normal or rise during chemotherapy Various criteria can be used to divide patients into better or worse prognostic groups However, the prognostic information gained from CA125 alone is not sufficiently accurate to manage individual patients during chemotherapy *M-CSF *IL-6 *TPS *Kallikreins	CA125 Reflects clinical course in >90% of positive Serial values should be used. Numerous criteria have been suggested—only criteria validated are those by Rustin et al.	CA125 Among patients with elevated antigen levels at diagnosis, relapse is often preceded by an elevation of serum with a median lead-time of 63–99 days Impact on survival and quality of life of therapeutic intervention based on CA1 25 levels is currently being assessed in a MRC/EORTC trial. Until the results are known, the consensus is that CA125 should not be routinely monitored and its measurement should be reserved as an aid to diagnosis of relapse when clinically suspected *TPS *Kallikreins

Ovarian cancers	*Screening*	*Differential diagnosis*	*Prognostic indiutor*	*Monitoring response to treatment*	*Detection of recurrence*
Germ cell tumors		AFP: tumors with yolk sac elements hCG: tumors with chorionic elements *serum M-CSF for dysgerminomas		AFP: tumors with yolk sac elements hCG: tumors with chorionic elements	AFP: tumors with yolk sac elements hCG: tumors with chorionic elements
Sex cord stromal tumors		Inhibin B Estradiol in granulosa tumors			Inhibin B Estradiol in granulosa tumors

Further discussion and references are to be found in the accompanying text.
*Potential role. Not used in routine clinical practice.
CEA, carcinoembryonic antigen; CA 125, cancer antigen 125; LPA, lysophosphatidic acid; AFP, alpha-fetoprotein; hCG, human chorionic gonadotrophin;
M-CSF, macrophage colony-stimulating factor.

with ovarian cancer. While there is some correlation with disease state, this is less satisfactory than that obtained with the other described markers (Onsrud 1991, Roman et al. 1998).

Alpha-fetoprotein

Alpha-fetoprotein (AFP) is an oncofetal glycoprotein produced by the fetal yolk sac, liver and upper gastrointestinal tract. Elevated levels are seen in pregnancy and in benign liver disease. Serum levels are raised in most patients with liver tumors and in some with gastric, pancreatic, colon and bronchogenic malignancies (Onsrud 1991). Levels are elevated in endodermal sinus tumors and a proportion of immature teratomas and dysgerminomas (Kawai et al. 1992). In women with endodermal sinus tumors and embryonal carcinomas, AFP is a reliable marker for monitoring response to therapy and detecting recurrences early (Chow et al. 1996, Zalel et al. 1996). It accurately predicts the presence of yolk sac elements in mixed germ cell tumors (Olt et al. 1990).

Human chorionic gonadotrophin

Human chorionic gonadotrophin (hCG) is synthesized in pregnancy by the syncytiotrophoblast. It is a glyco-protein hormone made up of two dissimilar noncovalently linked subunits termed a and β. Tumor production of hCG is accompanied by varying degrees of release of the free subunits into the circulation. In patients with gestational trophoblastic disease (hydatiform mole, invasive mole and choriocarcinoma) hCG is elevated in virtually all cases and serves as an ideal tumor marker. There is close correlation between hCG levels and tumor burden, and clinical management decisions are based almost solely on the level of the marker. This hormone can also be found in the serum of patients with non-trophoblastic cancers. Although, gynecologic malignancies are prominent in this group, the sensitivity is below that of other markers in current use except in germ cell tumors with a chorionic component (Mann and Hoermann 1993). In recent years, urinary gonadotrophin fragment (UGF), which is a mixture of human chorionic gonadotrophin, free β-subunit and its fragments, has been investigated. Initial studies reported elevated levels in 56–84% of ovarian cancer patients (Kinugasa et al. 1995, Cole et al. 1996). However, more recent reports suggest that CA125 as a single test discriminates malignant from benign ovarian disease better than UGP (Schutter et al. 1999). More recently, serum βhCG has been reported as an independent prognostic factor in epithelial ovarian cancer with a prognostic value similar to that of grade and stage (Vartiainen et al. 2001).

Inhibin

Inhibins and activins are structurally related dimeric proteins, which were first isolated from ovarian follicular fluid on the basis of their ability to modulate pituitary follicle-stimulating hormone secretion. They are members of a larger group of diverse proteins, the transforming growth factor-β superfamily that are involved in cell growth and differentiation. Inhibin is a heterodimeric glycoprotein composed of a common α-subunit and one of two β-subunits, resulting in inhibin A(αβA) and inhibin B(αβB), for which specific immunoassays are now available. In addition, the serum also contains immunoreactive forms of the α-subunit which are not attached to the β-subunit, the most abundant of which is believed to be pro-αC and pro-αN-αC. These precursor forms of inhibin are measured using the pro-αC assay. The original Monash assay detected immunoreactive inhibin that included a range of inhibin-related peptides in addition to biologically active inhibin dimers.

In 1989, Lappohn et al. studied nine women with granulosa cell tumor and found serum immunoreactive inhibin concentrations to be elevated (Lappohn et al. 1992). Numerous studies have confirmed serum inhibin elevation in ovarian sex cord/stromal tumors and established their role in the differential diagnosis and surveillance of these malignancies (Jobling et al. 1994, Cooke et al. 1995, Boggess et al. 1997). It is easier to interpret assay results in women who have had bilateral oophorectomy or are postmenopausal. Interpretation of results in women with residual inhibin secretion is complicated by the variations in inhibin levels during the normal cycle. In such situations, it is best to measure levels during menstruation, when secretion of immunoreactive inhibin is at its lowest. Bioactive dimeric inhibin A and B are the major molecular forms detected, with the latter being produced by all granulosa tumors (Yamashita et al. 1997, Petraglia et al. 1998). Since these tumors are relatively rare, serial monitoring is probably best done nationally or regionally by a tumor marker laboratory able to maintain the necessary quality control

(Groome and Evans 2000). In recent years, inhibins have been investigated together with other monoclonal antibodies (those directed against CD99, müllerian-inhibiting substance, relaxin-like factor, melan A and calretinin) to aid immunocytochemical diagnosis of ovarian sex cord/stromal tumors. Of all investigated, anti-alpha-inhibin appears to be of most diagnostic value. It must, however, be stressed that these antibodies should always be used as part of a larger panel and not in isolation (McCluggage 2000). In epithelial ovarian cancers, the role of the inhibin peptides remains to be defined. Serum inhibin levels, measured using the initial non-specific Monash assay, are elevated in 25–90% of women with epithelial ovarian cancers (Blaakaer et al. 1993, Healy et al. 1993, Phocas et al. 1996) with mucinous tumors most likely to be associated with raised levels (Cooke et al. 1995, Burger et al. 1996). The epithelial cancers, unlike granulosa cell tumors make little dimeric inhibin A. Best results are obtained using less specific assays that recognize all molecular forms of inhibin, including bioactive dimeric forms and free α-subunits (Lambert-Messerlian et al. 1997, Burger et al. 1998, Menon et al. 2000). A new α-subunit monoclonal antibody-based ELISA that is amenable to wider clinical use is being developed as a diagnostic test (Robertson et al. 2004). At 95% specificity, the new ELISA detected 83% mucinous cancers and 37–54% of other epithelial ovarian cancers. It was not able to differentiate between benign and malignant mucinous types, similar to that seen previously with the other assays (Robertson et al. 2002). The enhanced detection of mucinous tumors leads to increased sensitivity for detection of epithelial ovarian cancer when combined with CA125 (Lambert-Messerlian et al. 1997, Robertson et al. 1999).

Activin is a dimer of the two β-subunits of inhibin and exists as activin A(βAβA), activin B(βBβB) and activin AB(βAβB). Serum activin A has been found to be significantly elevated in epithelial ovarian cancers (Welt et al. 1997, Petraglia et al. 1998, Menon et al. 2000) with highest levels detected in undifferentiated tumors. Preliminary data suggest that there is poor correlation of activin with clinical course of disease (Petraglia et al. 1998).

In conclusion, functional inhibin is secreted by all granulosa cell tumors of the ovary studied and is superior to estradiol as a tumor marker to determine response to therapy and predict recurrence (Stuart and Dawson 2003). However, further study using the new inhibin assays is needed before its role in the clinical management of epithelial ovarian cancer can be defined.

Estrogen/androgen

Estrogen secretion is associated with granulosa cell tumors. Since the assessment of malignant potential of granulosa cell tumors is difficult on histological grounds, serial estradiol levels are of significant value in monitoring these patients after surgery. Androgen levels are elevated in women with Sertoli-Leydig cell tumors.

Lysophosphatidic acid

Lysophosphatidic acid (LPA) is a bioactive phospholipid with mitogenic and growth factor-like activities that stimulates the proliferation of cancer cells. LPA has been implicated as a growth factor present in ascites of ovarian cancer patients (Xu et al. 1995); it increases cell proliferation, cell survival, resistance to cisplatin, and production of vascular endothelial growth factor in ovarian cancer cells but not in normal ovarian surface epithelial cells (Fang et al. 2000). LPA levels were significantly higher in ascites from ovarian cancer patients than in malignant effusions from other cancer patients suggesting a role for LPA-like lipids in the peritoneal spread of ovarian cancer (Westermann et al. 1998). Elevated plasma LPA levels were detected in 9 of 10 patients with stage I ovarian cancer, all 24 patients with stage II, III and IV ovarian cancer, and all 14 patients with recurrent ovarian cancer. In comparison, only 28 of 47 had elevated CA125 levels, including 2 of 9 patients with stage I disease. LPA levels were also elevated in patients with other gynecologic cancers. Raised plasma LPA levels were detected in 5 of 48 controls and 4 of 17 patients with benign gynecologic diseases and in no women with breast cancer or leukemia (Xu et al. 1998). Using a new highly specific, sensitive and reproducible assay, Bast and coworkers demonstrated elevated levels of LPA in more than 90% of ovarian cancer patients at stage I or II, less than 50% having elevated levels of CA125 levels (Bast et al. 1998). Plasma LPA may represent a potential biomarker for ovarian and other gynecologic cancers.

Cytokines

Cytokines are soluble mediator substances produced by cells that exercise a specific effect on other target cells. They have assumed increasing importance in tumor biology. It is reasonable to assume that in malignancy, they may serve to promote the unregulated growth of tumor cells and metastasis. It is also likely that cytokines produced by tumors will modulate immune responses that favor tumor progression (Nash et al. 1999). It is clear that cytokines do not fulfill the classic criteria for tumor markers. They are invariably produced by non-malignant tissue, may be elevated in a number of pathological conditions, are not specific for one cell type and in the malignant scenario are often produced by the surrounding tissue in response to the tumor rather then by the tumor itself. Despite this, measurements of cytokines and their soluble receptors may provide valuable clinical information regarding prognosis and response to treatment. Most of the markers are at an early stage of evaluation and in some cases, studies have produced conflicting results. Serum interleukin 6 (IL-6) and macrophage colony-stimulating factor (M-CSF) may have a prognostic role in women with ovarian cancer.

IL-6 levels are raised in ovarian cancer patients compared to healthy controls but it does not appear to be as sensitive or as useful a marker as CA125 in either differential diagnosis or monitoring of disease (Scambia et al. 1994b, 1995, Tempfer et al. 1997). Its potential role lies in the independent negative prognostic value of a high level (Berek et al. 1991, Gastl et al. 1993, Scambia et al. 1995, Tempfer et al. 1997). One explanation is that high levels of IL-6 block apoptosis induced by cytotoxic agents or p53.

Serum M-CSF is the most important of the cytokines to be studied so far, in the context of ovarian cancers. It is produced constitutively by normal as well as neoplastic ovarian epithelium (Lidor et al. 1993). It appears to be a marker with high specificity for ovarian malignancy with elevation related to stage and independent of histologic type (Suzuki et al. 1993, 1995). Elevated serum levels were associated with poor outcome following adjustment for stage, grade and degree of surgical clearance (Price et al. 1993, Scholl et al. 1994). While M-CSF may have a role in differential diagnosis and screening (Suzuki et al. 1993, Woolas et al. 1993, van Haaften-Day et al. 2001), it is not useful in the follow-up of women with advanced ovarian cancer (Gadducci et al. 1998). Suzuki et al. (1998) have suggested that serum M-CSF may be highly sensitive and specific for malignant germ cell tumors of the ovary, especially dysgerminoma.

Cytokeratins

Cytokeratins are intermediate filaments that are part of the cytoskeleton of all epithelial cells. They are specific markers of epithelial differentiation and interestingly, they continue to be expressed by epithelial cells after malignant transformation. They play an increasingly significant role in distinguishing carcinomas metastatic to the ovary from ovarian primaries. On immunohistochemical staining, colon cancer metastatic to the ovary is cytokeratin 7 negative and cytokeratin 20 positive in the majority of cases; in contrast, most primary ovarian carcinomas are keratin 7 positive and keratin 20 negative (Cathro and Stoler 2002, Park et al. 2002, Nishizuka et al. 2003). In contrast to Cytokeratins themselves, fragments of Cytokeratins are soluble in the serum and therefore can be detected and measured with the aid of monoclonal antibodies. Those currently being studied as tumor markers in ovarian cancer are tissue polypeptide-specific antigen (TPS), a proliferation marker recognized by a monoclonal antibody raised against cytokeratin 18 and CYFRA 21–1, a soluble serum fragment of cytokeratin 19. Elevated TPS levels may add to the diagnostic value of serum CA125 in ovarian cancer (Shabana and Onsrud 1994, Sliutz et al. 1995, Harlozinska et al. 1997, Padungsutt et al. 2000). Determination of serum TPS improved the prognostic accuracy of CA125 levels after surgery (Senapad et al. 2000, Van Dalen et al. 2000) and improved detection of recurrent disease, especially in those patients who had elevated TPS serum levels prior to therapy (Sliutz et al. 1995). The potential usefulness of CYFRA 21–1 as a tumor marker for ovarian malignancy needs to be explored further before any firm conclusions can be drawn (Hasholzner et al. 1994, Mazurek et al. 1998, Tempfer et al. 1998b, Gadducci et al. 2001).

Kallikrein

Kallikreins are a subgroup of serine proteases with diverse physiological functions. The human kallikrein gene family has now been fully characterized and includes 15 members located on chromosome 19q13.4. Two members of the human kallikrein gene family, prostate-specific antigen and human kallikrein 2, have already found important clinical application as prostate cancer biomarkers. Strong experimental evidence now supports a link between kallikreins and ovarian cancer. Since the first report describing significant elevations of human kallikrien 6 (HK6) in serum of ovarian cancer patients (Diamandis et al. 2000), numerous other members of this serine protease family have been reported to have potential as serological markers for ovarian cancer diagnosis, prognosis and monitoring. Those of interest are HK5 (Yousef et al. 2003), HK6 (Diamandis et al. 2000, 2003), HK8 (Magklara et al. 2001, Kishi et al. 2003), HK10 (Luo et al. 2001, 2003) HK11 (Diamandis et al. 2002) and HK13 (Scorilas et al. 2004). A multiparametric kallikrein expression profile may be a useful tool when used either alone or in conjunction with existing markers.

Proteomic patterns

In the new era of proteomics, in addition to individual markers, there has been a great deal of interest in identifying global patterns of serum proteins and peptides that relate to cancer risk. Serum, by its nature, can reflect organ-confined events and the pattern, rather than its component parts, is the diagnostic. Wide ranges of techniques are now available for protein identification and characterization where high sensitivity and specificity is combined with high throughput. Surface-enhanced laser desorption ionization time-of-flight (SELDI-TOF) analysis and matrix-associated laser desorption ionization time-of-flight (MALDI-TOF) technology have the potential to identify patterns or changes in thousands of small proteins (<20 kDa). When combined with matrices that selectively absorb certain serum proteins, these approaches can globally analyze almost all small proteins in complex solutions, such as serum or plasma (Mills et al. 2001, Baak et al. 2003). Combinations of mass spectra generated by these new technologies and artificial intelligence-based informatic algorithms have been used to discover small sets of key protein values that discriminate normal from ovarian cancer patients. A preliminary study reported that using SELDI-TOF to analyze the proteomic spectra patterns generated from 50 women with and 50 without ovarian cancer, the algorithm identified a cluster pattern that, in the training set, completely segregated cancer from non-cancer. The discriminatory pattern correctly identified all 50 ovarian cancer cases in the masked set including all 18 stage I cases. Of the 66 cases of non-malignant disease, 63 were recognized as not cancer. This result yielded a sensitivity of 100% (95% CI 93%–100%), specificity of 95% (95% CI 87%–99%), and positive predictive value of 94% (95% CI 84%–99%) (Petricoin et al. 2002). Although the limitations of this study design and its analysis have been discussed in some detail in the literature (Diamandis 2002, Elwood 2002, Pearl 2002, Sorace and Zhan 2003), the implications of such proteomic spectrum analysis for the identification of novel tumor markers is huge. While further validation is needed to confirm that ovarian cancer serum protein signature patterns can be a robust biomarker approach, it is likely that in the future, the early detection of ovarian and other cancers will involve high-throughput proteomic profiling either alone or in combination with markers already in use.

Novel tumor markers

New technologies are emerging that facilitate the identification of diagnostic tumor markers. In particular, high-throughput techniques using microarray technology and proteomic screening of tumors and cell lines, has made it possible to identify overexpression of genes for secretory proteins. Prostasin, a serine protease normally secreted by the prostate gland was identified as a potential ovarian tumor marker in this manner (Mok et al. 2001). Subsequent investigation revealed that levels of serum prostasin were found to be higher in patients with ovarian cancer compared to controls with levels declining after surgery. In non-mucinous ovarian cancers, the combination of CA125 and prostasin resulted in greater sensitivity (92%) than CA125 alone (64.9%) for the same specificity (Mok et al. 2001). Osteopontin, another biomarker was similarly identified. Osteopontin expression was higher in tissue samples from patients with invasive and borderline ovarian cancer than benign tumors and normal ovaries. Plasma levels of Osteopontin were also significantly higher in patients with epithelial ovarian cancer compared to controls (Kim et al. 2002). Proteomic profiling patterns are also resulting in the identification of new biomarkers that are being investigated for use in ovarian cancer (e.g. haptoglobin-derived alpha-subunit) (Kozak et al. 2003, Ye et al. 2003).
Multiple novel serum markers are now being assessed in isolation and in various combinations in women with ovarian cancer, both in the context of screening and for assessing prognosis and monitoring disease recurrence. Although no single agent or combination has emerged as having a clear clinical advantage over CA125, except in specific tumor subtypes (germ cell tumors with yolk sac or chorionic elements and granulosa cell tumors), many of those being investigated have promising potential.

Endometrial cancers

There are no serum tumor markers with a definite role in clinical management of endometrial cancer. Serum

CA125 is raised in 10–27% of patients with endometrial carcinoma (Patsner et al. 1990, Takeshima et al. 1994, Hakala et al. 1995) with elevations noted in 60% of women with extrauterine spread compared to 15% of those with early-stage disease (Gadducci et al. 1990, Tomas et al. 1990, Cherchi et al. 1999, Kukura et al. 2003). While authors agree that raised levels reflect advanced stage and portend a poor prognosis, there is controversy as to whether this adds any information to that gained by history, physical examination, preoperative imaging and surgery (Cherchi et al. 1999, Schneider et al. 1999). CA125 rises progressively with worsening grade. It was suggested that it may have a role in post-treatment surveillance of patients with early-stage endometrial cancer. However, levels can be falsely elevated in the presence of severe radiation injury (Rose et al. 1994) and isolated recurrences in the vagina do not cause elevation (Patsner et al. 1990). Recently, there have been conflicting reports about its utility in monitoring for recurrence in the absence of other clinical findings (Cole and Nam 1989, Price et al. 1998, Cherchi et al. 1999). Other markers which have been investigated and reported as useful in prognosis are CA15.3 (Lo et al. 1997) and CA 72–4 (Hareyama et al. 1996).

Cervical cancers

Screening for cervical cancer uses exfoliative cytology and currently there are no serological markers being explored in this context. However, in assessing prognosis, monitoring response to therapy and detecting recurrence, a variety of tumor markers are being investigated (Table 2). The main among them are squamous cell carcinoma antigen (SCC), tissue polypeptide antigen (TPA), CEA and CYFRA 21–1.

Squamous cell carcinoma antigen

Squamous cell carcinoma antigen (SCC) is one of 14 subfractions of tumor antigen TA-4, which was isolated from a cervical squamous cell carcinoma (Kato 1977). Elevated serum levels were found in 57–65% of women with primary squamous cell carcinoma of the cervix (Ngan et al. 1996, Lozza et al. 1997). Release into the circulation is independent of local tissue content as high antigen concentrations are found in the cytosol of normal cervical squamous epithelia but in these cases, serum levels are always in the normal range (Crombach et al. 1989). The antigen is, however, not specific for cervical squamous cell carcinoma. Elevated serum levels are also found in other squamous cell cancers of the head and neck, esophagus, lung, vulva, vagina, and adenocarcinoma of the uterus, ovary and lung. SCC levels can also be raised in skin diseases, such as psoriasis and eczema (Duk et al. 1989b).
SCC is probably a marker of cellular differentiation of squamous cells as the incidence of elevated serum levels is higher in women with well-differentiated (78%) and moderately differentiated carcinomas (67%) than in those with poorly differentiated tumors (38%) (Crombach et al. 1989). SCC pretreatment levels correlate with stage and tumor volume, depth of cervical invasion, lymphovascular space involvement and lymph node status (Duk et al. 1996, Scambia et al. 1996, Bolger et al. 1997, Massuger et al. 1997, Gaarenstroom et al. 2000). There are conflicting reports about the independent prognostic role of pretreatment SS levels (Scambia et al. 1994a, Gaarenstroom et al. 1995, Duk et al. 1996, Ngan et al. 1996, Bolger et al. 1997, Gaarenstroom et al. 2000, Pras et al. 2002, Takeda et al. 2002).
In SCC-positive patients, serial SCC determinations correlated with the clinical course in 72% of women (Gocze et al. 1994) with levels decreasing with effective therapy (Pectasides et al. 1994). Normalization of elevated levels was associated with a complete response (Rose et al. 1993) and an elevated post-treatment serum SCC level was associated with a poor survival rate (Bonfrer et al. 1997). There has been a suggestion that the presence of elevated levels of SCC post-treatment may indicate the need for additional salvage surgery (Pras et al. 2002). In recurrent carcinoma, a raised SCC level was found in 50–71% of cases, with a lead time ranging from 0 months to 12 months (Rose et al. 1993, Lozza et al. 1997, Tempfer et al. 1998a).

Tissue polypeptide antigen

Tissue polypeptide antigen (TPA) levels are raised in 40–70% of women with squamous cell carcinoma of the cervix (Ferdeghini et al. 1994, Ngan et al. 1996, Pattaranutaporn et al. 1997). Serum levels were related to stage and grade. However, on multivariate analysis, pretreatment serum TPA levels were not predictive of survival (Gaarenstroom et al. 1995, Sproston et al. 1995, Ngan et al. 1996, Bonfrer et al. 1997). There is a recent report that suggests that combined with SCC levels, TPA may be useful in predicting recurrence (Tempfer et al. 1998a, Hung et al. 2002).

CYFRA 21–1

CYFRA 21–1 was initially found to be elevated in squamous cell carcinoma of the lung. In squamous cell carcinoma of the cervix, elevated levels are found in over 50% of patients (Tsai et al. 1996, Callet et al. 1998, Suzuki et al. 2000). Levels are related to tumor stage and size (Bonfrer et al. 1994, Callet et al. 1998, Suzuki et al. 2000), and there is a positive correlation with SCC (Kainz et al. 1995, Nasu et al. 1996, Suzuki et al. 2000). However, it is less useful than SCC in predicting prognosis or monitoring patients with cervical cancer (Tsai et al. 1996, Bonfrer et al. 1997, Gaarenstroom et al. 1997).

CA125

Serum CA125 is elevated in only 13–21% of women with squamous cell carcinoma (Gocze et al. 1994, Tomas et al. 1991). However, in cervical adenocarcinoma, it is a better tumor marker then SCC (Duk et al. 1989b). When combined with SCC, preoperative serum CA125 could be useful in estimating lymph node status and prognosis (Duk et al. 1990, Sproston et al. 1995, Takeda et al. 2002). In progressive disease, very high serum CA125, SCC and CEA levels were found in patients with adenosquamous tumor, whereas patients with adenocarcinoma demonstrated only high CA125 levels (Duk et al. 1989a). CEA levels may be raised in patients with cervical adenocarcinoma.
SCC remains the best available marker for squamous cell carcinoma of the cervix and a potential tool for monitoring the efficacy of treatment in advanced and recurrent disease. CA125 may be useful in cervical adenocarcinoma. The evidence available so far does not justify routine measurement of multiple markers.

Vulvar and vaginal cancers

Tumors of the vulva and vagina are rare and there are relatively few studies of circulating markers in these conditions. Tissue polypeptide-specific antigen (TPS) has been shown to be elevated in 80% of vulvovaginal cancers (Salman et al. 1995) while SCC levels were elevated in 43% of patients with vulvar or vaginal cancer (Nam et al. 1990). Urinary gonadotropin peptide (UGP) or urinary beta-core was elevated in 20–40% of vulvovaginal malignancies (Carter et al. 1995, Schwarz-Roeger et al. 1997). Both at initial presentation and at recurrence, there was a highly significant difference in the survival curve between those with elevated levels and those with normal levels (Carter et al. 1995). Rising UGF levels at an earlier clinic visit predicted recurrence in 4 of 7 patients (Nam et al. 1990). While the numbers are small, until larger studies become available, the data suggest that for lower genital tract cancer the measurement of UGP may be useful as a prognostic indicator.

Conclusion

The potential use of most serum tumor markers is hampered by the fact that their production is neither confined to the malignant tumor cell nor connected to the malignant phenotype. Of all those studied, hCG in gestational trophoblastic disease remains closest to the ideal tumor marker. CA125 is the most reliable serum marker for ovarian carcinoma. It has a well-established role in the differential diagnosis of adnexal masses, particularly in postmenopausal women and in monitoring response to chemotherapy and follow-up of patients with ovarian carcinoma. Its role in screening is undergoing evaluation in randomized control trials. Serum AFP and βhCG are useful in the preoperative evaluation and management of nondys-germinomatous ovarian germ cell tumors, whereas elevated serum inhibin levels can be detected in patients with granulosa cell tumors of the ovary. In endometrial carcinoma, preoperative serum CA125 levels correlate with stage and clinical outcome. There are conflicting reports about its utility in monitoring for recurrence. SCC is the most reliable serum marker for squamous cell cervical carcinoma, and in patients with this malignancy pretreatment SCC levels are related to tumor stage and tumor size. Serial SCC levels parallel response to therapy and clinical course. Serum CYFRA 21–1 seems to be less sensitive than serum SCC for squamous cell cervical carcinoma. Elevated CA125 levels can be detected in patients with cervical adeno-carcinoma.
The future of tumor marker research is being expanded due to recent technological advances in genomics and proteomics. There are numerous novel tumor markers that are being investigated either alone or in combination with standard markers in ovarian cancer screening. Many have promising prognostic

Table 2 Other potential turnor markers in endometrial cancer that are not referred to in detail in the text.

Tumor maker	*Reference*	*Finding*
CA15–3	(Lo et al. 1997)	CA15–3, CA 125, CA19.9, CEA and TPA were analyzed in 97 patients with endometrial cancer. The incidence of individual elevated tumor markers was 2 1–3 1%. Elevations of CA1 25 and CA1 5.3 were significantly associated with poor prognostic clinical factors. In multivariate analysis, CA1 5.3 was highly significant and had a larger hazard ratio then CA1 25
	(Matorras et al. 1992)	CA 125, SCC, CA 19.9 and CA 15.3 were evaluated in the follow-up of 105 patients with endometrial carcinoma. The tumor markers were of limited value for the prediction of recurrences
CA19–9	(Takeshima et al. 1990)	CA19–9 was elevated in 24% of 225 patients with primary endometrial carcinoma. Elevated CA125 levels were found in 27% and the combined assay detected in 39%. Serum levels of both CA125 and CA19–9 were significantly increased with surgical staging. The combined assay demonstrated a 72% positive rate at the time of detection of recurrence in 32 patients (66% for CA125 44% for CA19–9). In 34% of the 32 recurrent cases, elevated levels of the tumor markers were the first sign of recurrence. The use of CA19–9 in combination with CA125 may be useful in the management of endometrial carcinoma
Aminoterminal propeptide of type III procollagen	(Tomas et al. 1990)	PIIINP is an indicator of collagen metabolism. Serum levels were increased in 35% of 148 patients with endometrial carcinoma and elevated levels were more often seen in advanced (63%) than early disease (31%). In monitoring advanced endometrial disease, the authors found that it is of use when combined with CA125
Placental protein 4 (PP4)	(Ota et al. 1990)	Raised levels were detected in 48% of patients with endometrial carcinoma and 18% of patients with uterine myomata

Tumor marker	*Reference*	*Finding*
CYFRA 21–1	(Inaba et al. 1995)	Elevated in 52% of endometrial malignancies
CA72–4	(Hareyama et al. 1996)	Increased levels in 32% of 72 patients with endometrial carcinoma. Levels correlated with depth of myometrial invasion, adnexal metastasis, lymphovascular space involvement, and pelvic and para-aortic lymph node metastasis. On multivariate analysis significant correlation with adnexal metastasis
OVX1 antigen	(Xu et al. 1995)	Levels elevated in 64% of 45 patients with endometrial cancer but only in 5% of 184 healthy persons and 9% of 58 patients with endometriosis. Elevation more frequent in patients with deep myometrial invasion and poorly differentiated tumors
Soluble interleukin-2 receptor (sIL-2R)	(Ferdeghini et al. 1993)	Elevated serum levels of sIL-2R, CA 125 and SCC were detected in 52%, 11% and 14%? of 35 patients with endometrial cancer, respectively, rendering sIL-2R the most sensitive antigen for endometrial cancer among the three markers studied
Macrophage colony-stimulating factor (m-CSF)	(Hakala et al. 1995)	Elevated in 73% of 183 patients with endometrial adenocarcinoma. Levels correlated with clinical course of disease and measurement of CA125 or the aminoterminal peptide of type III procollagen levels did not further enhance accuracy

potential which will aid the development of novel treatment strategies in the future. The role of markers in monitoring therapeutic response and detecting recurrence has yet to be fully exploited.

References

Alagoz T, Buller RE, Berman M, et al. (1994) What is a normal CA125 level? *Gynecol Oncol* **53**:93–7.

Andersen ES, Knudsen A, Rix P, Johansen B (2003) Risk of malignancy index in the preoperative evaluation of patients with adnexal masses. *Gynecol Oncol* **90**:109–12.

Aslam N, Tailor A, Lawton F, et al. (2000) Prospective evaluation of three different models for the pre-operative diagnosis of ovarian cancer. *BJOG* **107**:1347–53.

Baak JP, Path FR, Hermsen MA, et al. (2003) Genomics and proteomics in cancer. *Eur J Cancer* **39**:1199–215.

Bast RC, Jr, Feeney M, Lazarus H, et al. (1981) Reactivity of a monoclonal antibody with human ovarian carcinoma. *J Clin Invest* **68**:1331–7.

Bast RC, Jr, Klug TL, St John E, et al. (1983) A radio-immunoassay using a monoclonal antibody to monitor the course of epithelial ovarian cancer. *N Engl J Med* **309**:883–7.

Bast RC, Jr, Xu FJ, Yu YH, et al. (1998) CA 125: the past and the future. *Int J Biol Markers* **13**:179–87.

Berek JS, Chung C, Kaldi K, et al. (1991) Serum inter-leukin-6 levels correlate with disease status in patients with epithelial ovarian cancer. *Am J Obstet Gynecol* **164**:1038–42 [discussion 1042–3].

Blaakaer J, Micic S, Morris ID, et al. (1993) Immuno-reactive inhibin-production in post-menopausal women with malignant epithelial ovarian tumors. *Eur J Obstet Gynecol Reprod Biol* **52**:105–10.

Boggess JF, Soules MR, Goff BA, et al. (1997) Serum inhibin and disease status in women with ovarian granulosa cell tumors. *Gynecol Oncol* **64**:64–9.

Bolger BS, Dabbas M, Lopes A, Monaghan JM (1997) Prognostic value of preoperative squamous cell carcinoma antigen level in patients surgically treated for cervical carcinoma. *Gynecol Oncol* **65**:309–13.

Bon GG, Kenemans P, Verstraeten R, et al. (1996) Serum tumor marker immunoassays in gynecologic oncology: establishment of reference values. *Am J Obstet Gynecol* **174**:107–14.

Bonfrer JM, Gaarenstroom KN, Kenter GG, et al. (1994) Prognostic significance of serum fragments of cytokeratin 19 measured by Cyfra 21–1 in cervical cancer. *Gynecol Oncol* **55**:371–5.

Bonfrer JM, Gaarenstroom KN, Korse CM, et al. (1997) Cyfra 21–1 in monitoring cervical cancer: a comparison with tissue polypeptide antigen and squamous cell carcinoma antigen. *Anticancer Res* **17**:2329–34.

Bourne TH, Campbell S, Reynolds K, et al. (1994) The potential role of serum CA 125 in an ultrasound-based screening program for familial ovarian cancer. *Gynecol Oncol* **52**:379–85.

Bridgewater JA, Nelstrop AE, Rustin GJ, et al. (1999) Comparison of standard and CA-125 response criteria in patients with epithelial ovarian cancer treated with platinum or paclitaxel. *J Clin Oncol* **17**:501–8.

Buller RE, Vasilev S, DiSaia PJ. (1996) CA 125 kinetics: a cost-effective clinical tool to evaluate clinical trial outcomes in the 1990s. *Am J Obstet Gynecol* **174**:1241–53 [discussion 1253–4].

Burger HG, Robertson DM, Cahir N, et al. (1996) Characterization of inhibin immunoreactivity in postmenopausal women with ovarian tumours. *Clin Endocrinol (Oxf)* **44**:413–18.

Burger HG, Baillie A, Drummond AE, et al. (1998) Inhibin and ovarian cancer. *J Reprod Immunol* **39**:77–87.

Burke W, Daly M, Garber J, et al. (1997) Recommendations for follow-up care of individuals with an inherited predisposition to cancer. II. BRCA1 and BRCA2. Cancer Genetics Studies Consortium. *JAMA* **277**:997–1003.

Callet N, Cohen-Solal Le Nir CC, Berthelot E, Pichon MF (1998) Cancer of the uterine cervix: sensitivity and specificity of serum Cyfra 21.1 determinations. *Eur J Gynaecol Oncol* **19**:50–6.

Canney PA, Moore M, Wilkinson PM, James RD (1984) Ovarian cancer antigen CA125: a prospective clinical assessment of its role as a tumour marker. *Br J Cancer* **50**:765–9.

Carter PG, lies RK, Neven P, et al. (1995) Measurement of urinary beta core fragment of human chorionic gonadotrophin in women with vulvovaginal malignancy and its prognostic significance. *Br J Cancer* **71**:350–3.

Cathro HP, Stoler MH (2002) Expression of cytokeratins 7 and 20 in ovarian neoplasia. *Am J Clin Pathol* **117**:944–51.

Cherchi PL, Dessole S, Ruiu GA, et al. (1999) The value of serum CA 125 and association CA 125/CA 19–9 in endometrial carcinoma. *Eur J Gynaecol Oncol* **20**:315–17.

Chow SN, Yang JH, Lin YH, et al. (1996) Malignant ovarian germ cell tumors. *Int J Gynaecol Obstet* **53**:151–8.

Cole LA, Nam JH (1989) Urinary gonadotropin fragment (UGF) measurements in the diagnosis and management of ovarian cancer. *Yale J Biol Med* **62**:367–78.
Cole LA, Tanaka A, Kim GS, et al. (1996) Beta-core fragment (beta-core/UGF/UGP), a tumor marker: a 7-year report. *Gynecol Oncol* **60**:264–70.
Cooke I, O'Brien M, Charnock FM, et al. (1995) Inhibin as a marker for ovarian cancer. *Br J Cancer* **71**:1046–50.
Crombach G, Scharl A, Vierbuchen M, et al. (1989) Detection of squamous cell carcinoma antigen in normal squamous epithelia and in squamous cell carcinomas of the uterine cervix. *Cancer* **63**:1337–42.
Cruickshank DJ, Terry PB, Fullerton WT (1991) The potential value of CA125 as a tumour marker in small volume, non-evaluable epithelial ovarian cancer. *Int J Biol Markers* **6**:247–52.
Davies AP, Jacobs I, Woolas R, Fish A, Oram D (1993) The adnexal mass: benign or malignant? Evaluation of a risk of malignancy index. *Br J Obstet Gynaecol* **100**:927–31.
de Bruijn HW, van der Zee AG, Aalders JG. (1997) The value of cancer antigen 125 (CA 125) during treatment and follow-up of patients with ovarian cancer. *Curr Opin Obstet Gynecol* **9**:8–13.
Diamandis EP (2002) Proteomic patterns in serum and identification of ovarian cancer. *Lancet* **360**:170 [author reply 170–1].
Diamandis EP, Yousef GM, Soosaipillai AR, Bunting P (2000) Human kallikrein 6 (zyme/protease M/ neurosin): a new serum biomarker of ovarian carcinoma. *Clin Biochem* **33**:579–83.
Diamandis EP, Okui A, Mitsui S, et al. (2002) Human kallikrein 11: a new biomarker of prostate and ovarian carcinoma. *Cancer Res* **62**:295–300.
Diamandis EP, Scorilas A, Fracchioli S, et al. (2003) Human kallikrein 6 (hK6): a new potential serum biomarker for diagnosis and prognosis of ovarian carcinoma. *J Clin Oncol* **21**:1035–43.
Dorum A, Heimdal K, Lovslett K, et al. (1999) Prospectively detected cancer in familial breast/ovarian cancer screening. *Acta Obstet Gynecol Scand* **78**:906–11.
Duk JM, Aalders JG, Fleuren GJ, et al. (1989a) Tumor markers CA 125, squamous cell carcinoma antigen, and carcinoembryonic antigen in patients with adenocarcinoma of the uterine cervix. *Obstet Gynecol* **73**:661–8.
Duk JM, van Voorst Vader PC, ten Hoor KA, et al. (1989b) Elevated levels of squamous cell carcinoma antigen in patients with a benign disease of the skin. *Cancer* **64**:1652–6.
Duk JM, De Bruijn HW, Groenier KH, et al. (1990) Adenocarcinoma of the uterine cervix. Prognostic significance of pretreatment serum CA 125, squamous cell carcinoma antigen, and carcinoembryonic antigen levels in relation to clinical and histopathologic tumor characteristics. *Cancer* **65**:1830–7.
Duk JM, Groenier KH, de Bruijn HW, et al. (1996) Pretreatment serum squamous cell carcinoma antigen: a newly identified prognostic factor in early-stage cervical carcinoma. *J Clin Oncol* **14**:111–18.
Einhorn N, Bast RC, Jr, Knapp RC, et al. (1986) Preoperative evaluation of serum CA 125 levels in patients with primary epithelial ovarian cancer. *Obstet Gynecol* **67**:414–16.
Elwood M (2002) Proteomic patterns in serum and identification of ovarian cancer. *Lancet* **360**:170 [author reply 170–1].
Engelen MJ, de Bruijn HW, Hollema H, et al. (2000) Serum CA 125, carcinoembryonic antigen, and CA 19–9 as tumor markers in borderline ovarian tumors. *Gynecol Oncol* **78**:16–20.
Fang X, Gaudette D, Furui T, et al. (2000) Lyso-phospholipid growth factors in the initiation, progression, metastases, and management of ovarian cancer. *Ann N Y Acad Sci* **905**:188–208.
Payers PM, Rustin G, Wood R, et al. (1993) The prognostic value of serum CA 125 in patients with advanced ovarian carcinoma: an analysis of 573 patients by the Medical Research Council Working Party on Gynaecological Cancer. *Int J Gynecol Cancer* **3**:285–92.
Ferdeghini M, Gadducci A, Prontera C et al (1993). Serum soluble interleukin-2 receptor assay in cervical and endometrial cancer. Preliminary data. *Anticancer Res* **13**: 709–13.
Ferdeghini M, Gadducci A, Prontera C, et al. (1994) Determination of serum levels of different cytokeratins in patients with uterine malignancies. *Anticancer Res* **14**:1393–7.
Fioretti P, Gadducci A, Ferdeghini M, et al. (1992) The concomitant determination of different serum tumor markers in epithelial ovarian cancer: relevance for monitoring the response to chemotherapy and follow-up of patients. *Gynecol* Oncol **44**:155–60.
Fritsche HA, Bast RC (1998) CA 125 in ovarian cancer: advances and controversy. *Clin Chem* **44**:1379–80.
Gaarenstroom KN, Bonfrer JM, Kenter GG, et al. (1995) Clinical value of pretreatment serum Cyfra 21–1, tissue polypeptide antigen, and squamous cell carcinoma antigen levels in patients with cervical cancer. *Cancer* **76**:807–13.

Gaarenstroom KN, Bonfrer JM, Korse CM, et al. (1997) Value of Cyfra 21–1, TPA, and SCC-Ag in predicting extracervical disease and prognosis in cervical cancer. *Anticancer Res* **17**:2955–8.
Gaarenstroom KN, Kenter GG, Bonfrer JM, et al. (2000) Can initial serum cyfra 21–1, SCC antigen, and TPA levels in squamous cell cervical cancer predict lymph node metastases or prognosis? *Gynecol Oncol* **77**:164–70.
Gadducci A, Ferdeghini M, Prontera C, et al. (1990) A comparison of pretreatment serum levels of four tumor markers in patients with endometrial and cervical carcinoma. *Eur J Gynaecol Oncol* **11**:283–8.
Gadducci A, Zola P, Landoni F, et al. (1995) Serum half-life of CA 125 during early chemotherapy as an independent prognostic variable for patients with advanced epithelial ovarian cancer: results of a multicentric Italian study. *Gynecol Oncol* **58**:42–7.
Gadducci A, Ferdeghini M, Castellani C, et al. (1998) Serum macrophage colony-stimulating factor (M-CSF) levels in patients with epithelial ovarian cancer. *Gynecol Oncol* **70**:111–14.
Gadducci A, Ferdeghini M, Cosio S, et al. (2001) The clinical relevance of serum CYFRA 21–1 assay in patients with ovarian cancer. *Int J Gynecol Cancer* **11**:277–82.
Gallion HH, Hunter JE, van Nagell JR, et al. (1992) The prognostic implications of low serum CA 125 levels prior to the second-look operation for stage III and IV epithelial ovarian cancer. *Gynecol Oncol* **46**:29–32.
Gastl G, Plante M, Finstad CL, et al. (1993) High IL-6 levels in ascitic fluid correlate with reactive thrombocytosis in patients with epithelial ovarian cancer. *Br J Haematol* **83**:433–41.
Gocze PM, Vahrson HW, Freeman DA (1994) Serum levels of squamous cell carcinoma antigen and ovarian carcinoma antigen (CA 125) in patients with benign and malignant diseases of the uterine cervix. *Oncology* **51**:430–4.
Gold P, Freedman SO (1965) Specific carcinoembryonic antigens of the human digestive system. *J Exp Med* **122**:467–81.
Groome NP, Evans LW (2000) Does measurement of inhibin have a clinical role? *Ann Clin Biochem* **37**(Pt 4):419–31.
Hakala A, Kacinski BM, Stanley ER, et al. (1995) Macrophage colony-stimulating factor 1, a clinically useful tumor marker in endometrial adenocarcinoma: comparison with CA 125 and the aminoterminal propeptide of type III procollagen. *Am J Obstet Gynecol* **173**:112–19.
Hareyama H, Sakuragi N, Makinoda S, Fujimoto S (1996) Serum and tissue measurements of CA72–4 in patients with endometrial carcinoma. *J Clin Pathol* **49**:967–70.
Hareyama H, Sakuragi N, Makinoda S et al. (1996) Serum and tissue measurements of CA72–4 in patients with endometrial carcinoma. *J Clin Pathol* **49**:967–70.
Harlozinska A, Sedlaczek P, Van Dalen A, et al. (1997) TPS and CA 125 levels in serum, cyst fluid and ascites of patients with epithelial ovarian neoplasms. *Anticancer Res* **17**:4473–78.
Hasholzner U, Baumgartner L, Stieber P, et al. (1994) Significance of the tumour markers CA 125 II, CA 72–4, CASA and CYFRA 21–1 in ovarian carcinoma. *Anticancer Res* **14**:2743–6.
Hawkins RE, Roberts K, Wiltshaw E, et al. (1989a) The prognostic significance of the half-life of serum CA 125 in patients responding to chemotherapy for epithelial ovarian carcinoma. *Br J Obstet Gynaecol* **96**:1395–9.
Hawkins RE, Roberts K, Wiltshaw E, et al. (1989b) The clinical correlates of serum CA125 in 169 patients with epithelial ovarian carcinoma. *Br J Cancer* **60**:634–7.
Healy DL, Burger HG, Mamers P, et al. (1993) Elevated serum inhibin concentrations in postmenopausal women with ovarian tumors. *N Engl J Med* **329**:1539–42.
Hung YC, Shiau YC, Chang WC, et al. (2002) Early predicting recurrent cervical cancer with combination of tissue polypeptide specific antigen (TPS) and squamous cell carcinoma antigen (SCC). *Neoplasma* **49**:415–17.
Inaba N, Negishi Y, Fukasawa I et al. (1995) Cytokeratin fragment 21–1 in gynecologic malignancy: comparison with cancer antigen 125 and squamous cell carcinoma-related antigen. *Tumour Biol* **16**:345–52.
Jacobs I, Bast RC, Jr (1989) The CA 125 tumour-associated antigen: a review of the literature. *Hum Reprod* **4**:1–12.
Jacobs I, Oram D, Fairbanks J, et al. (1990) A risk of malignancy index incorporating CA 125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. *Br J Obstet Gynaecol* **97**:922–9.
Jacobs I, Davies AP, Bridges J, et al. (1993) Prevalence screening for ovarian cancer in postmenopausal women by CA 125 measurement and ultrasonography. *BMJ* **306**:1030–4.
Jacobs IJ, Skates S, Davies AP, et al. (1996) Risk of diagnosis of ovarian cancer after raised serum CA 125 concentration: a prospective cohort study. *BMJ* **313**:1355–8.

Jacobs IJ, Skates SJ, MacDonald N, et al. (1999) Screening for ovarian cancer: a pilot randomised controlled trial. *Lancet* **353**:1207–10.
Jobling T, Mamers P, Healy DL, et al. (1994) A prospective study of inhibin in granulosa cell tumors of the ovary. *Gynecol Oncol* **55**:285–9.
Kabawat SE, Bast RC, Jr, Bhan AK, et al. (1983) Tissue distribution of a coelomic-epithelium-related antigen recognized by the monoclonal antibody OC125. *Int J Gynecol Pathol* **2**:275–85.
Kainz C, Sliutz G, Mustafa G, et al. (1995) Cytokeratin subunit 19 measured by CYFRA 21–1 assay in follow-up of cervical cancer. *Gynecol Oncol* **56**:402–5.
Karlan BY, Baldwin RL, Lopez-Luevanos E, et al. (1999) Peritoneal serous papillary carcinoma, a phenotypic variant of familial ovarian cancer: implications for ovarian cancer screening. *Am J Obstet Gynecol* **180**:917–28.
Kato HTT (1977) Radioimmunoassay for tumour antigen of human squamous cell carcinoma. *Cancer* **40**:1621–8.
Kauff ND, Satagopan JM, Robson ME, et al. (2002) Risk-reducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. *N Engl J Med* **346**:1609–15.
Kawai M, Kano T, Kikkawa F, et al. (1992) Seven tumor markers in benign and malignant germ cell tumors of the ovary. *Gynecol Oncol* **45**:248–53.
Kenemans P, van Kamp GJ, Oehr P, Verstraeten RA (1993) Heterologous double-determinant immunoradiometric assay CA 125 II: reliable second-generation immunoassay for determining CA 125 in serum. *Clin Chem* **39**:2509–13.
Kim JH, Skates SJ, Uede T, et al. (2002) Osteopontin as a potential diagnostic biomarker for ovarian cancer. *JAMA* **287**:1671–9.
Kinugasa M, Nishimura R, Koizumi T, et al. (1995) Combination assay of urinary beta-core fragment of human chorionic gonadotropin with serum tumor markers in gynecologic cancers. *Jpn J Cancer Res* **86**:783–9.
Kishi T, Grass L, Soosaipillai A, et al. (2003) Human kallikrein 8, a novel biomarker for ovarian carcinoma. *Cancer Res* **63**:2771–4.
Kozak KR, Amneus MW, Pusey SM, et al. (2003) Identification of biomarkers for ovarian cancer using strong anion-exchange ProteinChips: potential use in diagnosis and prognosis. *Proc Natl Acad Sci USA* **100**:12343–8.
Kukura V, Zovko G, Ciglar S, et al. (2003) Serum CA-125 tumor marker in endometrial adenocarcinoma. *Eur J Gynaecol Oncol* **24**:151–3.
Lambert-Messerlian GM, Steinhoff M, Zheng W, et al. (1997) Multiple immunoreactive inhibin proteins in serum from postmenopausal women with epithelial ovarian cancer. *Gynecol Oncol* **65**:512–16.
Lappohn RE, Burger HG, Bouma J, et al. (1992) Inhibin as a marker for granulosa cell tumor. *Acta Obstet Gynecol Scand Suppl* **155**:61–5.
Lavin PT, Knapp RC, Malkasian G, et al. (1987) CA 125 for the monitoring of ovarian carcinoma during primary therapy. *Obstet Gynecol* **69**:223–7.
Lloyd KO, Yin BW, Kudryashov V (1997) Isolation and characterization of ovarian cancer antigen CA 125 using a new monoclonal antibody (VK-8): identification as a mucin-type molecule. *Int J Cancer* **71**:842–50.
Lo SS, Cheng DK, Ng TY, et al. (1997) Prognostic significance of tumour markers in endometrial cancer. *Tumour Biol* **18**:241–9.
Lozza L, Merola M, Fontanelli R, et al. (1997) Cancer of the uterine cervix: clinical value of squamous cell carcinoma antigen (SCC) measurements. *Anticancer Res* **17**:525–9.
Luo LY, Bunting P, Scorilas A, Diamandis EP (2001) Human kallikrein 10: a novel tumor marker for ovarian carcinoma? *Clin Chim Acta* **306**:111–18.
Luo LY, Katsaros D, Scorilas A, et al. (2003) The serum concentration of human kallikrein 10 represents a novel biomarker for ovarian cancer diagnosis and prognosis. *Cancer* Res **63**:807–11.
Ma S, Shen K, Lang J (2003) A risk of malignancy index in preoperative diagnosis of ovarian cancer. *Chin Med J (Engl)* **116**:396–9.
Magklara A, Scorilas A, Katsaros D, et al. (2001) The human KLK8 (neuropsin/ovasin) gene: identification of two novel splice variants and its prognostic value in ovarian cancer. *Clin Cancer Res* **7**:806–11.
Makar AP, Kristensen GB, Kaern J, et al. (1992) Prognostic value of pre- and postoperative serum CA 125 levels in ovarian cancer: new aspects and multivariate analysis. *Obstet Gynecol* **79**:1002–10.
Makar AP, Kristensen GB, Bormer OP, Trope CG (1993a) Is serum CA 125 at the time of relapse a prognostic indicator for further survival prognosis in patients with ovarian cancer? *Gynecol Oncol* **49**:3–7.
Makar AP, Kristensen GB, Bormer OP, Trope CG (1993b) Serum CA 125 level allows early identification of nonresponders during induction chemotherapy. *Gynecol Oncol* **49**:73–9.

Manjunath AP, Pratapkumar Sujatha K, Vani R (2001) Comparison of three risk of malignancy indices in evaluation of pelvic masses. *Gynecol Oncol* **81**:225–9.
Mann KSB, Hoermann R (1993) Clinical use of HCG and hCG beta determinations. *Scand J Clin Lab Invest* **216S**:97–104.
Massuger LF, Koper NP, Thomas CM, et al. (1997) Improvement of clinical staging in cervical cancer with serum squamous cell carcinoma antigen and CA 125 determinations. *Gynecol Oncol* **64**:473–6.
Matorras R, Rodriguez-Escuderoi FJ, Diez J et al. (1992) Monitoring endometrial adenocarcinoma with a four tumor marker combination. CA 125, squamous cell carcinoma antigen, CA 19–9 and CA 15.3. *Acta Obstet Gynecol Scand* **71**: 458–64.
Mazurek A, Niklinski J, Laudanski T, Pluygers E (1998) Clinical tumour markers in ovarian cancer. *Eur J Cancer Prev* **7**:23–35.
McCluggage WG (2000) Recent advances in immunohistochemistry in the diagnosis of ovarian neoplasms. *J Clin Pathol* **53**:327–34.
Meden H, Fattahi-Meibodi A (1998) CA 125 in benign gynecological conditions. *Int J Biol Markers* **13**:231–7.
Memarzadeh S, Lee SB, Berek JS, Farias-Eisner R (2003) CA125 levels are a weak predictor of optimal cytoreductive surgery in patients with advanced epithelial ovarian cancer. *Int J Gynecol Cancer* **13**:120–4.
Menon U, Jacobs I (2002) Screening for ovarian cancer. *Best Pract Res Clin Obstet Gynaecol* **16**:469–82.
Menon U, Riley SC, Thomas J, et al. (2000) Serum inhibin, activin and follistatin in postmenopausal women with epithelial ovarian carcinoma. *BJOG* **107**:1069–74.
Meyer T, Rustin GJ (2000) Role of tumour markers in monitoring epithelial ovarian cancer. *Br J Cancer* **82**:1535–8.
Mills GB, Bast RC, Jr, Srivastava S (2001) Future for ovarian cancer screening: novel markers from emerging technologies of transcriptional profiling and proteomics. *J Natl Cancer Inst* **93**:1437–9.
Mok SC, Chao J, Skates S, et al. (2001) Prostasin, a potential serum marker for ovarian cancer: identification through microarray technology. *J Natl Cancer Inst* **93**:1458–64.
Morgan RJ, Jr, Speyer J, Doroshow JH, et al. (1995) Modulation of 5-fluorouracil with high-dose leucovorin calcium: activity in ovarian cancer and correlation with CA-125 levels. *Gynecol Oncol* **58**:79–85.
Morgante G, la Marca A, Ditto A, De Leo V (1999) Comparison of two malignancy risk indices based on serum CA125, ultrasound score and menopausal status in the diagnosis of ovarian masses. *Br J Obstet Gynaecol* **106**:524–7.
Nagele F, Petru E, Medl M, et al. (1995) Preoperative CA 125: an independent prognostic factor in patients with stage I epithelial ovarian cancer. *Obstet Gynecol* **86**:259–64.
Nam JH, Chang KC, Chambers JT, et al. (1990) Urinary gonadotropin fragment, a new tumor marker. III. Use in cervical and vulvar cancers. *Gynecol Oncol* **38**:66–70.
Nap M (1998) Immunohistochemistry of CA 125. Unusual expression in normal tissues, distribution in the human fetus and questions around its application in diagnostic pathology. *Int J Biol Markers* **13**:210–15.
Nash M A, Ferrandina G, Gordinier M, et al. (1999) The role of cytokines in both the normal and malignant ovary. *Endocr Relat Cancer* **6**:93–107.
Nasu K, Etoh Y, Yoshimatsu J, et al. (1996) Serum levels of cytokeratin 19 fragments in cervical cancer. *Gynecol Obstet Invest* **42**:267–70.
Ngan HY, Cheung AN, Lauder, IJ, et al. (1996) Prognostic significance of serum tumour markers in carcinoma of the cervix. *Eur J Gynaecol Oncol* **17**:512–17.
Nishizuka S, Chen ST, Gwadry FG, et al. (2003) Diagnostic markers that distinguish colon and ovarian adenocarcinomas: identification by genomic, proteomic, and tissue array profiling. *Cancer Res* **63**:5243–50.
Nustad K, Bast RC, Jr, Brien TJ, et al. (1996) Specificity and affinity of 26 monoclonal antibodies against the CA 125 antigen: first report from the ISOBM TD-1 workshop. International Society for Oncodevelopmental Biology and Medicine. *Tumour Biol* **17**:196–219.
Olt G, Berchuck A, Bast RC, Jr (1990) The role of tumor markers in gynecologic oncology. *Obstet Gynecol Surv* **45**:570–7.
Onsrud M (1991) Tumour markers in gynaecologic oncology. *Scand J Clin Lab Invest Suppl* **206**:60–70.
Ota Y, Inaba N, Shirotake S et al. (1990) Enzyme immunoassay for placental protein 4 (PP4) and its possible diagnostic significance in patients with genital tract cancer. *Arch Gynecol Obstet* **247**:139–47.
Padungsutt P, Thirapagawong C, Senapad S, Suphanit I (2000) Accuracy of tissue polypeptide specific antigen (TPS) in the diagnosis of ovarian malignancy. *Anticancer Res* **20**:1291–5.
Park SY, Kim HS, Hong EK, Kim WH (2002) Expression of cytokeratins 7 and 20 in primary carcinomas of the stomach and colorectum and their value in the differential diagnosis of metastatic carcinomas to the ovary. *Hum Pathol* **33**:1078–85.

Parker D, Bradley C, Bogle SM, et al. (1994) Serum albumin and CA125 are powerful predictors of survival in epithelial ovarian cancer. *Br J Obstet Gynaecol* **101**:888–93.
Patsner B, Orr JW, Jr, Mann WJ, Jr (1990) Use of serum CA 125 measurement in posttreatment surveillance of early-stage endometrial carcinoma. *Am J Obstet Gynecol* **162**:427–9.
Pattaranutaporn P, Chansilpa Y, Tangkarat S, et al. (1997) Serum tissue polypeptide specific antigen (TPS) in patients with cervical carcinoma: preliminary report. *Anticancer Res* **17**:2309–12.
Pearl DC (2002) Proteomic patterns in serum and identification of ovarian cancer. *Lancet* **360**:169–70 [author reply 170–1].
Pectasides D, Economides N, Bourazanis J, et al. (1994) Squamous cell carcinoma antigen, tumor-associated trypsin inhibitor, and carcinoembryonic antigen for monitoring cervical cancer. *Am J Clin Oncol* **17**:307–12.
Peters-Engl C, Obermair A, Heinzl H, et al. (1999) CA 125 regression after two completed cycles of chemotherapy: lack of prediction for long-term survival in patients with advanced ovarian cancer. *Br J Cancer* **81**:662–6.
Petraglia F, Luisi S, Pautier P, et al. (1998) Inhibin B is the major form of inhibin/activin family secreted by granulosa cell tumors. *J Clin Endocrinol Metab* **83**:1029–32.
Petricoin EF, Ardekani AM, Hitt BA, et al. (2002) Use of proteomic patterns in serum to identify ovarian cancer. *Lancet* **359**:572–7.
Phocas I, Sarandakou A, Sikiotis K, et al. (1996) A comparative study of serum alpha-beta A immunoreactive inhibin and tumor-associated antigens CA125 and CEA in ovarian cancer. *Anticancer Res* **16**:3827–31.
Pras E, Willemse PH, Canrinus AA, et al. (2002) Serum squamous cell carcinoma antigen and CYFRA 21–1 in cervical cancer treatment. *Int J Radiat Oncol Biol Phys* **52**:23–32.
Price FV, Chambers SK, Chambers JT, et al. (1993) Colonystimulating factor-1 in primary ascites of ovarian cancer is a significant predictor of survival. *Am J Obstet Gynecol* **168**:520–7.
Price FV, Chambers SK, Carcangiu ML, et al. (1998) CA 125 may not reflect disease status in patients with uterine serous carcinoma. *Cancer* **82**:1720–5.
Rebbeck TR, Lynch HT, Neuhausen SL, et al. (2002) Prophylactic oophorectomy in carriers of BRCA1 or BRCA2 mutations. *N Engl J Med* **346**:1616–22.
Robertson DM, Cahir N, Burger HG, et al. (1999) Combined inhibin and CA125 assays in the detection of ovarian cancer. *Clin Chem* **45**:651–8.
Robertson DM, Pruysers E, Burger HG, et al. (2004) Inhibins and ovarian cancer. Mol Cell Endocrinol **225**: 65–71.
Robertson DM, Stephenson T, Pruysers E, et al. (2002) Inhibins/activins as diagnostic markers for ovarian cancer. *Mol Cell Endocrinol* **191**:97–103.
Roman LD, Muderspach LI, Burnett AF, Morrow CP (1998) Carcinoembryonic antigen in women with isolated pelvic masses. Clinical utility? *J Reprod Med* **43**:403–7.
Rose PG, Baker S, Fournier L, et al. (1993) Serum squamous cell carcinoma antigen levels in invasive cervical cancer: prediction of response and recurrence. *Am J Obstet Gynecol* **168**:942–6.
Rose PG, Sommers RM, Reale FR, et al. (1994) Serial serum CA 125 measurements for evaluation of recurrence in patients with endometrial carcinoma. *Obstet Gynecol* **84**:12–16.
Rosman M, Hay den CL, Thiel RP, et al. (1994) Prognostic indicators for poor risk epithelial ovarian carcinoma. *Cancer* **74**:1323–8.
Rustin GJ, Nelstrop AE, McClean P, et al. (1996a) Defining response of ovarian carcinoma to initial chemotherapy according to serum CA 125. *J Clin Oncol* **14**:1545–51.
Rustin GJ, Nelstrop AE, Tuxen MK, Lambert HE (1996b) Defining progression of ovarian carcinoma during follow-up according to CA 125: a North Thames Ovary Group Study. *Ann Oncol* **7**:361–4.
Rustin GJ, Nelstrop AE, Crawford M, et al. (1997) Phase II trial of oral altretamine for relapsed ovarian carcinoma: evaluation of defining response by serum CA125. *J Clin Oncol* **15**:172–6.
Rustin GJ, Nelstrop AE, Bentzen SM, et al. (2000) Selection of active drugs for ovarian cancer based on CA-125 and standard response rates in phase II trials. *J Clin Oncol* **18**:1733–9.
Salman T, el-Ahmady O, Sawsan MR, Nahed MH (1995) The clinical value of serum TPS in gynecological malignancies. *Int J Biol Markers* **10**:81–6.
Scambia G, Benedetti Panici P, Foti E, et al. (1994a) Squamous cell carcinoma antigen: prognostic significance and role in the monitoring of neoadjuvant chemotherapy response in cervical cancer. *J Clin Oncol* **12**:2309–16.

Scambia G, Testa U, Panici PB, et al. (1994b) Interleukin-6 serum levels in patients with gynecological tumors. *Int J Cancer* **57**:318–23.
Scambia G, Testa U, Benedetti Panici P, et al. (1995) Prognostic significance of interleukin 6 serum levels in patients with ovarian cancer. *Br J Cancer* **71**:354–6.
Scambia G, Benedetti P, Foti E, et al. (1996) Multiple tumour marker assays in advanced cervical cancer: relationship to chemotherapy response and clinical outcome. *Eur J Cancer* **32A**:259–63.
Schneider J, Centeno M, Saez F, et al. (1999) Preoperative CA-125, CA 19–9 and nuclear magnetic resonance in endometrial carcinoma: correlation with surgical stage. *Tumour Biol* **20**:25–9.
Scholl SM, Bascou CH, Mosseri V, et al. (1994) Circulating levels of colony-stimulating factor 1 as a prognostic indicator in 82 patients with epithelial ovarian cancer. *Br J Cancer* **69**:342–6.
Schorge JO, Muto MG, Welch WR, et al. (1998) Molecular evidence for multifocal papillary serous carcinoma of the peritoneum in patients with germline BRCA1 mutations. *J Natl Cancer Inst* **90**:841–5.
Schutter EM, Mijatovic V, Kok A, et al. (1999) Urinary gonadotropin peptide (UGP) and serum CA 125 in gynaecologic practice, a clinical prospective study. *Anticancer Res* **19**:5551–7.
Schwarz-Roeger U, Petzoldt B, Waldschmidt R, et al. (1997) UGP—a tumor marker of gynecologic and breast malignancies? Specificity and sensitivity in pretherapeutic patients and the influence of hormonal substitution on the expression of UGP. *Anticancer Res* **17**:3041–5.
Scorilas A, Borgono CA, Harbeck N, et al. (2004) Human kallikrein 13 protein in ovarian cancer cytosols: a new favorable prognostic marker. *J Clin Oncol* **22**:678–85.
Senapad S, Neungton S, Thirapakawong C, et al. (2000) Predictive value of the combined serum CA 125 and TPS during chemotherapy and before second-look laparotomy in epithelial ovarian cancer. *Anticancer Res* **20**:1297–300.
Sevelda P, Schemper M, Spona J (1989) CA 125 as an independent prognostic factor for survival in patients with epithelial ovarian cancer. *Am J Obstet Gynecol* **161**:1213–16.
Shabana A, Onsrud M (1994) Tissue polypeptide-specific antigen and CA 125 as serum tumor markers in ovarian carcinoma. *Tumour Biol* **15**:361–7.
Sjovall K, Nilsson B, Einhorn N. (2002) The significance of serum CA 125 elevation in malignant and nonmalignant diseases. *Gynecol Oncol* **85**:175–8.
Skates SJ, Pauler DK, Jacobs IJ (2001) Screening based on the risk of cancer calculation from Bayesian hierarchical change point and mixture models of longitudinal markers. *J Am Stat Assoc* **96**:429–35.
Skates SJ, Menon U, MacDonald N, et al. (2003) Calculation of the risk of ovarian cancer from serial CA-125 values for preclinical detection in postmenopausal women. *J Clin Oncol* **21**:206–10.
Sliutz G, Tempfer C, Kainz C, et al. (1995) Tissue polypeptide specific antigen and cancer associated serum antigen in the follow-up of ovarian cancer. *Anticancer Res* **15**:1127–9.
Sorace JM, Zhan M (2003) A data review and re-assessment of ovarian cancer serum proteomic profiling. *BMC Bioinformatics* **4**:24.
Sproston AR, Roberts SA, Davidson SE, et al. (1995) Serum tumour markers in carcinoma of the uterine cervix and outcome following radiotherapy. *Br J Cancer* **72**:1536–40.
Stenman UH, Alfthan H, Vartiainen J, Lehtovirta P (1995) Markers supplementing CA 125 in ovarian cancer. *Ann Med* **27**:115–20.
Stuart GC, Dawson LM (2003) Update on granulosa cell tumours of the ovary. *Curr Opin Obstet Gynecol* **15**:33–7.
Suresh MR (1996) Classification of tumor markers. *Anticancer Res* **16**:2273–7.
Suzuki M, Ohwada M, Aida I, et al. (1993) Macrophage colony-stimulating factor as a tumor marker for epithelial ovarian cancer. *Obstet Gynecol* **82**:946–50.
Suzuki M, Kobayashi H, Ohwada M, et al. (1998) Macrophage colony-stimulating factor as a marker for malignant germ cell tumors of the ovary. *Gynecol Oncol* **68**:35–7.
Suzuki Y, Nakano T, Ohno T, et al. (2000) Serum CYFRA 21–1 in cervical cancer patients treated with radiation therapy. *J Cancer Res Clin Oncol* **126**:332–6.
Takeda M, Sakuragi N, Okamoto K, et al. (2002) Preoperative serum SCC, CA125, and CA19–9 levels and lymph node status in squamous cell carcinoma of the uterine cervix. *Acta Obstet Gynecol Scand* **81**:451–7.
Takeshima N, Shimizu Y, Umezawa S, et al. (1994) Combined assay of serum levels of CA125 and CA19–9 in endometrial carcinoma. *Gynecol Oncol* **54**:321–6.
Tamakoshi K, Kikkawa F, Shibata K, et al. (1996) Clinical value of CA125, CA19–9, CEA, CA72–4, and TPA in borderline ovarian tumor. *Gynecol Oncol* **62**:67–72.

Tempfer C, Zeisler H, Sliutz G, et al. (1997) Serum evaluation of interleukin 6 in ovarian cancer patients. *Gynecol Oncol* **66**:27–30.
Tempfer C, Hefler L, Haeusler G, et al. (1998a) Tissue polypeptide specific antigen in the follow-up of ovarian and cervical cancer patients. *Int J Cancer* **79**:241–4.
Tempfer C, Hefler L, Heinzl H, et al. (1998b) CYFRA 21–1 serum levels in women with adnexal masses and inflammatory diseases. *Br J Cancer* **78**:1108–12.
Timmerman D, Verrelst H, Bourne TH, et al. (1999) Artificial neural network models for the preoperative discrimination between malignant and benign adnexal masses. *Ultrasound Obstet Gynecol* **13**:17–25.
Tingulstad S, Hagen B, Skjeldestad FE, et al. (1996) Evaluation of a risk of malignancy index based on serum CA125, ultrasound findings and menopausal status in the pre-operative diagnosis of pelvic masses. *Br J Obstet Gynaecol* **103**:826–31.
Tingulstad S, Hagen B, Skjeldestad FE, et al. (1999) The risk-of-malignancy index to evaluate potential ovarian cancers in local hospitals. *Obstet Gynecol* **93**:448–52.
Tomas C, Penttinen J, Risteli J, et al. (1990) Serum concentrations of CA 125 and aminoterminal propeptide of type III procollagen (PIIINP) in patients with endometrial carcinoma. *Cancer* **66**:2399–406.
Tomas C, Risteli J, Risteli L, et al. (1991) Use of various epithelial tumor markers and a stromal marker in the assessment of cervical carcinoma. *Obstet Gynecol* **77**:566–72.
Tsai SC, Kao CH, Wang SJ (1996) Study of a new tumor marker, CYFRA 21–1, in squamous cell carcinoma of the cervix, and comparison with squamous cell carcinoma antigen. *Neoplasma* **43**:27–9.
Van Dalen A, Favier J, Baumgartner L, et al. (2000) Serum levels of CA 125 and TPS during treatment of ovarian cancer. *Anticancer Res* **20**:5107–8.
van der Burg ME, Lammes FB, van Putten WL, Stoter G (1988) Ovarian cancer: the prognostic value of the serum half-life of CA125 during induction chemotherapy. *Gynecol Oncol* **30**:307–12.
van Haaften-Day C, Shen Y, Xu F, et al. (2001) OVX1, macrophage-colony stimulating factor, and CA-125-II as tumor markers for epithelial ovarian carcinoma: a critical appraisal. *Cancer* **92**:2837–44.
Vartiainen J, Lehtovirta P, Finne P, et al. (2001) Preoperative serum concentration of hCGbeta as a prognostic factor in ovarian cancer. *Int J Cancer* **95**:313–16.
Venesmaa P, Lehtovirta P, Stenman UH, et al. (1994) Tumour-associated trypsin inhibitor (TATI): comparison with CA125 as a preoperative prognostic indicator in advanced ovarian cancer. *Br J Cancer* **70**:1188–90.
Vergote IB, Bormer OP, Abeler VM (1987) Evaluation of serum CA 125 levels in the monitoring of ovarian cancer. *Am J Obstet Gynecol* **157**:88–92.
Welt CK, Lambert-Messerlian G, Zheng W, et al. (1997) Presence of activin, inhibin, and follistatin in epithelial ovarian carcinoma. *J Clin Endocrinol Metab* **82**:3720–7.
Westermann AM, Havik E, Postma FR, et al. (1998) Malignant effusions contain lysophosphatidic acid (LPA) like activity. *Ann Oncol* **9**:437–42.
Woolas RP, Xu FJ, Jacobs IJ, et al. (1993) Elevation of multiple serum markers in patients with stage I ovarian cancer. *J Natl Cancer Inst* **85**:1748–51.
Xu Y, Gaudette DC, Boynton JD, et al. (1995) Characterization of an ovarian cancer activating factor in ascites from ovarian cancer patients. *Clin Cancer Res* **1**:1223–32.
Xu Y, Shen Z, Wiper DW, et al. (1998) Lysophosphatidic acid as a potential biomarker for ovarian and other gynecologic cancers. *JAMA* **280**:719–23.
Yamashita K, Yamoto M, Shikone T, et al. (1997) Production of inhibin A and inhibin B in human ovarian sex cord stromal tumors. *Am J Obstet Gynecol* **177**:1450–7.
Ye B, Cramer DW, Skates SJ, et al. (2003) Haptoglobinalpha subunit as potential serum biomarker in ovarian cancer: identification and characterization using proteomic profiling and mass spectrometry. *Clin Cancer Res* **9**:2904–11.
Yedema CA, Kenemans P, Thomas CM, et al. (1993a) CA 125 serum levels in the early post-operative period do not reflect tumour reduction obtained by cytoreductive surgery. *Eur J Cancer* **29A**:966–71.
Yedema CA, Kenemans P, Voorhorst F, et al. (1993b) CA 125 half-life in ovarian cancer: a multivariate survival analysis. *Br J Cancer* **67**:1361–7.
Yousef GM, Polymeris ME, Grass L, et al. (2003) Human kallikrein 5: a potential novel serum biomarker for breast and ovarian cancer. *Cancer Res* **63**:3958–65.
Zalel Y, Piura B, Elchalal U, et al. (1996) Diagnosis and management of malignant germ cell ovarian tumors in young females. *Int J Gynaecol Obstet* **55**:1–10.

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4
Cross-sectiona imaging

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Introduction

Modern pelvic imaging is largely achieved using the cross-sectional modalities of ultrasonography computed tomography and magnetic resonance imaging. These techniques can all elegantly display pelvic anatomy but have different strengths and weaknesses for the evaluation of gynecologic malignancies. Imaging may be used at presentation for diagnosis, in the assessment of disease extent prior to operation, and postoperatively for residual or recurrent disease evaluation. Imaging is also central to the assessment of response to adjuvant chemotherapy. Although, at present, cross-sectional imaging is not part of International Federation of Obstetrics and Gynaecology (FIGO) staging for any of the gynecologic malignancies, the role of imaging continues to expand in the management of these problems.

Carcinoma of the endometrium

In approximately 90% of cases, endometrial cancer is well-differentiated adenocarcinoma which typically presents with postmenopausal bleeding. Histopathological diagnosis is usually confirmed by hysteroscopy and curettage, which despite a small false-negative rate of 2–6% remains the ‘gold standard’ for differentiating benign from malignant endometrium. At presentation, 75% of women have tumor confined to the endometrium (stage IA) for whom the 5-year survival rate is 80% following total hysterectomy (Creasman et al. 1987). The FIGO committee recommends staging by total hysterectomy, bilateral salpingo-oophorectomy and lymphadenectomy.

Role of imaging

Imaging aids detection of endometrial carcinoma and helps select those postmenopausal women with bleeding who need dilatation and curettage for histo-pathological diagnosis. Once a diagnosis has been made, imaging plays a crucial role in preoperative assessment. It can identify patients with extensive advanced disease where surgery may no longer be suitable. It can also help identify patients who are at high risk of nodal metastasis and may need more extensive lymph node sampling (Barakat and Hricak 2002). It is particularly important to identify this second group to allow definite surgery to be performed initially, thus reducing the morbidity and mortality associated with multiple operations. Several factors are associated with increased risk of nodal metastasis. These include certain histological groups, isthmus or corpus extension and deep myometrial invasion (Ascher and Reinhold 2000).

Ultrasonography

An office endometrial biopsy may be the initial investigation of postmenopausal bleeding; pelvic ultrasonography may be used to select patients in whom hysteroscopy, dilatation and curettage are indicated. The normal endometrium is visualized as a highly reflective band in the center of the uterus. Transvaginal sonography allows more precise measurement of endometrial thickness than transabdominal sonography as the higher-frequency ultrasound probe gives images of improved spatial resolution. In addition, the role of transabdominal sonography is limited by difficulty in obtaining adequate images in obese patients, those with a retroflexed uterus and those with multiple fibroids. Normal endometrial thickness and appearance vary with hormonal status (prepubertal, menstrual age or postmenopausal) and phase of the menstrual cycle. Early in the menstrual cycle the endometrium is visualized as a thin reflective line. In the proliferative phase, the endometrium appears as a triple line (Figure 1), and in the secretory phase of the endometrium is at its greatest thickness, with homogeneously increased reflectivity and greater through transmission.

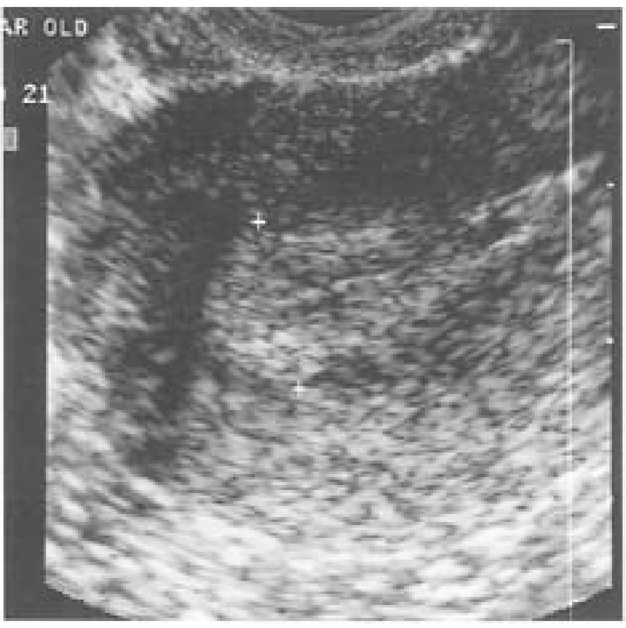


Figure 1

Transvaginal ultrasound. Normal hyperreflective endometrial appearances during the proliferative phase of the cycle. The endometrium is homogeneous in reflectivity and clearly delineated in outline

In women with postmenopausal bleeding a thin endometrium measuring 4 mm or less obviates the need for endometrial biopsy. Endometrial carcinoma is characterized by increased endometrial thickness, often with heterogeneous reflectivity and an irregular, ill-defined margin. However, there is overlap between the sonographic appearances of endometrial polyps, hyperplasia (associated with hormone replacement and tamoxifen therapy) and carcinoma in postmenopausal women with bleeding. From a meta-analysis transvaginal sonography (TVS) appears to be very sensitive at detecting endometrial carcinoma (94.3%) but has a poor specificity (52.4%), giving it an overall accuracy of only 57%. However, it does have a very high negative predictive value (98.6%) (Timmermann et al. 1997). Although morphological characteristics and Doppler characteristics of the endometrium have been investigated in the hope of improving the specificity of TVS for endometrial carcinoma, at present these are not helpful (Ascher et al. 2002).
Sonohysterography (transvaginal ultrasound scanning during the instillation of saline into the uterine cavity) can be helpful in further evaluating focal endometrial thickening and it also appears to be very sensitive in identifying significant uterine pathology. Although the technique has been shown to have better accuracy than endovaginal sonography alone in diagnosing endometrial pathology its exact role in the evaluation of women presenting with postmenopausal bleeding is still unclear. Its particular strength appears to be in identifying focal abnormalities and in directing biopsy.

Computed tomography

The main role of CT (both conventional and helical) to date has been in the staging of endometrial cancer, specifically to assess lymph node status, and in assessment of depth of myometrial invasion. CT has been reported to have accuracy of 84–88% for staging (Ascher and Reinhold 2002), however, only a single study has assessed helical CT (Hardesty et al. 2001). This study showed CT to have poor sensitivity and specificity for both deep myometrial invasion (sensitivity 83%, specificity 42%) and cervical invasion (sensitivity 25%, specificity 70%), when compared to magnetic resonance imaging (MRI) (myometrial invasion sensitivity 92%, specificity 90%, cervical invasion sensitivity 86%, specificity 97%). Dynamic contrast-enhanced computed tomography may show endometrial tumors as hypodense masses in the endometrial cavity or myometrium. In locally advanced disease it may show an eccentric mass extending into the parametrial tissues. Occasionally, the uterus may be fluid-filled secondary to tumor obstruction of the endocervical canal or owing to tumor necrosis.

The strength of CT lies in its ability to evaluate more advanced disease where there is pelvic side-wall tumor spread. It is also useful in identifying both local and retroperitoneal lymph node enlargement, which if present, should encourage lymphadenectomy at surgery. It may also identify distant metastases to the lungs, liver, bone and brain, which will aid in the planning of appropriate therapy.

Magnetic resonance imaging

On T_2-weighted imaging the uterus has a clearly delineated zonal anatomy which allows staging of the depth of myometrial invasion in endometrial carcinoma (Figure 2). In the normal patient the endometrium has a high signal intensity and is separated from the peripheral myometrium by the inner myometrium or junctional zone which has a very low signal intensity because of its low water content and scanty extracellular matrix. The outermost layer identified on MRI, the peripheral myometrium, has a moderately high signal intensity which is slightly greater than that of striated muscle.

On T_2-weighted sequences endometrial carcinoma has a relatively high signal intensity, which widens the

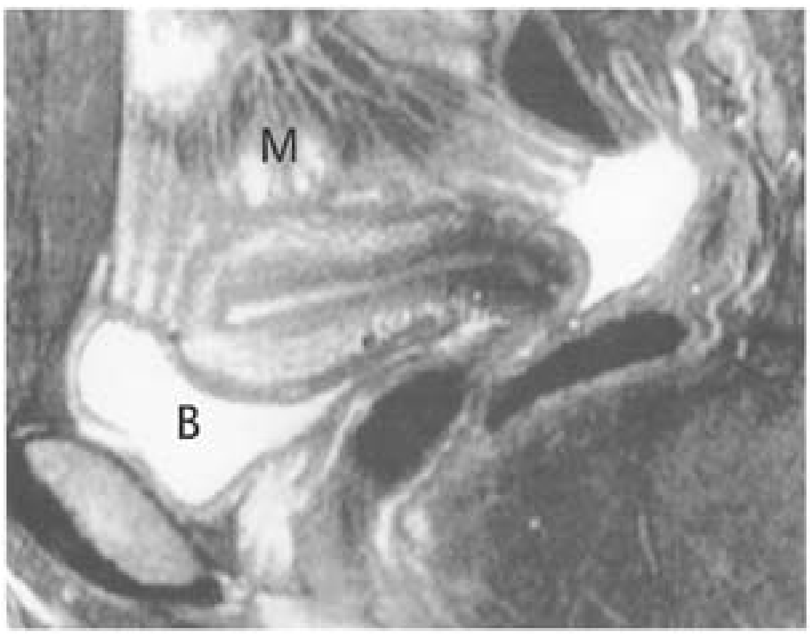


Figure 2

Sagittal T_2-weighted magnetic resonance imaging (MRI) scan through a normal uterus. The normal signal characteristics of the uterus are demonstrated, with a relatively increased signal in the peripheral myometrium, a reduced signal from the junctional zone or inner myometrium and a high signal from the endometrium. The endometrial high signal continues into the cervical canal. The body of the cervix is generally of homogeneously low signal intensity owing to the lower water content. B, urinary bladder; M, small bowel mesentery

endometrial canal or causes its signal intensity to be more heterogeneous. These changes may be the only abnormality in stage IA carcinoma. On T_2-weighted sequences the signal intensity of the endometrial carcinoma is usually equal to (or less than) that of myometrium, and the tumor may be difficult to delineate (Figure 4a). On T_2-weighted sequences, the normal low signal of the junctional zone is replaced by hyperintense tumor in stage IB tumors (Figure 4). In stage IC tumors there is extension through the junctional zone into the outer half of the myometrium.

On T_2-weighted imaging the cervix also has a zonal anatomy, with high signal central secretions, an inner low signal band and an outer intermediate signal band (see Figure 2). Disruption of the normal appearance allows identification of high signal tumor extension into the cervical stroma, indicating stage II disease (Figure 5).

Overestimation of myometrial invasion is more common than its underestimation, especially in bulky tumors within a small uterus where the zonal anatomy is distorted, or if the junctional zone is atrophied, which commonly occurs in the menopause.

Contrast-enhanced T_1-weighted images of the uterus improve the accuracy of assessment of depth of invasion because endometrial carcinoma enhances to a lesser degree than the surrounding myometrium. This also aids detection of extension into the cervix and spread into the parametrial tissues.

Dynamic contrast enhancement, with rapid acquisition of images after a bolus injection of gadolinium DTPA, assists myometrial staging by the identification of a subendometrial zone. The region enhances before

Figure 3

Axial T_1-weighted gradient echo MRI scan through the body of the uterus. The signal from fat has been suppressed. There is an endometrial carcinoma bulging into the endometrial cavity (Ca). More posteriorly a low signal intensity uterine fibroid is present (arrows)

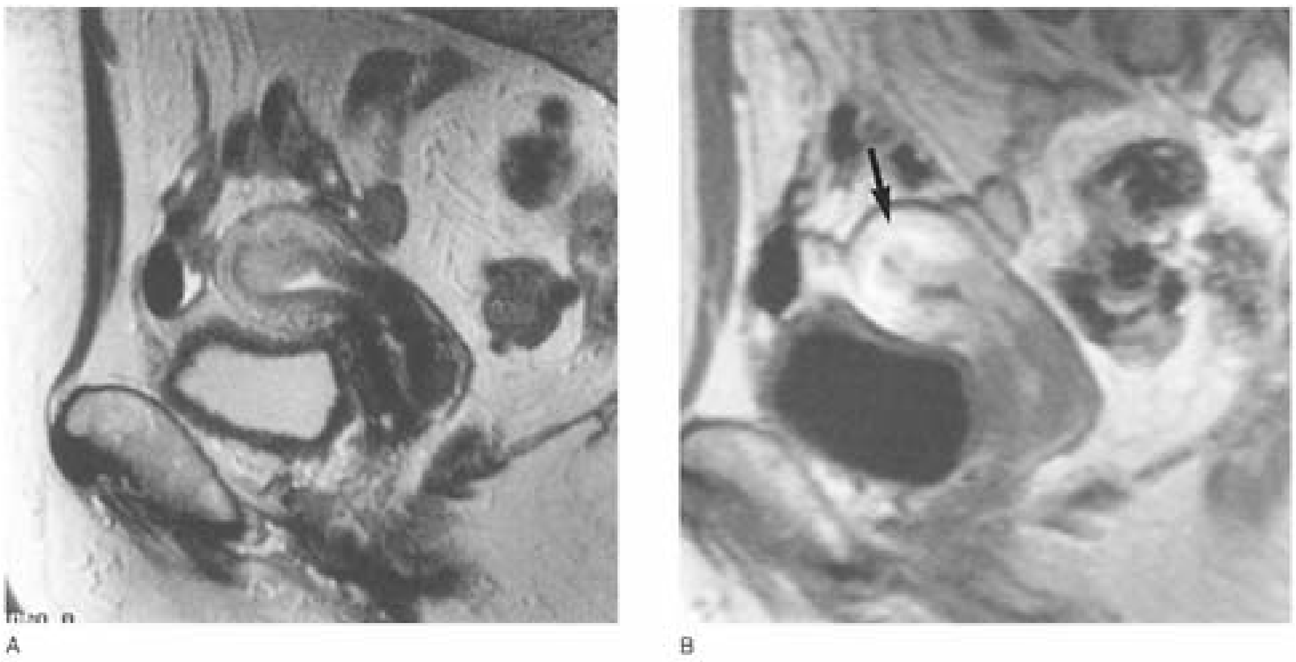


Figure 4

Stage IB endometrial carcinoma. (A) Sagittal T_2-weighted image demonstrates an endometrial carcinoma replacing the normal low-intensity junctional zone and bulging into the endometrial cavity. (B) The post-gadolinium contrast-enhanced T_1-weighted sagittal image demonstrates an intact and normally enhancing junctional zone (arrow), indicating that the tumor is confined to the inner myometrium without extension into the outer myometrium

the rest of the myometrium and corresponds histologically to the innermost part of the junctional zone (see Figure 4). Overall, the sensitivity and accuracy of MRI for detecting deep myometrial invasion are significantly higher than transvaginal sonography or CT, ranging from 82% to 94% (Kinkel et al. 1999). MRI is the most accurate imaging modality for the assessment of pretreatment endometrial carcinoma. Two recent

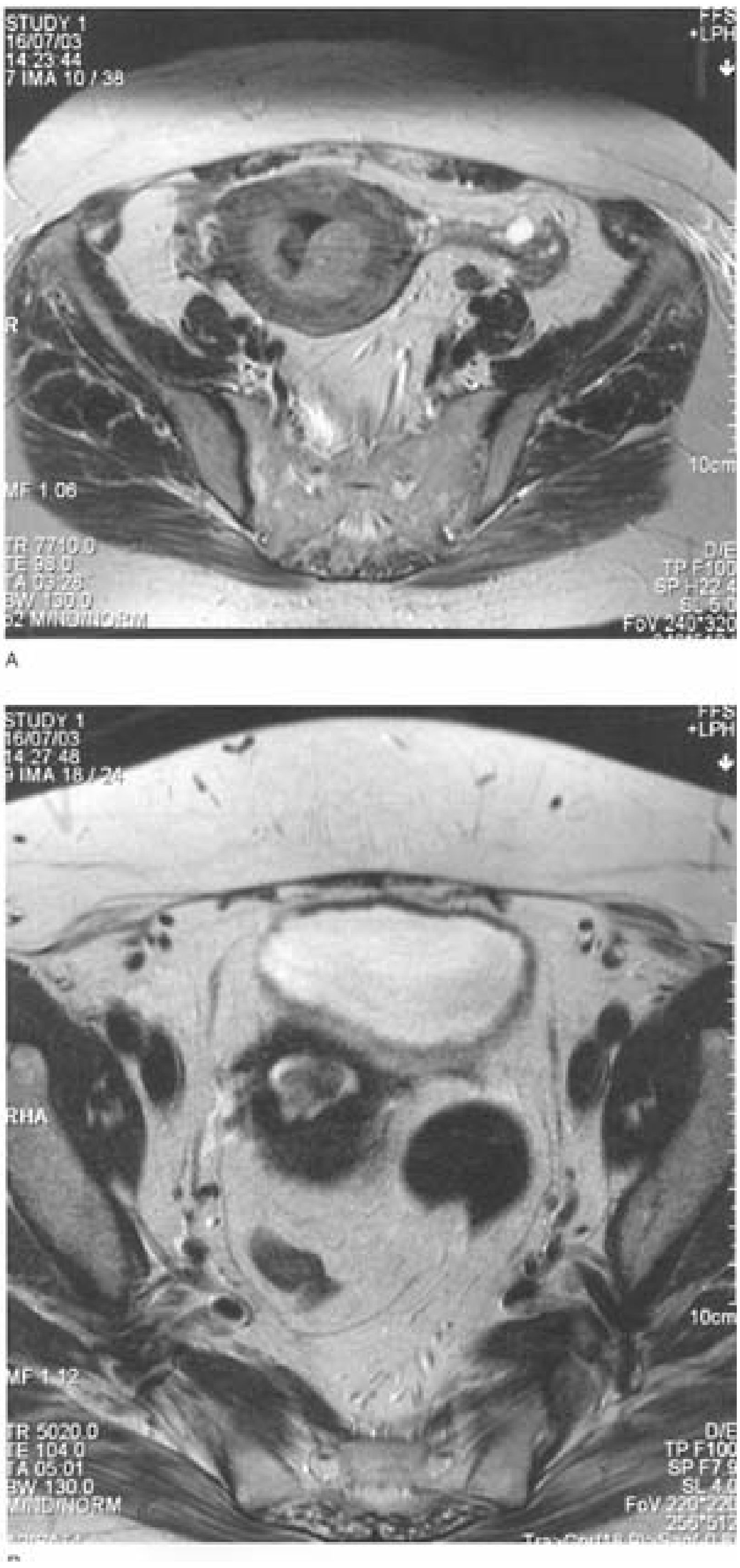
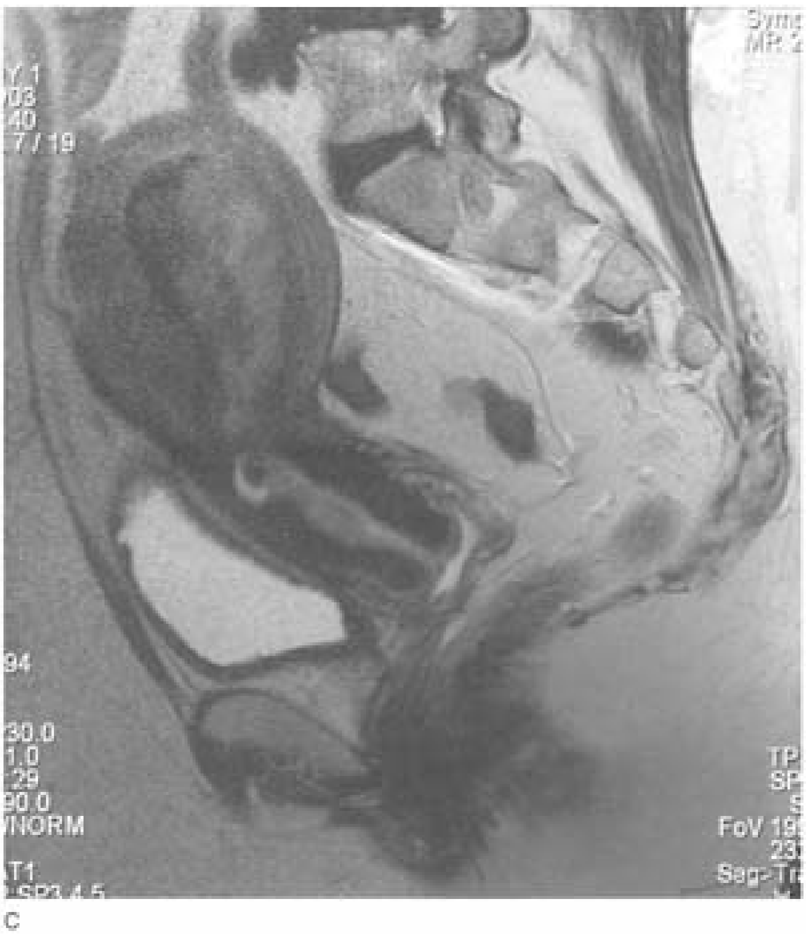


Figure 5

Axial and sagittal T_2-weighted MRI demonstrates a bulky tumor extending into the cervical canal. On the axial images the tumor is confined, and does not extend into more than 50% of the myometrium. The features are of a stage IIB tumor



meta-analyses have shown that contrast-enhanced MRI has greater accuracy than transvaginal ultrasound (TVUS), CT or unenhanced MRI in assessment of deep myometrial invasion (Figure 6). Extension of tumor into the cervix is one of the important prognostic factors. MRI using T_2-weighted, contrast-enhanced T_1-weighted sequences and dynamic contrast enhancement has been shown recently to have accuracy of between 85% and 95% (Seki et al. 2000).
allow acquisition of information during a single With the advent of rapid imaging sequences that breath-hold, the ability of MRI to detect more advanced disease in the retroperitoneum and liver is improving. However, older studies report a poor sensitivity (17%) and positive predictive value (50%) for MRI detection of advanced disease.

Carcinoma of the cervix

Invasive carcinoma of the cervix is most frequently squamous in histological type (80–90% of cases), developing at the squamocolumnar junction. Adeno-carcinoma and adenosquamous carcinomas tend to arise deeper in the endocervical canal and may remain occult until they are advanced. Histological examination establishes the diagnosis and determines whether disease is preinvasive (cervical intraepithelial neoplasia) or invasive.

Role of imaging

The FIGO committee recommends a clinical staging system with vaginal examination under anesthesia, even though this strategy has obvious limitations in advanced disease. Errors have been reported in up to 22% of patients with stage I disease and 75% with stage III (Scheidler and Heuck 2002). Although not officially part of the FIGO system of staging, crosssectional imaging techniques are increasingly used to assess volume of the disease and lymph node status, both important prognostic indicators. The critical distinction in cervical carcinoma is between potentially

Figure 6

Axial, coronal and sagittal T_2-weighted images through the pelvis. There is a large pelvic mass of mixed signal extending to the pelvic side-wall on the right and causing a right hydronephrosis. Enlarged right external iliac nodes are demonstrated. The mass proved to be a uterine sarcoma

operable (stage IIa or lower) tumors and those treated with radiotherapy. The presence or absence of involved lymph nodes markedly affects prognosis and may determine the extent of lymphadenectomy. The size of the tumor is important because tumors of greater than 4 cm in diameter (IB2) have a higher incidence of recurrence, thought to be due to the inability of intercavitary sources to encompass the entire tumor. Patients with parametrial spread (stage IIB, IIIB disease) are treated with chemotherapy to achieve downstaging prior to surgery or with radiotherapy rather than surgery (Barakat and Hricak 2002).

Ultrasonography

The role of ultrasound (US) is very limited in the assessment of cervical cancer.
Cervical tumors are usually hypoechoic on transvaginal and transrectal ultrasound scans. Some reports suggest that local staging of early cervical cancer is equivalent to MRI and better than spiral CT (Yang et al. 1996), although this is not accepted practice.
Parametrial extension is suggested when there is soft tissue stranding laterally from the tumor, but because of its limited focal range neither transvaginal nor transrectal techniques can evaluate parametrial spread in bulky tumors or detect pelvic lymphadenopathy.

Computed tomography

Computed tomography has no role in the early stages of cervical cancer in terms of local spread. Local tumor may be identified on dynamic postcontrast images as an area of low attenuation in normally enhancing cervical stroma. A CT scan may identify parametrial spread as poor definition of the cervix with the surrounding fat or soft tissue stranding in the parametrial fat. False-positive diagnoses are frequent, because hyperemia and pericervical inflammatory changes (which are very common) can have similar appearances. Reliance on CT therefore often leads to overestimates of the extent of local disease, resulting in varying reports of accuracy in local staging of disease of 58% to 88%. More reliable signs of local spread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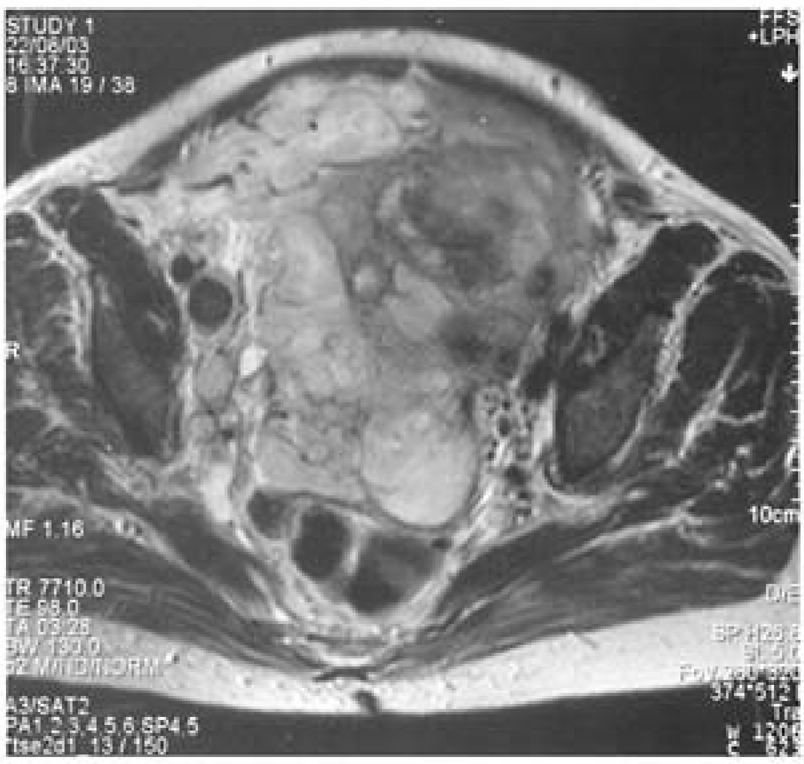
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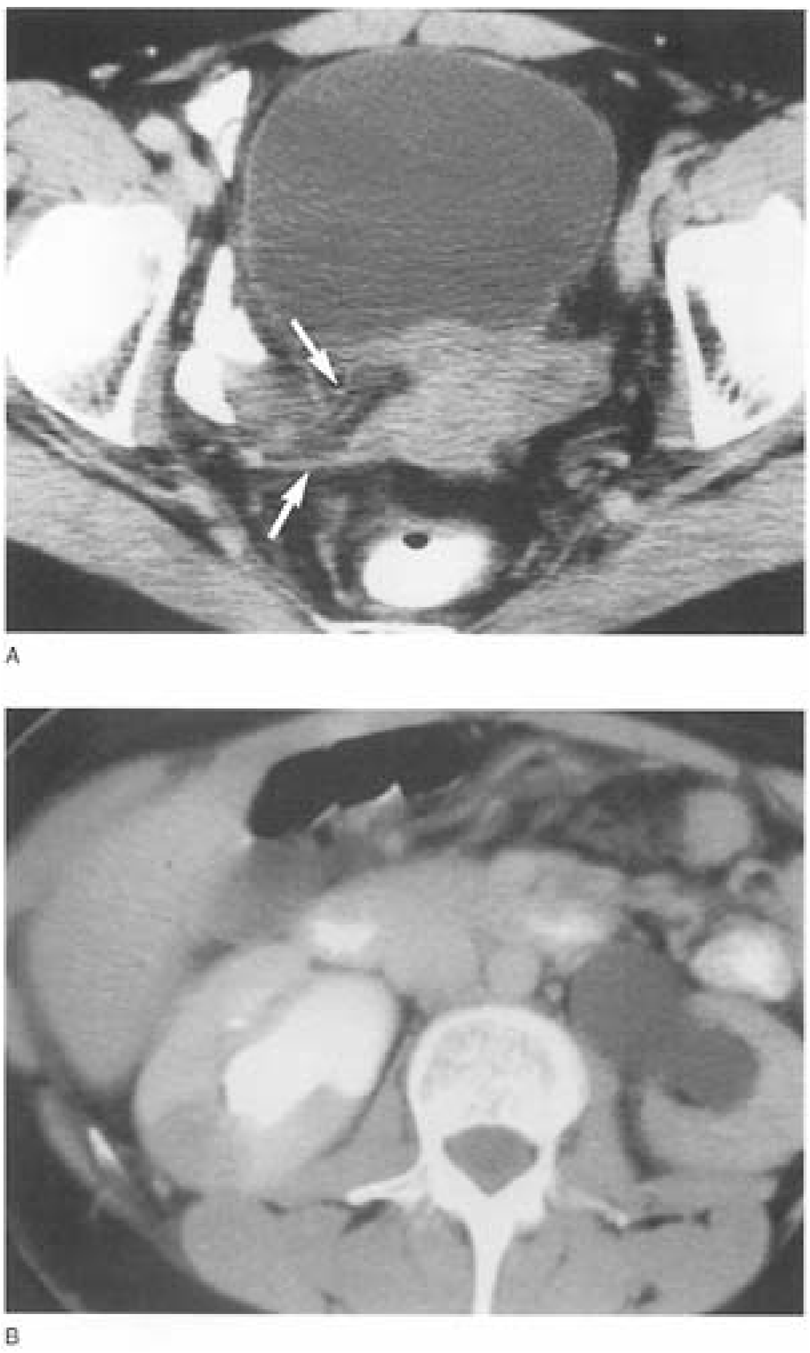

Figure 7

Computed tomography. (A) Contrast-enhanced scan through the cervix. There is bilateral parametrial invasion and thickening of the posterior bladder wall due to direct extension of carcinoma of the cervix into the adjacent tissue. Note the soft tissue density stranding in the paracervical fat, best seen on the right (arrows). (B) Scan through the level of the kidneys demonstrates partial obstruction of the right kidney and complete obstruction of the left kidney with bilateral hydronephrosis. No contrast has passed into the collecting system on the left because of the greater degree of obstruction (stage III)

include obliteration of the pericervical fat planes or an eccentric parametrial soft tissue mass (Vick et al. 1984).

More recent work suggests that helical CT may improve the differentiation between normal parametrial vessels and ligaments from adenopathy and tumor extention (Yang et al. 2000). Pelvic side-wall extension is characterized by tumor reaching the obturator internus or piriformis muscles. Bladder and rectal involvement is suggested if there is loss of the fat plane and asymmetric wall thickening of the adjacent viscera, nodular thickenings or contiguous masses extending into these organs, or by the demonstration of a fistula (Figure 7). Overall accuracy of diagnosing tumor extension to the pelvic side wall is over 90%.

Computed tomography will identify more distant spread by revealing retroperitoneal lymph node enlargement, hydronephrosis and liver metastases, which are infrequently present at the time of presentation.

Recurrent disease is also accurately assessed by CT, which has a high sensitivity and specificity for detecting recurrent pelvic tumor or pelvic and para-aortic lymph node enlargement. However, CT is not accurate in the differentiation of radiation fibrosis from post-surgical change or from recurrent disease. Vesico-vaginal and rectovaginal fistulas can also be difficult to delineate on CT.

Magnetic resonance imaging

Magnetic resonance imaging, like CT, is not part of the formal FIGO staging system. However, it is frequently able to make a significant contribution to the staging of cervical cancer. This is especially so in bulky tumors, endocervical tumors, or tumors difficult to assess on examination under anesthesia. In these cases, MRI will aid evaluation of local tumor extent and can identify para-aortic and pelvic lymph node enlargement.

Invasive cervical carcinoma that is less than stage IB is not usually identified on MRI, but the site of the

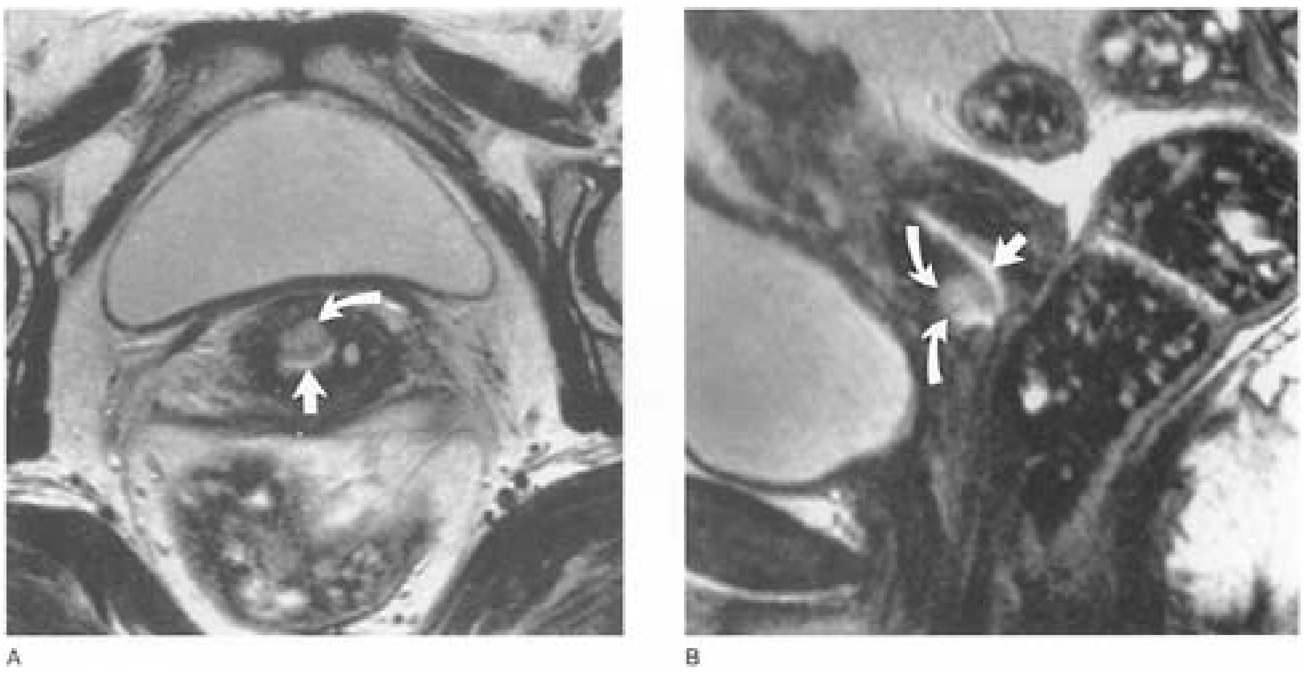

Figure 8

Stage I carcinoma of the cervix. (A) The axial T_2-weighted image through the cervix demonstrates the relatively high-signal carcinoma (curved arrow) surrounded by the low-signal normal cervical stroma. Normal high signal is demonstrated in the cervical canal (straight arrow). A nabothian follicle is also present as a round area of high intensity adjacent to the canal. (B) Sagittal image in the same patient. The normal cervical canal is demonstrated (short arrow) with a small carcinoma in the anterior lip of the cervix (curved arrows)

cervical biopsy is usually easily identified because of edema and blood products. Tumors are usually of intermediate or high signal intensity on T_2-weighted images, surrounded by the very low signal intensity of the cervical stroma (Figure 8). Preservation of this low-intensity rim around the tumor on T_2-weighted imaging and a smooth interface with the surrounding parametrium (Figure 9) are reliable signs of tumor confined to the cervix (stage IB) (specificity 96–99%). Small tumors (IB1) can sometimes be difficult to appreciate. Several reports suggest that dynamic contrast-enhanced images can make them easier to see. Extension into the vagina is readily identified on sagittal or coronal MRI; it may be into the upper third (stage IIA) or the lower third (stage IIIA). The accuracy of MRI for assessing vaginal extension is reported to be 86–93%.

Extension of tumor through the cervical stroma and into the surrounding parametrial fat is best seen on dynamic images (stage IIB) (Figure 10). Magnetic resonance imaging will detect 95% of stage IB tumors and has an overall accuracy of detecting parametrial invasion of 86–92%. Similarly, stage IIIB tumor, which extends to the muscles of the pelvic side wall

Figure 9

Carcinoma of the cervix (stage Bii). There is extension of a bulky cervical tumor into the uterus (arrows), and preservation of the normal low-signal vaginal wall in the posterior fornix (small arrows)

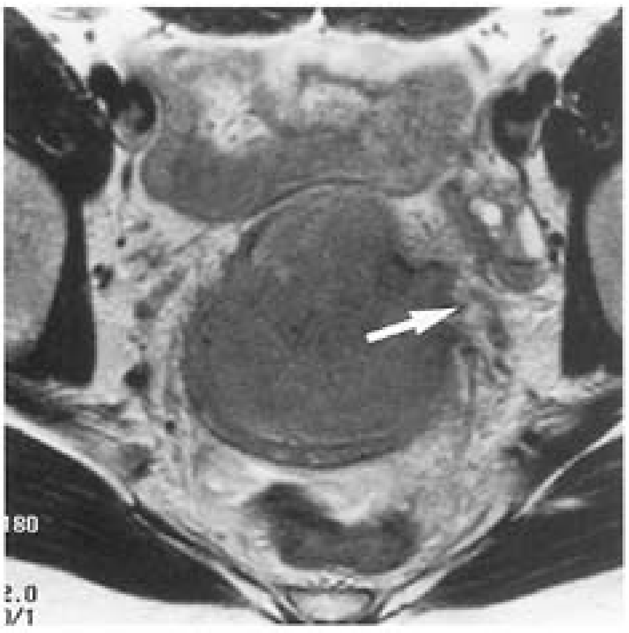

Figure 10

Axial T_2-weighted image through a cervical carcinoma. There is direct extension into the left parametrium with strands of tissue extending into the paracervical fat (arrow), indicating a stage IIB tumor

or obstructs the lower end of the uterus, is clearly seen on T_1- and T_2-weighted imaging. The use of MRI also allows detection of stage IVA disease by demonstration of extension into the bladder or rectum (Figure 11). Obliteration of the intervening fat planes can be iden-

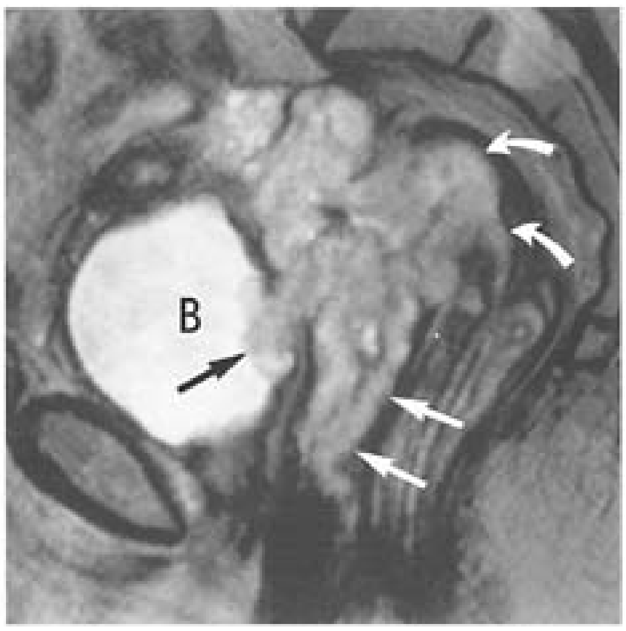

Figure 11

Carcinoma of the cervix, stage IVA. There is a large and exophytic adenocarcinoma of the cervix. On this T_2-weighted sagittal image there is direct extension through the posterior wall of the bladder, outlined by high-signal urine (arrow). There is also extension into the vagina (white arrows) and into the rectum (curved arrows). B, bladder

tified on T_1-weighted images and disruption of the low signal intensity bladder or rectal wall can be identified on T_2-weighted images (Kaur et al. 2003).

Cervical carcinoma spreads first to the parametrial lymph nodes, then to the obturator nodes and the internal and external iliac chains. Differentiating benign and malignant nodes on MRI and CT is based on enlargement. Although size criteria are still debated, a short axis greater than 1 cm is considered enlarged. Lymph node enlargement on MRI is best detected on T_2-weighted images. Magnetic resonance imaging performs similarly to CT in its ability to detect lymph node metastases, with accuracy ranging from 76% to 88%. A useful feature is central necrosis, which when present has a positive predictive value of 100% (Yang et al. 2000). Both CT and MRI have a low specificity of 24–70%, because of the inability to detect metastasis in normal-sized nodes. A recent area of interest is the use of 2[18F]-fluro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) imaging to assess lymph node metastasis. FDG is a radiolabeled analog of glucose. It is taken up by metabolically active cells, and also by many neoplastic cells—91% of cervical tumors show uptake. Although patient numbers are still small the majority of studies show PET to be more accurate than MRI for staging of pelvic lymph nodes (accuracy of 85–97%). Small nodes remain a problem, however, the positive predictive value of PET is reported as 90–100% (Zimny and Siggelow 2003).

Like CT, MRI can be used to detect recurrent disease, but it is not always possible confidently to distinguish recurrent disease from postsurgical and radiotherapy changes which can appear as high signal areas on T_2-weighted imaging for a prolonged time (Figure 12) (Yamashita et al. 1996). Dynamic contrast-enhanced MRI with quantitative analysis of the time-enhancement curves may allow separation of recurrent disease from irradiated tissue.

Magnetic resonance imaging is very good for the evaluation of vaginal fistulas (Figure 13), and furthermore can be used to distinguish fistulas associated with recurrent disease from those that are a complication of surgery or radiotherapy (Healy et al. 1996).

Carcinoma of the ovary

Ovarian cancer accounts for about 4% of all female cancers but is the most frequent cause of death from gynecologic malignancy. Primary ovarian tumors arise from one of three ovarian components, namely the surface epithelium, germ cells or stroma of the ovary. The age distribution varies according to tumor histology. Epithelial ovarian cancer is commonly a disease

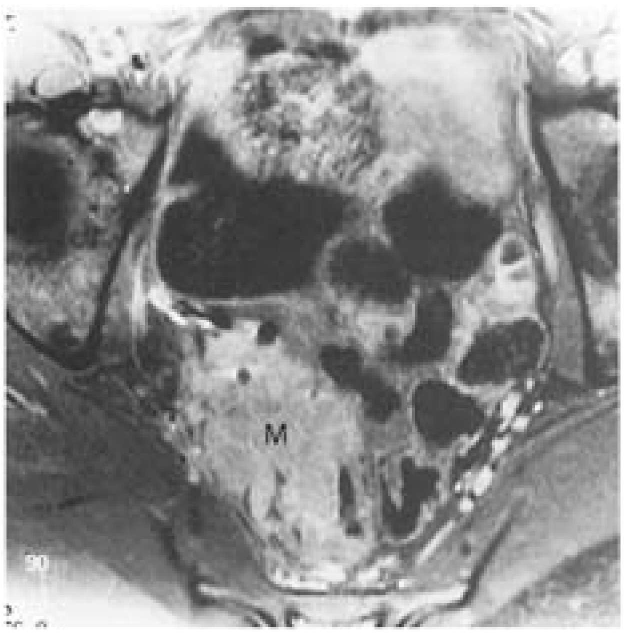

Figure 12

Postcontrast T_1-weighted fat-suppressed images through the pelvis of a patient following radical surgery for carcinoma of the cervix. There is a right posterolateral recurrent tumor mass (M) confirmed by needle biopsy

of postmenopausal women, with approximate age at diagnosis of 60 years, whereas ovarian germ cell tumors and sex cord stromal tumors are most prevalent in the second and third decades. The majority of patients do not present until the tumor is large and there has been spread beyond the ovary, usually with intraperitoneal dissemination.

No satisfactory screening test exists for ovarian cancer, and thus early detection is very difficult. The value of cancer antigen 125 (CA125) in screening for ovarian cancer was assessed in 22 000 females by a study that highlights the difficulty in the early detection of these tumors. Amongst this large cohort, 11 cancers were identified, of which 7 were advanced stage III and IV tumors. Seven patients with normal screening CA125 levels subsequently presented with ovarian cancer, two within a year of the normal result (Jacobs et al. 1993).

Once the diagnosis of ovarian cancer has been established FIGO recommends a staging system based on laparotomy with specified parameters for sampling high-risk areas, such as the omentum and peritoneal reflections.

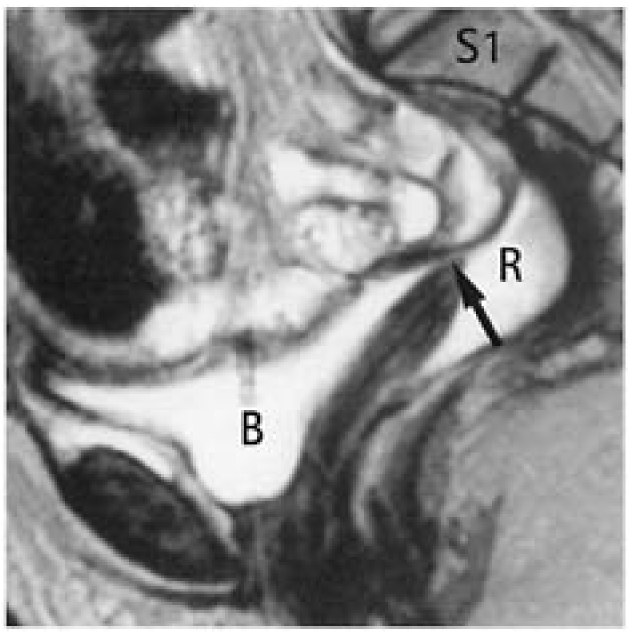

Figure 13

Rectovesical fistula following surgery and radiotherapy for carcinoma of the cervix. Sagittal T_2-weighted image demonstrating communication between the rectal and bladder contents via a fistulous tract (arrow). B, bladder; R, rectum; S1, first sacral segment

Role of imaging

At presentation, imaging is important for identifying the organ of origin of a palpable pelvic mass, and aids characterization. Although imaging acts as a guideline for the differentiation of malignant from benign tumors, it is not sufficiently accurate to preclude the need for tissue diagnosis. Characterization is usually initially achieved using ultrasound. Cross-sectional imaging may be performed before surgery when the diagnosis is uncertain.

When the diagnosis of epithelial ovarian cancer is suspected or made, cross-sectional imaging may also be helpful. One of the most important prognostic factors for epithelial cancer is the volume of disease that remains after surgical cytoreduction. If the diameter of residual disease (disease remaining after surgical debulking) is less than 1 cm then chemotherapy can cure patients or put them into long-term remission. If optimal debulking is not achieved, then there is no survival benefit to surgery (Coakley 2002). Although, at present, there is no accurate way to predict which patients can be optimally debulked, imaging can help plan surgical procedure and allow accurate assessment of residual disease postoperatively

Ultrasonography

Ultrasonography is a valuable method of detecting and characterizing ovarian masses. This examination may be performed via a transabdominal or transvaginal approach and benefits from being quick, inexpensive and non-invasive. Transvaginal Ultrasonography is especially sensitive for detecting small tumors in postmenopausal females and is said to provide additional diagnostic information in 70% of cases, particularly in distinguishing malignant from benign pathology. Unilocular simple cysts with a thin wall, measuring less than 5 cm, are likely to be benign and can be followed up with imaging (Higgins et al. 1989; Fleischer 1991).

Malignant ovarian masses range from entirely cystic to solid masses. Sonographic features that suggest malignancy include soft tissue vegetations on the cyst wall, irregular cyst wall thickening, a partially solid mass, a homogeneously solid mass, the presence of ascites, and peritoneal nodules. However, there is a significant overlap between the appearances of benign and of malignant masses, preventing accurate characterization by imaging criteria alone.

Color flow Doppler studies may give some information regarding tumor vascularity, but again there is considerable overlap between the flow characteristics of benign and of malignant masses, and there is also regional variation in flow characteristics within malignant lesions (Figure 14).

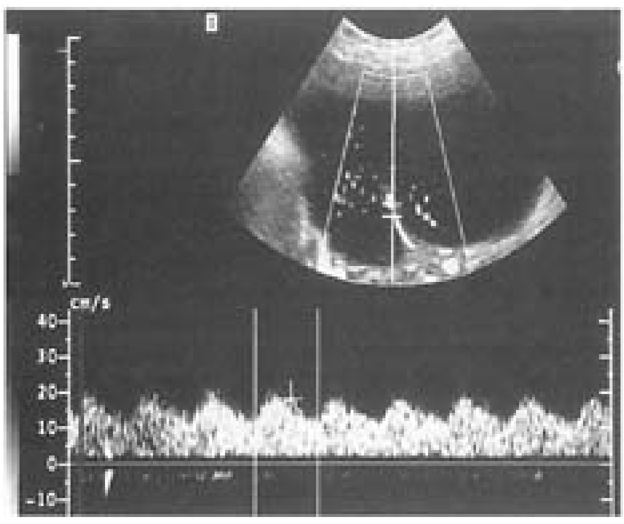

Figure 14

Ultrasound of septate, predominantly cystic pelvic mass. Doppler ultrasound scan of a septal vessel reveals a low-resistance waveform consistent with malignancy

Ultrasound is not widely used for staging ovarian malignancy because bowel gas can obscure deposits related to serosal surfaces and to peritoneal reflections. The overall staging accuracy is consequently poor (50–60%). Ultrasonography has an accuracy of 90% for detecting recurrent tumor within the pelvis but is not very sensitive for the identification of recurrent disease elsewhere within the peritoneum.

Computed tomography

Computed tomography is currently the most widely used imaging technique for staging ovarian cancer. On CT, malignant ovarian masses frequently appear solid, partially solid/cystic, or cystic with papillary projections (Figure 15). Contrast enhancement is variable within septa, cyst walls and solid components. This imaging method has an accuracy in detecting ovarian masses of up to 95% but its ability to distinguish benignity from malignancy is reported to range from 64% to 94%. Signs of disseminated malignancy include invasion of adjacent organs or pelvic side-wall spread (stages II and III), and ascites, peritoneal and omental deposits (stage III).
On CT, peritoneal deposits may appear as rounded, cake-like, stellate or ill-defined masses (Figure 16).

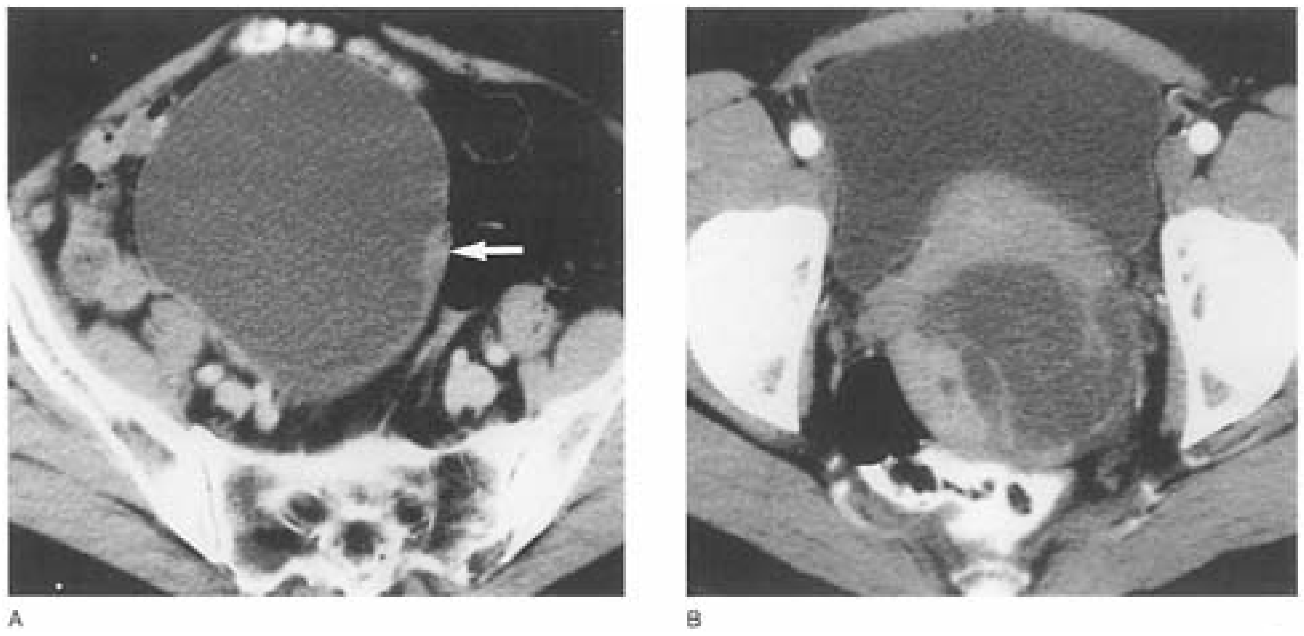

Figure 15

Ovarian carcinoma. (A) Contrast-enhanced CT scan through the pelvis demonstrating predominantly cystic carcinoma of the ovary with some mural thickening (arrow). (B) Mixed solid and cystic ovarian carcinoma in a different patient

These tumor deposits may show contrast enhancement or uniform peritoneal thickening, especially in the right subphrenic space, greater omentum and pouch of Douglas.
Omental tumor is seen as an increased density within the omentum, which can be subtle or mass-like. Computed tomography can identify psammomatous calcification in plaque-like peritoneal metastases, seen especially with serous cystadenocarcinoma. Distinctive mucinous peritoneal deposits are seen with mucinous cystadenocarcinoma, which produces pseudomyxoma peritonei characterized by low-attenuation masses scalloping the liver margins and pushing the bowel posteriorly within the peritoneal cavity. The ability of CT to detect peritoneal deposits is somewhat limited, particularly with small-volume disease. Recent work suggests that multislice CT with coronal reformatted images may have advantages over previous techniques (Pannu et al. 2003).
Computed tomography is frequently used to detect recurrent ovarian cancer and to document response to chemotherapy (Figure 17). Patients with clinically suspected recurrence can pose diagnostic difficulties, CT having a sensitivity of 66.6%. Helical CT is more accurate, a small recent study showed accuracies of 59% to 100% for peritoneal disease (depending on the site of disease). Although there has been interest in FDG PET in recurrent ovarian carcinoma, borderline tumors and

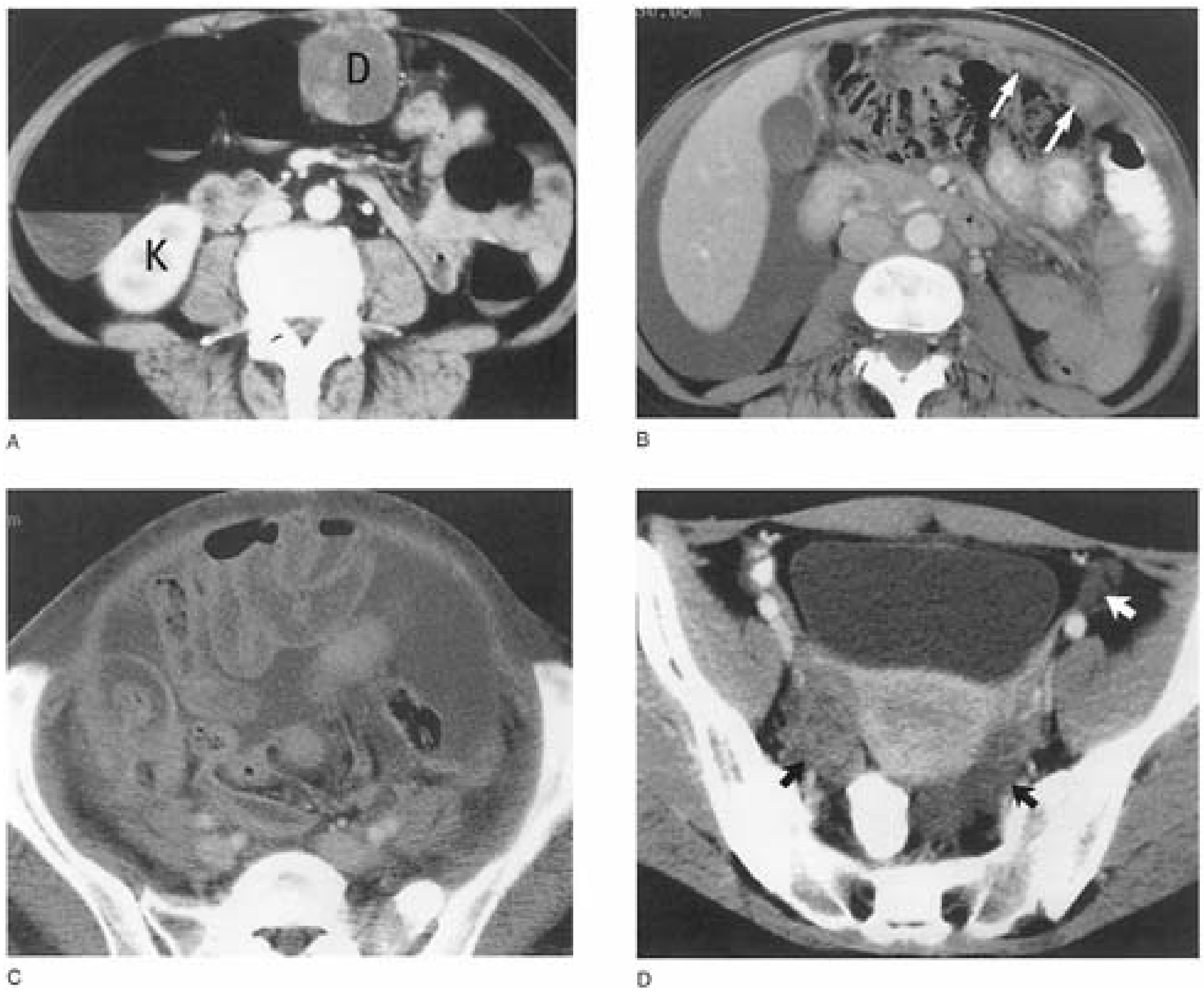

Figure 16

Manifestations of peritoneal spread from carcinoma of the ovary. (A) Partially necrotic, solid omental deposit (D) at the level of the lower pole of the right kidney. K, kidney. (B) Nodular omental deposits (arrows) and abdominal ascites. (C) Diffuse serosal thickening of the surface of the small bowel with extensive ascites due to low-volume peritoneal disease. (D) Bilateral ovarian carcinoma (black arrows) with a deposit in the left round ligament (white arrow)

well-differentiated adenocarcinomas are not identified. Patients suspected of recurrence due to a high CA125, may benefit from FDG PET, but this remains contentious (Cho et al. 2003). As stated above, CT cannot replace staging laparotomy but is useful for postoperative staging in patients with irresectable tumors or where surgery may have missed deposits—for example, posteriorly in the right lobe of the liver in a sub-capsular location, or when there are enlarged retroperitoneal or retrocrural lymph nodes. Consequently, CT is now the recommended imaging modality for staging, evaluating therapeutic response and detecting recurrence.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) offers some potential benefits for evaluating ovarian neoplasms because of its multiplanar capabilities, its superior soft tissue contrast resolution, and the absence of ionizing radiation. However, despite more rapid sequences, physiologic motion in the form of bowel peristalsis and breathing can degrade abdominal imaging, with consequent reduced spatial resolution when compared with CT. In the pelvis, these factors are less significant and in this location MRI is very good for evaluating ovarian pathology. At present, MRI has a role in the

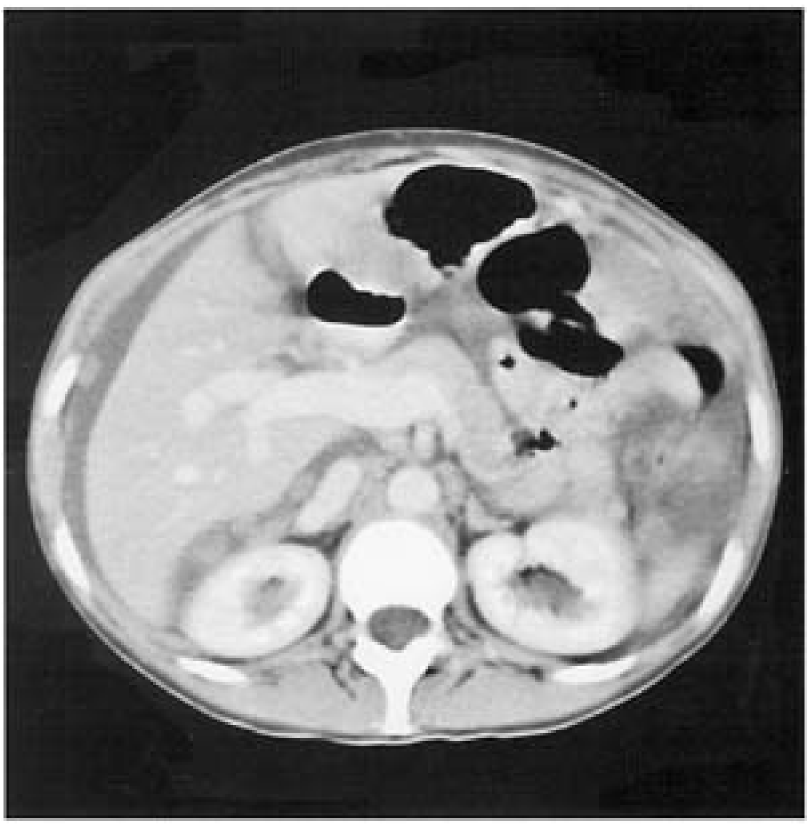

Figure 17

Carcinoma of the ovary producing ascites and perihepatic deposits in the hepatorenal pouch and diaphragmatic deposits on the right. Small para-aortic lymph nodes are seen together with abnormal soft tissue on the left, superficial to the small bowel

characterization of ovarian masses rather than staging ovarian malignancy.

Ovarian masses generally give a low to intermediate signal on T_1-weighted imaging and appear as complex masses with areas of low, intermediate and high signal on T_2-weighted images. The signal intensity of the cystic components of ovarian masses may vary depending on the protein content. Pure fluids will be high intensity on T_2-weighted images only, but mucinous or hemorrhagic cysts may be high intensity on T_1 and intermediate on T_2-weighted images. The high degree of contrast on T_1-weighting between pelvic fat and ovary enhances the ability to detect extraovarian pelvic spread (stage II). Magnetic resonance imaging is also useful at identifying fat within ovarian teratomas, but calcification is not so clearly seen as on CT or ultrasound. Intravenous gadolinium improves lesion characterization by making it easier to see nodules and septa in complex cystic adnexal masses (Figure 18) (Forstner et al. 1995).

Magnetic resonance imaging has an accuracy of 60–93% in distinguishing benign from malignant lesions. Its multiplanar capability means that it is superior to both ultrasound and CT in differentiating adnexal from uterine masses and also in identifying spread to the bladder and rectum.

Although MRI has a limited role in staging intraabdominal metastatic spread, peritoneal deposits greater than 1 cm can be identified with a similar sensitivity to CT Using intravenous gadolinium with fat-suppressed T_1-weighted images may increase the conspicuity of peritoneal implants (Tempany et al. 2000, Riche et al. 2003).

Despite some of the advantages of MRI, CT continues to be preferred for staging peritoneal disease, owing to the inferior spatial resolution of MRI and the degradation from bowel peristalsis and breathing artefact from the anterior abdominal wall.

Vulval carcinoma

Carcinoma of the vulva is a rare malignancy—85–90% are squamous cell carcinomas. Lymphatic spread is first to the superficial and then the deep inguinal nodes. Treatment normally consist of radical vulvectomy and bilateral inguinofemoral lymphadenectomy and sometimes pelvic lymphadenectomy, which is associated with considerable morbidity, wound break-down occurring in 85% and debilitation lymphedema in 70% (Sohaib et al. 2002).

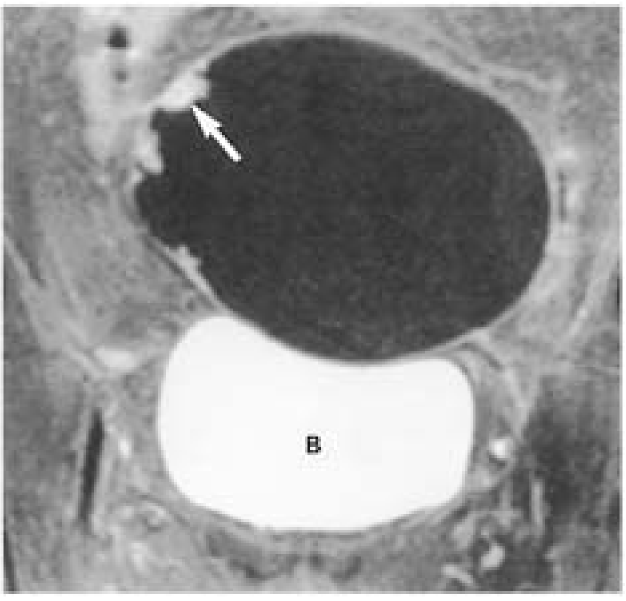

Figure 18

Coronal T_1-weighted image following gadolinium contrast through a predominantly cystic carcinoma of the ovary. Following gadolinium there is enhancement of tumor nodules within the cyst wall (arrow). B, bladder

Role of imaging

The emerging role of imaging in this malignancy is in trying to delineate which patients have lymph node metastasis. MRI demonstrates lymph nodes, but can only distinguish malignant and benign on size criteria as previously discussed. Recently ultrasound and FNA of inguinal nodes has shown promise (Hall et al. 2003).

Uterine sarcoma

Uterine sarcoma is a rare tumor, accounting for only 2–6% of gynecologic malignancies. Uterine sarcomas may be broadly divided into three subtypes. The first is the mixed müllerian sarcoma, which occurs most frequently in postmenopausal women. The other two types are endometrial stromal sarcomas and leio-myosarcomas, which usually present in younger women. Mixed müllerian sarcomas tend to be bulky, arising centrally within the uterus, and are frequently associated with necrosis (Figure 6). However, they have no imaging characteristics that aid their differentiation from endometrial carcinoma. Leiomyosarcomas also tend to be bulky tumors indistinguishable from benign fibroids on imaging. Malignancy should be suspected if the tumor shows marked contour irregularity, significant necrosis or evidence of metastatic disease.

Gestational trophoblastic disease

Gestational trophoblastic disease is caused by abnormal proliferation of trophoblastic elements in the fertilized ovum, which has the potential for malignant transformation. Complete hydatidiform mole is the most common subtype of this disease, accounting for 80% of cases. The uterine cavity becomes distended by a grape-like proliferation of chorionic villi. Sono-graphically, the uterus contains a complex multicystic/solid mass filling the uterine cavity, with anechoic spaces reflecting hydropic swelling of the villi. The process can be invasive with penetration of the uterine myometrium by trophoblastic elements. Malignant transformation into choriocarcinoma can also occur. Ultrasonography cannot reliably distinguish between complex hydatidiform mole confined to the uterus and invasive forms of the disease, such as chorio-carcinoma, but can sometimes show myometrial invasion. Computed tomography and MRI are of limited value in routine management, but do have a role in demonstrating metastatic disease to the lungs or central nervous system (Newlands et al. 1995).

References

Ascher SM, Reinhold C (2002) Imaging of the endometrium. *Radiol Clin N Am* **40**:563–76.
Barakat RR, Hricak H (2002) What do we expect from imaging? *Radiol Clin N Am* **40**:521–6.
Belhocine T (2003) An appraisal of 18F-FDG PET imaging in post therapy surveillance of uterine cancers: Clinical evidence and a research proposal. *Int J Gynecol Cancer* **13**:228–33.
Cho SM, Ha HK, Byun JY et al. (2002) Usefulness of FDG PET for assessment of early recurrent epithelial ovarian cancer. *Am J Roentgenol* **179**:391–5.
Coakley FV (2002) Staging ovarian cancer: role of imaging. *Radiol Clin N Am* **40**:609–36.

Creasman WT, Morrow CP, Bundy BN, et al. (1987) Surgical pathologic spread patterns of endometrial cancer. A Gynaecologic Oncology Group Study. *Cancer* **60**(8 suppl):2035–41.
Fleischer AC (1991) Transabdominal and transvaginal sonography of ovarian masses. *Clin Obstet Gynecol* **34**:433–42.
Forstner R, Hricak H, Occhipinti KA, et al. (1995) Ovarian cancer: staging with CT and MR imaging. *Radiology* **197**:619–26.
Hall T Barton DP, Trott PA, et al. (2003) The role of ultrasound-guided cytology of groin lymph nodes in the management of squamous cell carcinoma of the vulva: 5-year experience in 44 patients. *Clin Radiol* **58**:367–71.
Hardesty L, Sumkin JH, Hakim C, et al. (2001) The ability of helical CT to preoperatively stage endometrial carcinoma. *Am J Roentgenol* **176**:603–6.
Healy JC, Phillips RR, Reznek RH, et al. (1996) The MR appearance of vaginal fistulas. *Am J Roentgenol* **167**:1487–9.
Higgins RV, van Nagell JR, Donaldson ES, et al. (1989) Transvaginal sonography as a screening method for ovarian cancer. *Gynecol Oncol* **34**:402–6.
Jacobs I, Davies AP, Bridges J, et al. (1993) Prevalence screening for ovarian cancer in postmenopausal women by CA 125 measurement and ultrasonography. *BMJ* **306**:1030–4 [see comments].
Kaur H, Silverman P, Iyer R, et al. (2003) Diagnosis, staging and surveillance of cervical carcinoma. *Am J Roentgenol* **180**:1621–32.
Kinkel K Kaji Y, Yu KK, et al. (1999) Radiologic staging in patients with endometrial cancer: A meta-analysis. *Radiology* **212**:711–18.
Newlands ES, Price P, Sikora K, eds (1995) *Treatment of cancer*, 3rd edn. London: Chapman & Hall: 721–34.
Pannu HK, Horton KM, Fishman EK (2003) Thin section dual-phase multidetector-row computed tomography detection of peritoneal metastases in gynaecologic cancers. *J Comput Assist Tomogr* **27**(3):333–40.
Ricke J, Sehouli J, Hack C, et al. (2003) Prospective evaluation of contrast-enhanced MRI in the depiction of peritoneal spread in primary or recurrent ovarian cancer. *Eur Radiol* **13**:943–9.
Scheidler J, Heuck AF (2002) Imaging of cancer of the cervix. *Radiol Clin N Am* **40**:577–90.
Seki H, Takano T, Sakai K (2000) Value of dynamic MR imaging in assessing endometrial carcinoma involvement of the cervix. *Am J Roentgenol* **175**:171–6.
Sohaib SA Richards PS, Ind T, et al. (2002) MR imaging of carcinoma of the vulva. *Am J Roentgenol* **178**:373–7.
Tempany CM, Zou KH, Silverman SG, et al. (2000) Staging of advanced ovarian cancer: comparison of imaging modalities—report from the Radiological Diagnostic Oncology Group. *Radiology* **215**:761–7.
Timmermann D, Vergote I, Brosens I, Wamsteker K, eds (1997) *Diagnostic imaging in obstetrics and gynaecology: a practical guide.* London: WB Saunders: 200.
Vick CW, Walsh JW, Wheelock JB, Brewer WH (1984) CT of the normal and abnormal parametria in cervical cancer. *Am J Roentgenol* **143**:597–603.
Yamashita Y, Harada M, Torashima M, et al. (1996) Dynamic MR imaging of recurrent postoperative cervical cancer. *J Magn Reson Imaging* **6**:167–71.
Yang WT, Walkden SB, Ho S, et al. (1996) Transrectal ultrasound in the evaluation of cervical carcinoma and comparison with spiral computed tomography and magnetic resonance imaging. *Br J Radiol* **69**(823):610–16.
Yang WT, Lam WWM, Yu MY, et al. (2000) Comparison of dynamic helical CT and dynamic MR imaging in the evaluation of pelvic lymph nodes in cervical carcinoma. *Am J Roentgenol* **175**:759–66.
Zimny M, Siggelkow W (2003) Positron emission tomography scanning in gynaecologic and breast cancers. *Curr Opin Obstet Gynecol* **15**:69–75.

5
Sigmoidoscopy, cystoscopy and stenting

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David J Corless

Sigmoidoscopy

Indications

Sigmoidoscopy forms part of the routine examination of patients who complain of colorectal symptoms. Patients presenting with rectal bleeding or a change in bowel habit should undergo either a rigid Sigmoidoscopy followed by a barium enema, or a colonoscopy. In addition, patients presenting with vulval carcinoma extending to the perineum should have anal and rectal assessment. Flexible Sigmoidoscopy can be used to confirm lesions in the distal colon and rectum, to obtain material, and in the follow-up of patients who have undergone colonic resections.

Preoperative preparation

Rigid Sigmoidoscopy can be performed in the outpatient department without any special preparation. Bowel preparation in most instances is unnecessary but in some cases feces in the rectum may limit views and the advancement of the sigmoidoscope. In these cases either a glycerine suppository or a phosphate enema can be used prior to the examination.
Flexible Sigmoidoscopy is usually carried out in the endoscopy suite with or without sedation. Adequate bowel preparation of the left colon and rectum is usually provided by a regimen of clear fluids for 24 hours and two sachets of sodium picosulfate taken the previous day.

Instrumentation

Rigid sigmoidoscope

The rigid sigmoidoscope (Figure 1) is approximately 25 cm long with a 19 mm internal diameter and an internal obturator to aid insertion. It has a detachable eye-piece, which allows instruments to be passed along the shaft, and a circumferential light source. Bellows attached to the distal end are used to insufflate the rectum with air. Newer instruments are disposable, being made of self-lubricating plastic. Useful appendages are a punch biopsy, grasping forceps and suction tubing.

Figure 1

Rigid sigmoidoscope and proctoscope

Flexible sigmoidoscope

The flexible sigmoidoscope (Figure 2) is 70–110 cm long and consists of a control head with eye-piece and controls, a multichannel flexible shaft and a controllable tip. The flexible shaft contains fiberoptic channels carrying the optics and light source to the visual field, as well as channels for suction, irrigation and insufflation of the colon, and the passage of instruments. Movement of the tip in two planes is produced by pulling wires operated at the control head. The eyepiece can be attached to a video camera and the image viewed on a monitor. Immediately after use, instruments should be washed in fresh disinfectant in accordance with the manufacturers' instructions.

Figure 2

Flexible sigmoidoscope or colonoscope

Operative procedure

Rigid sigmoidoscope

Patients are usually placed in the left lateral position on a couch or bed and a digital examination of the rectum is performed. The sigmoidoscope is held in the right hand with the left hand holding the buttocks for insertion. The instrument is lubricated and inserted into the anal canal, pointing towards the umbilicus with the obturator in place. When the instrument is felt to enter the rectum it is directed posteriorly and the obturator removed. Using the bellows the rectum is gently insufflated with air which allows the sigmoidoscope to be advanced while visualizing the whole circumference of the lumen. As the sigmoidoscope is passed through the rectum it follows an anterior curve formed by the hollow of the sacrum (Figure 3). Inspection of the whole mucosa can be achieved by rotating the instrument. Negotiation of the instrument at the rectosigmoid junction should be carried out with care; it can be achieved using gentle insufflation and manipulation in order to find the lumen of the sigmoid colon. The best views are often obtained while withdrawing the sigmoidoscope, and inspection of the mucosa—particularly around the horizontal rectal folds—should be carried out.

Rectal biopsy

The sigmoidoscope is manipulated so that the lesion is at the tip of the instrument. The glass eye-piece is removed; although this causes deflation of the rectum, the lesion should still be in view. Punch biopsy forceps

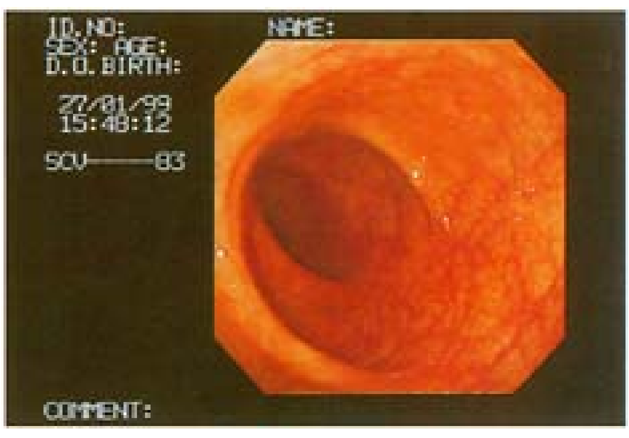

Figure 3

View of rectum at sigmoidoscopy

are passed along the sigmoidoscope and the biopsy is taken under direct vision. The jaws of the biopsy forceps are closed around the lesion and removal is aided by rotation of the closed forceps. Excessive bleeding at the site of the biopsy can easily be controlled with pressure from a cotton-wool swab or occasionally injection of 1 in 1000 adrenaline (epinephrine).

Polypectomy

Polyps with a long stalk can be removed using a diathermy snare technique through the rigid sigmoidoscope. The polyp is grasped with polyp-holding forceps which have been passed through the loop of a diathermy snare. The snare is then passed over the polyp and closure of the snare during application of diathermy coagulates the stalk. The polyp is then removed by the forceps and the excision site inspected for bleeding. It is important to avoid excessive traction on the forceps since this may result in removal of excess normal mucosa and hence perforation.

Flexible sigmoidoscope

Patients are placed in the left lateral position on a couch or bed and a digital examination of the rectum is performed. Intravenous sedation and oxygen may be administered via a face mask or nasal prongs and a pulse oximeter attached to the patient. The tip of the sigmoidoscope is lubricated and inserted into the anal canal for a distance of 4–5 cm. Initially inspection usually reveals a red blur as the tip of the sigmoidoscope rests against the rectal mucosa. The rectum is gently inflated and the tip position adjusted and withdrawn until the lumen comes into view. It may be necessary to adjust the focus, wash the lens and suck out any residual fluid or feces to optimize the image. With gentle insufflation and guidance of the tip, the sigmoidoscope is advanced through the lumen and the rectosigmoid junction negotiated under direct vision. If the lumen or movement across the mucosa is not seen, then the sigmoidoscope should be withdrawn until the lumen once again comes into view. Looping of the sigmoidoscope prevents advancement and in such cases the instrument should also be withdrawn. In most patients, a combination of manipulation of the tip and twisting of the shaft should make it possible to examine the whole left colon. The best views are once again seen on slow withdrawal of the sigmoidoscope, keeping the lumen in view all the way and aspirating as much air as possible. Biopsy can also be performed on withdrawal. The lesion is cleaned by injecting water down the irrigation channel and biopsy forceps are passed through the instrument port. The biopsy is taken under direct vision, the closure usually performed by an assistant who then removes the forceps while the operator directs the sigmoidoscope and the position of the biopsy. The incidence of perforation with a flexible sigmoidoscope is extremely low, but if the patient complains of excessive pain or discomfort then the examination should cease.

Postoperative care

No special postoperative care is necessary after routine sigmoidoscopy After a polypectomy or biopsy the patient should be observed for signs of excessive bleeding or perforation. Barium enema should not be performed for 10 days after biopsy because of the risk of extravasation of contrast.

Cystoscopy and stenting

Indications

Cystoscopy is the single most common urological procedure and is used in the investigation of urinary symptoms. Patients who present with urological symptoms such as frequency, dysuria and hematuria undergo cystoscopy for the diagnosis of lesions of the urethra and bladder. In addition, cystoscopy may be performed as part of the FIGO preoperative staging for cervical carcinoma or where it is suspected that tumors may involve the bladder and urethra. It can also be used to perform retrograde ureterography to provide X-ray visualization of the ureter and collecting system and the placement of retrograde ureteric stents. Stents provide ureteric drainage and can also be used to identify the position of the ureter. Where retrograde stenting proves impossible the interventional radiologist may well be able to pass antegrade stents or, failing this, to insert bilateral nephrostomy tubes.

Preoperative preparation

Rigid cystoscopy is carried out under general anesthesia in the operating theater with the patient in the lithotomy position. It is important to rule out severe osteoarthritis of the hips which may make examination

impossible. Antibiotic prophylaxis is given if there is any evidence or suspicion of a urinary tract infection.
Flexible cystoscopy is usually carried out in the endoscopy suite under local anesthesia. Lignocaine (lidocaine) gel inserted into the urethra acts as both lubricant and local anesthetic agent. If possible the patient should void prior to examination to ensure the bladder is empty.

Instrumentation

Rigid cystoscope

The rigid cystoscope (Figure 4) is composed of a sheath, a bridge and a telescope: it is 30 cm long. The sheath has both an inlet and an outlet port for irrigation and is attached to the bridge with a watertight lock. The endoscope is introduced into the sheath through the bridge, and is also fitted with a watertight lock. The telescope comprises a hollow metal cylinder containing a series of solid rod lenses and a magnifying eye-piece. In front of the eye-piece is a pillar connected to a fiberoptic light source which transmits light to the visual field. The bridge has one or two other ports for the introduction of biopsy forceps and electrodes, and a director which allows the passage of a ureteric catheter and its advancement into the ureteric orifice. Endoscopes with viewing angles of 0°, 30°, 70° and 90° are available.

Flexible cystoscope

The flexible cystoscope (Figure 5) is 35–40 cm long and consists of a control head with eye-piece and con-

Figure 4

Rigid cystoscope

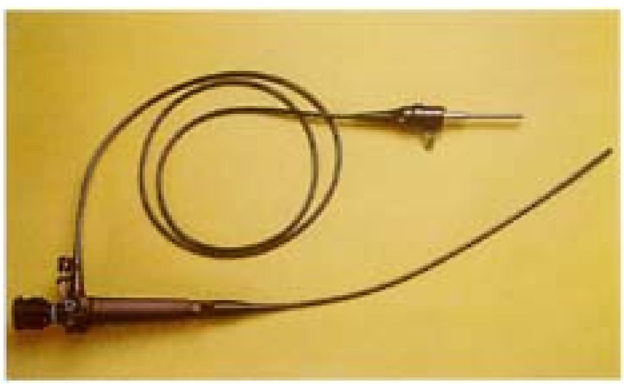

Figure 5

Flexible cystoscope

trols, a multichannel flexible shaft and a controllable tip. The flexible shaft contains fiberoptic channels carrying the optics and light source to the visual field, an irrigation channel and a biopsy channel. Movement of the tip occurs in one plane and ranges from 145° to 180°, controlled by a deflecting level adjacent to the eye-piece.

Operative procedure

Rigid cystoscope

The patient is placed on the operating table in the lithotomy position. The cystoscope sheath is lubricated and introduced into the urethra. The female urethra is about 4 cm long and has a relatively uniform caliber from the meatus to the bladder outlet. Upon entering the bladder the telescope is removed to allow the residual urine and irrigant to drain from the bladder: this may be sent for cytological and bacteriological analysis. Approximately 50 mL of saline is inserted and the fundus of the bladder is identified by finding the air bubble. With incomplete distension the bladder mucosa appears rugated, but as the irrigant fluid distends the bladder the mucosa becomes smooth. The ureteric orifices are visualized on the interureteric ridge at the superolateral corners of the trigone (Figure 6). By regular sweeping of the cystoscope backwards and forwards and rotation of the endoscope the entire bladder mucosa can be visualized. Views of the anteroinferior bladder are obtained by suprapubic compression with the hand. At the completion of the examination, the irrigating fluid is evacuated from the bladder by removing the telescope and

Figure 6

Ureteric orifices

the instrument is slowly withdrawn. A bimanual examination of the pelvis is performed after the procedure.

Bladder biopsy

Bladder biopsy (Figures 7, 8) is the procedure most commonly performed during cystoscopy. Biopsy forceps are introduced down the cystoscope sheath via a port in the bridge, sometimes together with a diathermy wire. This allows cup biopsies of the mucosa to be taken. If required, the biopsy sites are

Figure 7

Bladder biopsy

Figure 8

Bladder biopsy

then cauterized with diathermy to prevent excessive bleeding.

Ureteric catheterization and stenting

The instrumentation and stenting of ureters should only be performed by clinicians such as gynecologic oncologists trained in this procedure since it is easy to damage the ureteric orifices and ureters. Ureteric catheterization and the placement of double J stents is achieved with the 30° telescope. There is a special port for the introduction of the stents which can be directed towards the ureteric orifices. A floppy-tipped, Teflon-coated guide wire is first placed into the ureteric orifice and advanced under fluoroscopic control into the renal pelvis. The double J stent is slid over the guide wire through the channel of the cystoscope and into the ureter (Figure 9). The stent is radio-opaque and its position is monitored by fluoroscopic control. Excessive force used in insertion of the guide wire or stent should be avoided. The proximal and distal ends curl to form a J shape when they are correctly placed in the renal pelvis and bladder respectively.

Flexible cystoscope

The patient is placed on the operating table or bed in the 'frog-leg' position. The cystoscope is lubricated and introduced into the urethra. The end of the cystoscope is passed into the bladder and deflected upwards. The midline of the anterior bladder is examined by withdrawing the instrument until the bladder outlet is encountered. The cystoscope is then pushed back into the bladder, rotated 30° and withdrawn again. This process is continued until the entire bladder has been

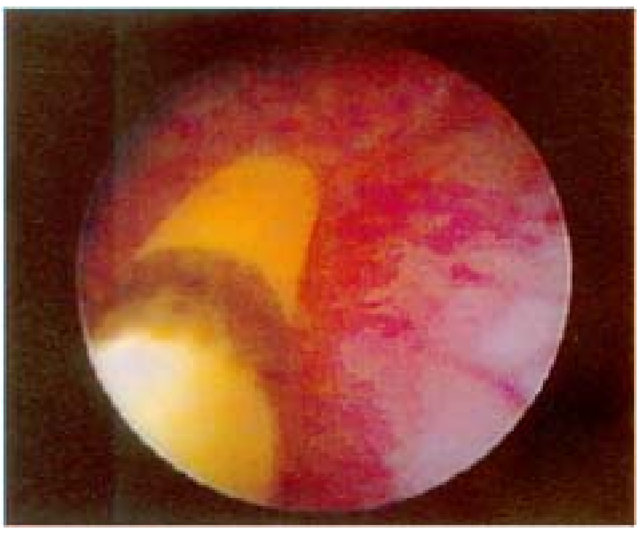

Figure 9

Introduction of the double J stent

inspected. Biopsy of the bladder mucosa can also be achieved by the passage of biopsy forceps down the instrumental channel of the cystoscope.

Postoperative care

No special postoperative measures are needed.

Bibliography

Calne RY, Pollard SG (1992) *Operative surgery*. London: Gower.
Carter DC, Russell RCG, Pitt HA (1996) *Atlas of general surgery*, 3rd edn. London: Chapman & Hall.
Cotton PB, Williams CB (1990) *Practical gastrointestinal endoscopy*, 3rd edn. Oxford: Blackwell.
Jackson E, Fowler JR (1992) *Urological surgery*. Mastery of Surgery series. New York: Little, Brown.
Reuter HJ (1987) *Atlas of urological endoscopy: diagnosis and treatment.* New York: Thieme.

6
Ovarian tissue cryopreservation and transplantation techniques

Erkan Buyuk
Kutluk H Oktay

Introduction

Modern improvements in cancer treatment regimens using aggressive chemotherapy radiotherapy, as well as bone marrow transplantation, can result in cure rates exceeding 90% for many cancers (Baird et al. 1999). However, this success has been accompanied by loss of fertility and premature menopause in many women cured of their disease. Ovarian cryopreservation and transplantation is one of the options aimed to preserve fertility in women who face a threat to their fertility. Discovery of modern cryoprotectants and progress in cryopreservation techniques led to successful cryopreservation of gametes, embryos and ovarian tissue. However, there is significant room for improvement in revascularization of tissues after auto-transplantation, as nearly two thirds of the ovarian reserve is lost during the initial ischemic state after grafting (Morales et al. 1995, Imthurn et al. 2000, Demirci et al. 2001).

Ovarian tissue cryopreservation

Ovarian tissue cryopreservation for future transplantation can be done in cancer patients as well as for other benign conditions where chemotherapy, radiotherapy, or surgically induced ovarian failure is anticipated. Table 1 summarizes the indications for ovarian tissue banking.

Tissue harvesting

As long as there is no contraindication, ovarian tissue is collected via laparoscopy In adult patients, we generally remove one ovary to obtain a large reserve of primordial follicles. However, in pediatric age groups, a large cortical biopsy may be enough since their ovaries harbor a larger number of follicles than the

Table 1 Indications for ovarian cryopreservation and transplantation

1.	**Cancer patients** Breast cancer (stage 0–III) Cervical cancer Childhood cancers • Hodgkin's lymphoma • non-Hodgkin's lymphoma (except Burkitt lymphoma) • Osteosarcoma • Ewing's sarcoma • Wilm's tumor
2.	**Bone marrow transplant patients** Aplastic anemia Sickle-cell anemia Autoimmune and immunodeficiency diseases (e.g. rheumatoid arthritis)
3.	**Autoimmune diseases** Collagen vascular diseases (e.g. SLE) Acute glomerulonephritis Behçet's disease
4.	**Adjunctive oophorectomy** Recurrent breast cancer Endometriosis
5.	**Benign ovarian tumors** Recurrent cysts Endometriosis
6.	**Prophylactic oopherectomy** BRCA-1 or -2 mutation carriers

SLE, systemic lupus erythematosus.

adult ovary (Newton et al. 1998). The whole ovary or ovarian cortical pieces are removed by a laparoscopic approach using a 5 mm scope inserted in the umbilicus and 5 mm and 12 mm trochars in the lower quadrants. Use of electrocautery is not recommended in order to avoid damage to ovarian cortex containing the follicles. The ipsilateral fallopian tube is left intact to allow a spontaneous pregnancy to occur in case an orthotopic transplantation is performed in the future. An endoscopic specimen bag is used to remove the ovary through the 12 mm trocar; the trocar is pulled out and the specimen is delivered through the 12 mm incision. This incision may need to be widened to extract a large ovary.

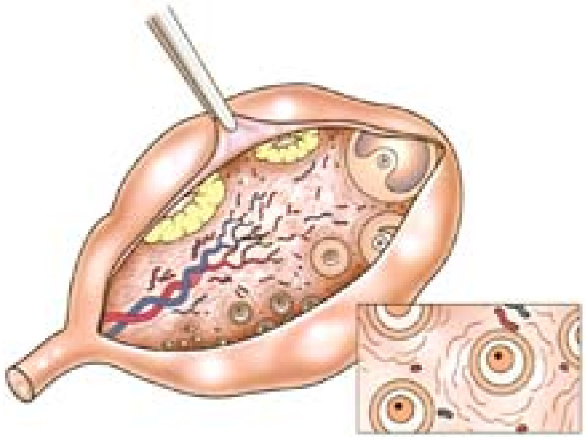

Figure 1

Preparation of ovarian tissue for cryopreservation. The ovary is bivalved through its hilum. Note that the primordial follicles are located predominantly in the cortex

Processing of the ovarian tissue

The aim of processing ovarian tissue before cryo-preservation is to obtain ovarian pieces small and thin enough for the cryoprotectants to easily permeate .The sample is transported to the laboratory on ice in Leibovitz L-15 medium. In the case of a whole ovary, it is bivalved through its hilum (Figure 1) and the cortex

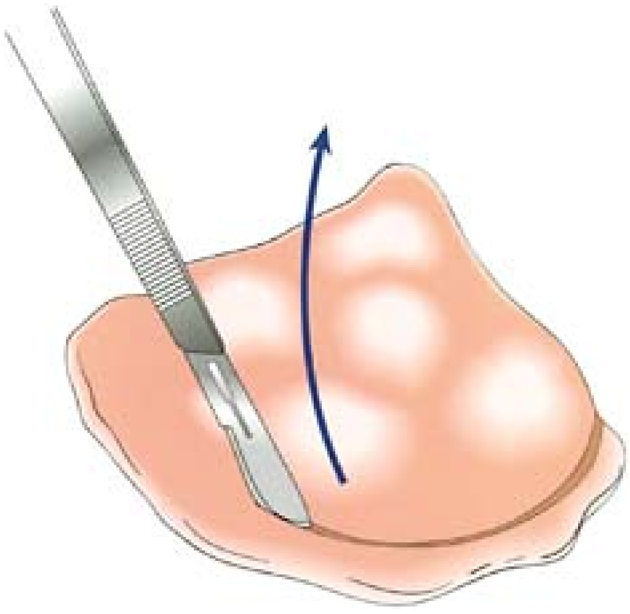

Figure 2

The cortex is dissected from the stroma

is separated from the medullary portion (stroma) using a number 10 blade (Figure 2). This step is undertaken because the primordial follicles are contained in the cortical portion and the medullary portion may decrease tissue permeation of cryoprotectants. The cortex is then divided into 10×5×1 mm strips using a no. 10 or 11 blade (Figure 3). The preparation is performed under a laminar flow hood and the tissue is kept in the medium throughout the process. The cortical pieces are then put in cryovials containing 1.5 ml of ovarian freeze solution (1.5 M 1,2 propanediol, 20% patient's own serum and 0.1 M sucrose in Leibovitz L-15 medium).

Cryopreservation and thawing

The cryovials are kept in ice for 30 minutes for the equilibration of the cryoprotectants. Cryopreservation is performed using a slow freeze protocol in a programmable freezer. The pieces are cooled to −7°C and seeded at this temperature. They are then cooled to −140°C and plunged into liquid nitrogen (Oktay 2001).
Thawing is done by a rapid thaw protocol in a 30°C water bath, followed by washing the tissues in decreasing gradients of cryoprotectant (Oktay 2001).

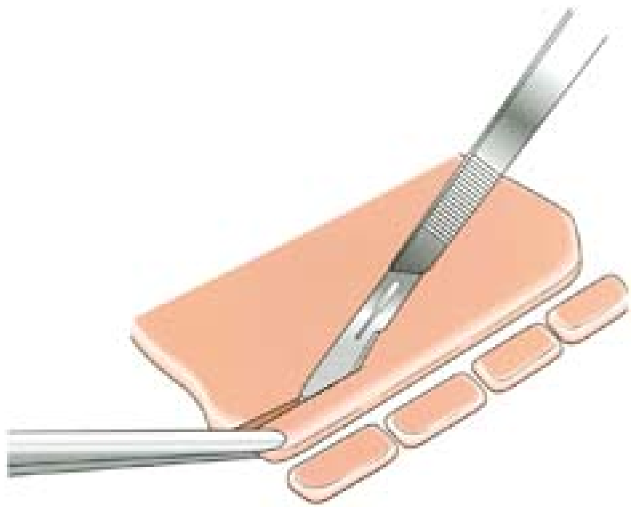

Figure 3

The cortex is divided into 10×5×1 mm strips

Ovarian transplantation techniques

Before performing ovarian transplantation, the risk of reseeding occult cancer cells should be kept in mind and the decision to perform ovarian transplantation should be made accordingly. Table 2 summarizes the risk of ovarian involvement in different cancers. For instance, the risk of ovarian involvement is higher in leukemia and neuroblastoma patients, compared to lymphoma or Wilm's tumor patients.
Transplantation can be done using an orthotopic or heterotopic approach. In orthotopic transplantation, the tissue is placed in the ovarian fossa (Oktay and Buyuk 2002). Although spontaneous pregnancy can in theory be achieved using this technique, the procedure is technically more challenging, and when there is a higher likelihood of ovarian involvement with cancer, it may be less desirable to graft ovarian tissue retroperitoneally. In heterotopic transplantation, the tissue is grafted into a place other than the ovarian fossa. The operation is done under local anesthesia and follow-up is easier with heterotopic transplantation.

Table 2 Risk of metastases to ovaries in various cancers

High risk
Leukemia
Neuroblastoma
Burkitt lymphoma
Moderate risk
Breast cancer
Stage IV
Infiltrative lobular histological subtype
Adenocarcinoma/adenosquamous carcinoma of the cervix
Colon cancer
Low risk
Breast cancer
Stages I–III
Infiltrative ductal histological subtype
Squamous cell carcinoma of the cervix
Non-Hodgkin's lymphoma
Hodgkin's lymphoma
Wilm's tumor
Ewing's sarcoma
Nongenital rhabdomyosarcoma
Osteogenic sarcoma

However, patients will always need an in vitro fertilization (IVF) procedure in order to conceive (Oktay et al. 2001a, b). In case of cancer recurrence, tissue sampling and removal will also be easily accomplished. The risk and significance of recurrent cancer at the transplant site are unknown.

Pelvic orthotopic transplantation

Following thawing and washing, the ovarian pieces are placed in a petri dish containing transport medium, and transported on ice to the operating room. In the operating room, 6–0 vicryl is used to string the strips by passing the needle between the cortex and the stroma of each strip under a microsurgical microscope (Figure 4). Several strings are formed depending on the number of the strips, and they are then anchored to a Surgicel frame (Ethicon, Somerville, NJ). 1–0 vicryl is used on the sides to further strengthen this frame. 0 vicryl sutures are then tagged to the apex and the base. Synchronously, the patient is anesthetized, and three trocars are inserted: an 11 mm one in the umbilicus, a 5 mm one in the right lower quadrant, and a 13 mm one (with fascia anchor) suprapubically. Using sharp and blunt dissection, a pocket is created in the ovarian fossa, posterior to the broad ligament, superior to the ureters, and inferior to iliac vessels in

Figure 4

The strips are strung on to 6–0 vicryl

Figure 5

The graft is loaded retrogradely into the 13 mm trocar

the supine position. The graft is then loaded retrogradely, into a 13 mm trocar (Figure 5), which is reinserted in the fascia anchor suprapubically. Pulling on the leading suture, the graft is dropped in the pelvis. The leading suture is then placed in the most dependent portion of the pocket, approximately 1 cm above the ureter, and the needle is passed through the peritoneum into the pelvic cavity (Figure 6). By pulling on this suture, the graft is wedged in the pelvic pocket. Next, the base suture is passed through the upper

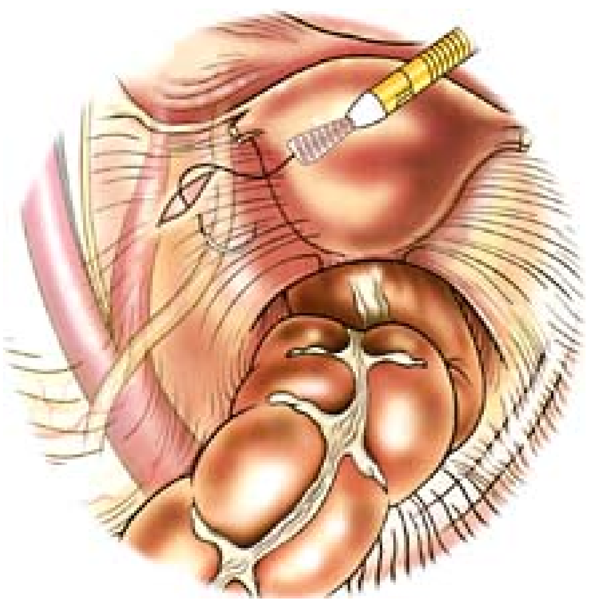

Figure 6

The leading suture is placed in the most dependent portion of the pelvic pocket

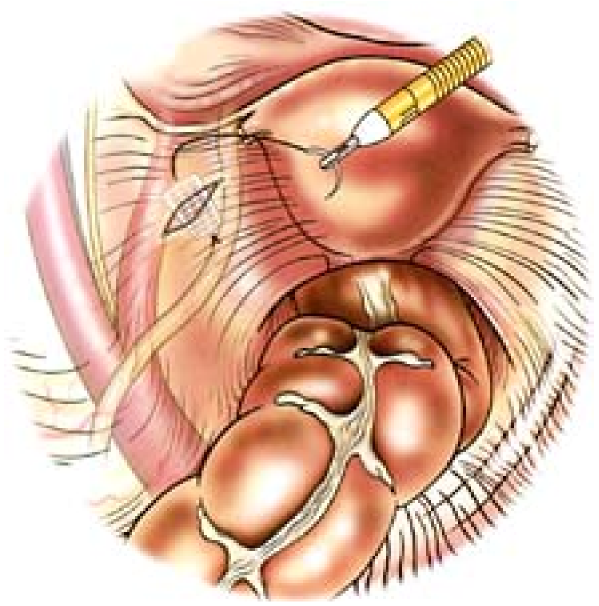

Figure 7

The graft is flattened and stretched against the pelvic side-wall

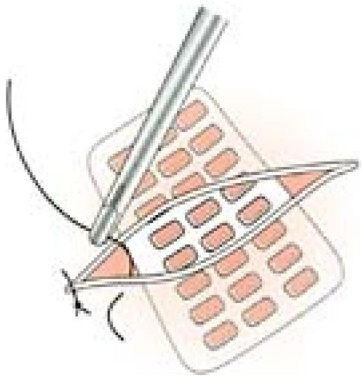

Figure 8

The pelvic peritoneum is closed with interrupted sutures

edge of the peritoneal pocket. The graft is stretched and flattened against the pelvic side-wall by pulling this suture from the intraperitoneal site (Figure 7). With an abundance of pieces, a second graft may be prepared and placed superior and caudal to the first one. Then, using an extracorporeal knot placement technique, the peritoneum is approximated with interrupted sutures (Figure 8). The base of the Surgicel frame is also included into the suture while closing the peritoneum to further secure the graft in place. The patient is given 150 IU/day of follicle-stimulating hormone (FSH) systemically for 7 days (Oktay et al. 2003). As beneficial effects on graft survival have been observed in animal studies (Richardson et al. 1987). The patient is also given 80 mg per day aspirin for 7 days, and started on hormone replacement therapy within 48 hours of the transplant, as it is thought that these treatments may enhance angiogenesis (Ries et al. 1999).

Forearm heterotopic transplantation

After thawing and washing as described previously, ovarian cortical strips are placed in phenol red-free Minimum Essential Medium Alpha Medium (with L-glutamine, ribonucleosides and deoxyribonucleosides, Invitrogen, cat. no. 41061–029), supplemented with 20% of the patient's own serum and 10 •g/mL cefotetan, and kept on ice. Then, each strip is tagged with 4–0 vicryl as described previously (Figure 9). The needle is cut, and the cortical pieces are left in the medium until the surgical site is ready for transplantation. To create a pocket for the graft under the skin of the forearm, a 1 cm transverse incision is made over the brachioradialis muscle, 5 cm below the antecubital fossa. If there is a cosmetic concern, the incision and the transplantation may be made more medially. A pocket is created between the fascia and the subcutaneous tissues using blunt dissection (Figure 10). Since this area is relatively vascular, attention must be given to avoid major bleeding. As the ovarian tissue will acquire its blood supply from these vessels, extensive cauterization should be avoided.

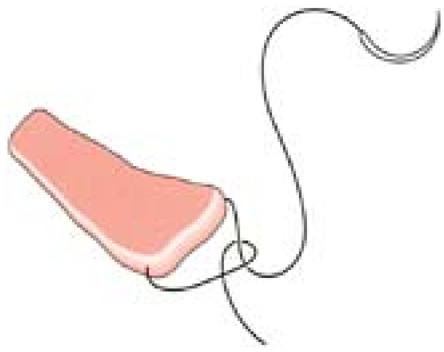

Figure 9

Each ovarian strip is tagged using 4–0 vicryl

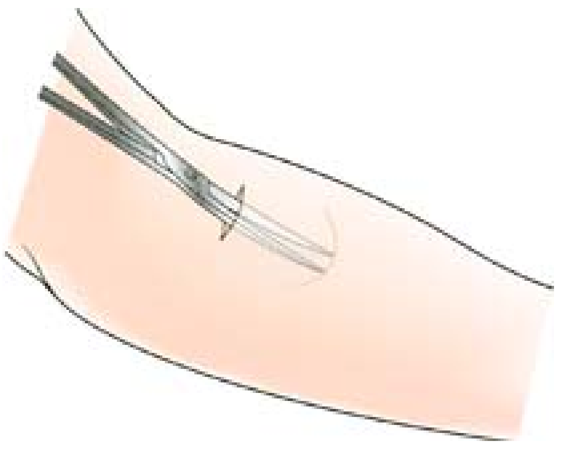

Figure 10 A pocket is created under the skin of the forearm

Following the creation of the pocket, the free end of the suture is threaded on to a reusable needle. A semi-circle cutting needle with a chord length of 25–38 mm (depending on the size of the strips) is inserted as far as possible into the subcutaneous pocket. It is then passed through the skin, and the cortical piece is wedged into the pocket by pulling on this suture (Figure 11). Care must be taken to place the strips with their cortical side facing up. The needle is removed, and the free end of the suture is held with a Mosquito clamp. The main purpose of this suture pull-through technique is to guide the tissue placement and to avoid overlapping the strips, rather than secur-

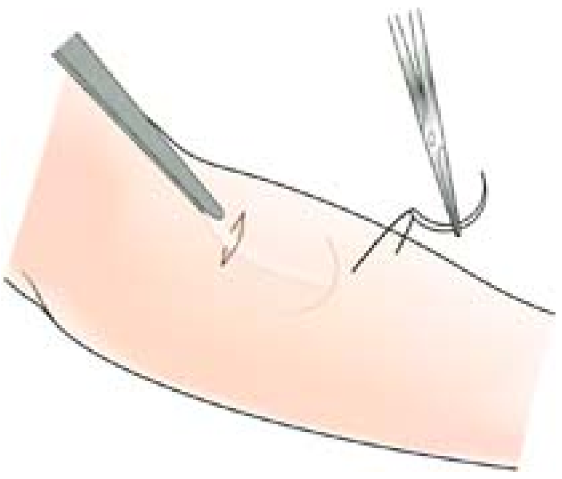

Figure 11 Each strip is inserted into the forearm pocket using a pull-through technique

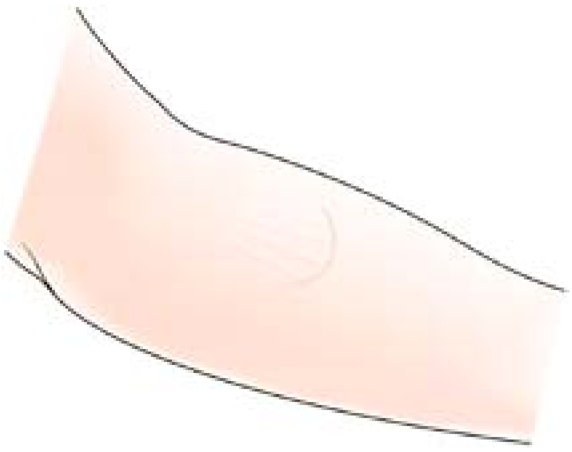

Figure 12 Ovarian cortical strips are fanned out under the skin of the forearm

ing them in place. Depending on the patient's forearm size, 5–15 cortical strips can be placed beneath the forearm skin (Figure 12). Following the placement of the last strip, the sutures are cut. Then the skin is closed subcuticularly and a non-pressure dressing is applied in order not to reduce the blood flow to the area, seventy five IU/day of FSH is injected directly in the grafts for 7 days, starting on the day of surgery. The patient's forearm is splinted for 72 hours to prevent dislodgment of the graft due to muscle movement. In addition, 80 mg per day aspirin is administered for 7 days, and hormone replacement is started within 48 hours of the surgery as in the case of orthotopic transplantation. The latter is stopped with the first sign of graft function. Ovarian function usually returns within 3 months.

References

Baird DT, Webb R, Campbell BK, et al. (1999) Long-term ovarian function in sheep after ovariectomy and transplantation of autografts stored at −196°C. *Endocrinology* **140**(1):462–71.

Demirci B, Lornage J, Salle B, et al. (2001) Follicular viability and morphology of sheep ovaries after exposure to cryoprotectant and cry op reservation with different freezing protocols. *Fertil Steril* **75**(4):754–62.

Imthurn B, Cox SL, Jenkin G, et al. (2000) Gonadotrophin administration can benefit ovarian tissue grafted to the body wall: implications for human ovarian grafting. *Mol Cell Endocrinol* **163**(1–2):141–6.

Morales DE, McGowan KA, Grant DS, et al. (1995) Estrogen promotes angiogenic activity in human umbilical vein endothelial cells in vitro and in a murine model. *Circulation* **91**(3):755–63.

Newton H, Fisher J, Arnold JR, et al. (1998) Permeation of human ovarian tissue with cryoprotective agents in preparation for cryopreservation. *Hum Reprod* **13**(2):376–80.

Oktay K (2001) Ovarian tissue cryopreservation and transplantation: preliminary findings and implications for cancer patients. *Hum Reprod Update* **7**:526–34.

Oktay K, Buyuk E (2002) The potential of ovarian tissue transplant to preserve fertility. *Expert Opin Biol Ther* **2**(4):36l–70.

Oktay K, Aydin BA, Karlikaya G (2001a) A technique for laparoscopic transplantation of frozen-banked ovarian tissue. *Fertil Steril* **75**(6):1212–16.

Oktay K, Economos K, Kan M, et al. (200 1b) Endocrine function and oocyte retrieval after autologous transplantation of ovarian cortical strips to the forearm. *JAMA* **286**:1490–3.

Oktay K, Buyuk E, Rosenwaks Z, Rucinski J (2003) A technique for transplantation of ovarian cortical strips to the forearm. *Fertil Steril* **80**:193–8.

Richardson SJ, Senikas V, Nelson JF (1987) Follicular depletion during the menopausal transition: evidence for accelerated loss and ultimate exhaustion. *J Clin Endocrinol Metab* **65**(6):1231–7.

Ries LAG, Percy CL, Bunun GR. (1999) Introduction. In: Ries LAG, Smith MA, Gurney JG, et al, eds. *Cancer incidence and survival among children and adolescents: United States SEER Program 1975–95*, National Cancer Institute, SEER program. Bethesda, MD: NIH Pub. No. 99–4649; 1999:1–15.

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7
Sentinel node mapping in gynecologic tumors

Robert L Coleman
Charles Levenback

Introduction

Advances in surgical management among the solid tumors have developed in response to a variety of catalysts over the years. One of these has been the pursuit of surgical precision—balancing maximal survival against morbidity of therapy. This relatively recent concept derives from a combination of an improved understanding of disease biology and the identification of effective adjuvant therapies, which have allowed modification of traditional surgical paradigms and procedures. Lymphatic mapping and sentinel node identification, new to gynecologic malignancies, represents one of these advances, which among diseases, such as malignant melanoma and breast cancer, have radically altered classic surgical practices once deemed 'the final achievement of surgery' (Way 1951). Integration of lymphatic mapping into triage and management has dramatically improved treatment precision by offering better disease characterization with the potential for reduced toxicity through less radical intervention. 'Proof-of-principle' studies are currently being undertaken. The purpose of this chapter is to introduce the concept of lymphatic mapping and sentinel node identification as it is being developed among the gynecologic cancers and to report on the early, albeit promising, experience, particularly in vulvar and cervical malignancy.

What is lymphatic mapping?

Lymphatic mapping is simply documentation of the regional lymphatic spillways from an organ of interest. While obvious in our current understanding of the metastatic process, the role of the regional lymphatics and their direct relationship with the major anatomic structures was somewhat elusive in early studies and anatomical dissections. Limited by evaluation of putrefied and fixed tissue, reliable identification of the lymphatic channels to the regional lymph nodes was a major challenge for early anatomists. Painstaking dissections led to the production of remarkable drawings of lymphatic anatomy, which served as reference materials for future generations of surgeons who ultimately designed operative procedures to remove these 'at-risk' sites. Indeed, the 'en bloc' resection championed by Halsted is heralded as one of the first great advances in the primary surgical treatment of solid tumors

Figure 1

Vulvar and perineal lymphatics as depicted by Sappey in 1874. Use of mercurial dyes in cadaveric tissue led to the erroneous depiction of lymphatic vessels in the vulva and perineum draining across the labiolcrural folds

(Halsted 1997). To aid the visualization of individual lymphatic vessels, various dyes were developed and used, including a number of mercurial compounds. While an important adjuvant, the dye technique most likely contributed to some early erroneous depictions of lymphatic anatomy, such as Sappey's illustration of vulvar lymphatics crossing the labiocrural fold (Parry-Jones 1963) (Figure 1). Subsequent development of more lymphotrophic dyes, techniques of administration and study of live tissues provided a more 'functional' understanding of the regional lymphatics. Focused on gynecology, these functional pathways have been well characterized by Plentyl and Friedman (1971) in their landmark monograph, *Lymphatic Anatomy of the Female Genital Tract*.

Historical perspective

The purpose of clinical lymphatic mapping is identification of the node or nodal group that receives the principal and primary flow from the target organ (Figure 2). Theoretically, these tissues hold the highest promise for disease characterization, as they should represent the first localization and highest statistical risk for early metastatic spread. In the early 20th century, the French gynecologists Leveuf and Godard (1923) studied the lymphatic anatomy of the cervix by injecting Gerotti blue into the services of neonatal cadavers. They found that the injected dye reproducibly drained to a lymph node usually found in the obturator space or at the bifurcation of the iliac vessels. They named this the *principal* lymph node. The term *sentinel node* is most often credited to Ernest Gould, who proposed that the lymph node found at the junction of the anterior and posterior facial veins was the first and most important basin for patients with parotid cancer (Gould et al. 1960). Based on observations in 28 patients, he reasoned that if a negative node in this anatomic region was found it would be unlikely that other regional nodes would contain disease and thus, one could forego a full neck

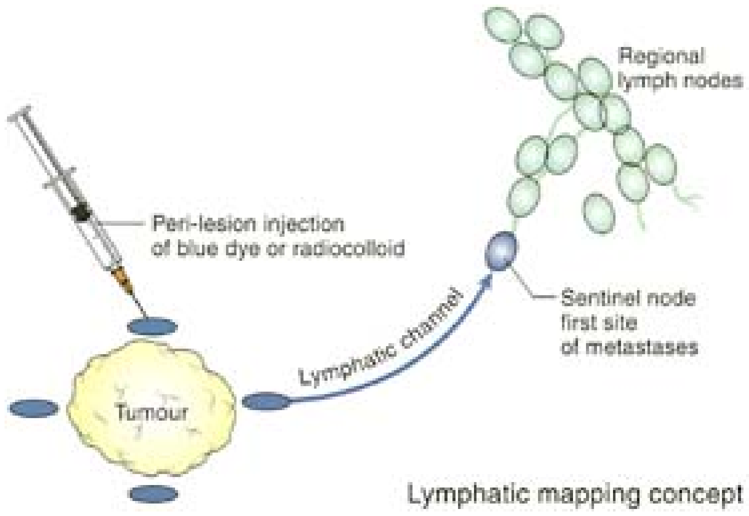

Figure 2

Schematic of the concept of lymphatic mapping. A preferred pathway from the tumor primary to the regional basin drains into the sentinel node dissection. However, it was Ramon Cabanas (1997), who combined the concepts of regional lymphatic flow and selective regional node identification into the technique of modern lymphatic mapping. Studying penile cancer patients with lymphography (performed via cut-down and canalization of the dorsal lymphatic of the penis), he found that a sentinel lymph node was always located among the superficial inguinal nodes. He also noted that the sentinel node was involved with disease in all patients who had metastases and that it was the only node positive in a proportion of patients (12 of 80 cases). He suggested that only those patients with a positive sentinel node required complete lymphadenectomy. These findings have been corroborated in other solid tumors including malignant melanoma and breast and vulvar carcinomas.

Mapping techniques

Blue dye

Developmental steps in refining the lymphatic mapping technique have been promulgated by a need to simplify the procedure and to develop an effective intraoperative strategy enabling precise nodal identification and treatment triage in one step. The first compounds used in this progression were selective lymphotrophic dyes. Wong et al. (1991) experimented with isosulfan blue, methylene blue and cyalumede in a feline model and found that isosulfan blue associated better with lymphatic vessel uptake and sentinel node identification (Figure 3). Alternative mapping materials that have been successful include flourescein and patent blue-V, however, the former requires a dark room and is associated with tissue extravasation (Bostick and Givliano 2000). Typically, 2–5 milliliters of dye is injected via a small gauge needle (e.g. 25 gauge) into the dermis or tissue surrounding the primary tumor. Intradermal injection is important in lesions of the vulva in order to access the superficial dermal lymphatics that communicate with the groin (Figure 4). Deep subcutaneous injection will result in uptake into the deep lymphatics accompanying the named vessels of the vulva and perineum to the pelvis. In the cervix and other solid organs, such as the uterus and ovaries, the injection is made deep enough to access the stromal lymphatic elements. These are generally located within 5 mm of the overlying epithelium. In some organs, such as the uterine corpus and the vagina, the anastomotic plexus is well developed and intercommunication throughout the entire organ can be

Figure 3

Vial of isosulfan blue trademarked as Lymphazurin 1% (5 cc)

accomplished with a single injection. However, preferred routes of lymphatic drainage exist even among these situations, best illustrated in the vagina where distal lesions drain into the inguinal femoral system and proximal lesion into the low pelvic lymphatics mirroring cervical drainage (Plentl and Friedman 1971) (Figure 5).

Once the dye is deposited, uptake is rapid and can be observed in real-time for some sites. Localization into the sentinel node occurs between 5 min and 15 min and may remain in the node for up to 60 min before dissipating. Procedures that require time to identify 'at-risk' nodal basins should take into account these temporal constraints prior to dye delivery For instance, in cases of cervical cancer mapping where laparotomy is planned, it is preferable to have the abdominal field exposed at the time of dye deposition, given the large number of potential lymphatic basins to be evaluated and the rapidity of the dye uptake in the vessel-rich parametrium.

Although these dyes are largely lymphotropic and weakly bound to serum proteins, side effects and complications have been observed. Fortunately, these

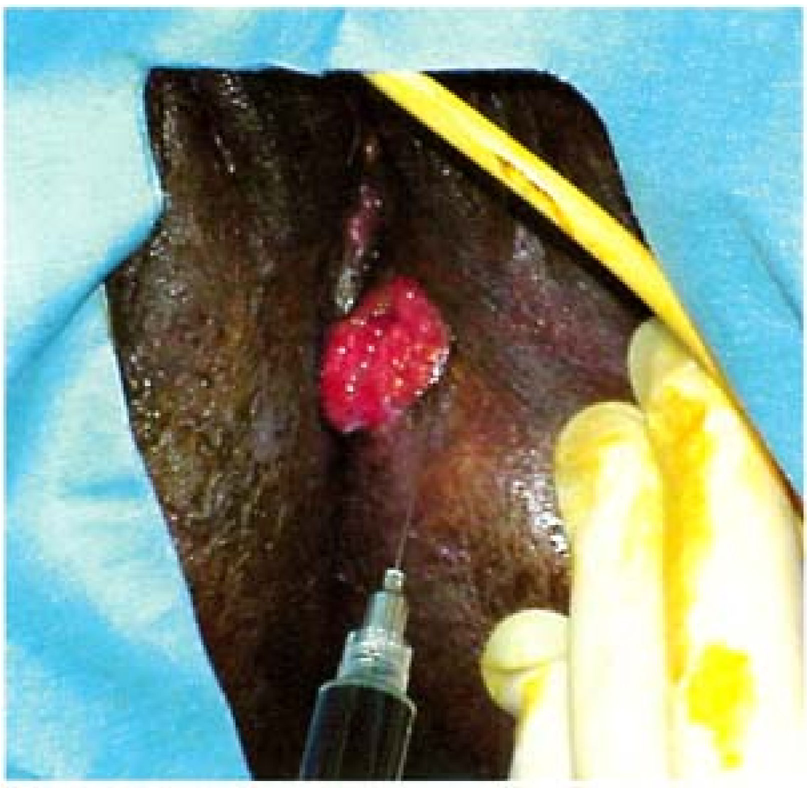

Figure 4

Intradermal injection around a vulvar carcinoma. Deeper injections will drain along the deep lymphatics that line the vascular supply to the vulva

are infrequent, occurring in approximately 1–2% of patients (Leong et al. 2000). Primary excretion of isosulfan blue is biliary and thus, patients with hepatic insufficiency may be at increased risk for complications. The most common effect seen with dye administration is a transient cohort change (gray or blue hue) in the skin with discoloration of the urine. In some cases it may be quite dramatic, albeit of limited duration. Allergic reaction and anaphylaxis have been rarely reported and manifest in classic manner with cardiovascular collapse, erythema, angioedema, bronchospasm, urticaria, gastrointestinal symptoms and pulmonary edema (Sadiq et al. 2001). While these effects are generally observed within 10 min of intravenous injection, most mapping procedures are performed by intradermal injection and thus, could be delayed as much as 30 min. Treatment is supportive. Occasionally, a pseudo-anaphylaxis clinical picture may present, usually first indicated by progressive loss of oxygen saturation. Compounded by gray skin coloring the condition is of concern but lacks features of cardiovascular collapse. Coleman et al. (1999) described this condition and hypothesized its etiology as related to dye interference with non-invasive pulse oximetry saturation algorithms. Peak absorbance of isosulfan blue is 646 nm which is very near that of oxyhemoglobin (660 nm), one of two hemoglobin species measured by non-invasive pulse oximetry. The short-lived condition may be confirmed by a simple arterial blood gas determination.

Radiocolloid and lymphoscintigraphy

The blue staining of a node with identification of at least one blue-stained afferent lymphatic channel entering the node remains the gold standard for assessment of whether a lymph node is or is not a true sentinel node. However, introduction of techniques, such as radioactive colloid injections and lymphoscintigraphy, have enhanced the accuracy of detecting the sentinel node. These have been particularly useful in identifying nodes outside of their routine anatomical landmarks of dissection and in aiding the surgeon intraoperatively via a hand-held gamma probe to identify sentinel nodes which have stained poorly or ambiguously

Historically, injection of radionuclides into human subjects to localize regional lymph nodes was first reported by Sherman and Ter-Pogossian in 1953. Numerous radiolabeled compounds have since been used for this purpose. The first gynecologic application of lymphoscintigraphy was in 1982, when

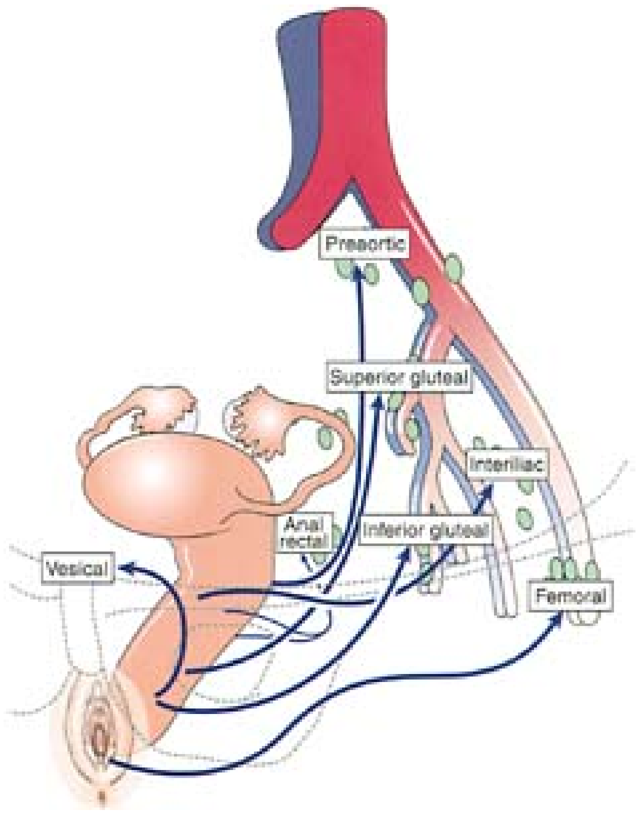

Figure 5

Lymphatic drainage of the vagina. A rich anastomotic network exists that allows intercommunication of lymph throughout the organ. However, specific locales of the vagina will preferentially drain to regional basins from the inguinofemoral nodes to the external iliac nodes

Iverson and Aas (1993) studied lymphatic drainage in 24 patents with stage IB cervical cancer. While they were unable to distinguish metastatic from non-metastatic nodes by radiocolloid uptake, they did remark that radioactivity was higher in certain nodes compared to the background—possibly an early representation of a sentinel node. However, it was Morton et al. in 1992, who brought this modality to the clinical arena by demonstrating its utility in identifying 'at-risk' node basins among 223 cutaneous melanoma patients. Since this report, validation of the strategy has occurred in a number of solid tumors including, head and neck, endocrine, gastrointestinal, genitourinary, breast and reproductive tract cancers.

The ideal radiocolloid must gain access to the lumen of the initial lymphatic channel in sufficient quantity for the lymph vessels to be seen on the dynamic scans. It should combine a rapid and predictable transport toward the sentinel node with persistent retention. The particle size of the radiocolloid is a critical factor in the ease with which these tracers enter the lymphatic system (Table 1). Large particles (500–2000 nm) remain trapped at the injection site and small particles (4–5 nm) will penetrate the capillary membranes and will not be available to migrate through the lymphatic channels (Ege 1976, Henze et al. 1982). In the United States, the most commonly used radiopharmaceutical is filtered technetium-99m sulfur colloid. This agent has a small particle size (<100 nm), it is uniformly dispersed, highly stable, and has a short half-life (gamma-emitter).

Injection flow rate of a radiocolloid is important in the success of sentinel node identification. Once the particles enter the lumen of the lymphatic capillaries, they will move freely and uniformly towards the draining lymph nodes. The valves in the lymphatic vessels will generally not allow retrograde flow. Lymphatic flow is fastest in the leg and foot and slowest in the head and neck. The study is performed by injection of 0.5–1 cc (1–2 mCi) intradermally and perilesionally as with blue dye. A lymphoscintigram is then made to visualize localized uptake (Figure 6). Dynamic images are usually acquired for a total of 20 min. The lymphatic channels are best appreciated by summing the individual dynamic frames to produce a composite dynamic image. Delayed scans are then performed at 2.5–3 h following injection of the radiocolloid tracer. These delayed scans should include all node fields that can possibly receive drainage from the injection site. Each static acquisition should be 5–10 min in length to ensure that even very faint sentinel nodes are detected (Uren and Howman-Giles 2002).

The intraoperative detection of the sentinel node relies not only on the visual inspection of the lymphatic basin, but also on the assessment of the radio-active colloid in the sentinel node through the aid of a gamma detection device. This hand-held sensor contains a gamma-sensitive crystal with a preamplifier, and a reading unit (Figure 7). There are several gamma probes for intraoperative use including laparoscopic devices that can be used in a large spectrum of clinical scenarios. Specificity and accuracy of these devices can be augmented with the use of collimation which will help to reduce background and 'bleed-through' radioactivity, frequently encountered in sites where the primary tumor is near its drainage lymphatic basin (Figure 8). The parametrial nodes in uterine cervical primary and the medial inguinofemoral nodes in an anterior vulvar cancer are good examples of challenging

Table 1 Characteristics of radionuclides (adapted from Wilhelm et al. 1999)

	^{99m}Tc-SC	*^{99m}Tc-HCA*	*^{99m}Tc-HSA*
Particle size (nm)	100–400 (Filtered: 15–50 nm)	5–80	2–3
Transit time to SN (min) Range (min)	11 (1–60)	10 (1–65)	5 (1–75)
Injection dose at site (3 h)	76%	83%	–
Visible nodes (30 min)±SD	2.1±1.9	2.1±1.3	2.2±0.9
Washout $T_{1/2}$±SD (h)	14±12.7	7.5±6.4	4.3±1.4

SN, sentinel node
^{99m}Tc-SC, technetium-99m sulfur colloid; ^{99m}Tc-HCA, technetium-99m human colloidal albumin; ^{99m}Tc-HAS, technetium-99m human serum albumin.

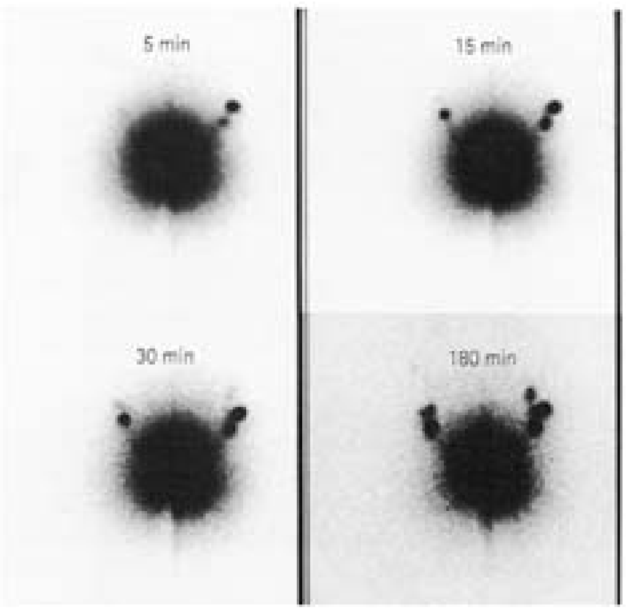

Figure 6

Example of the temporal relationship between time of injection and visualization of the regional basins. This example is from a woman with a stage II vulvar cancer. The time between scans is listed. It is debated as to whether the lateral and newly visualized nodes at 180 min represent secondary basins or ‘second echelon’ nodes

mapping areas. Use of these radiopharmaceuticals appears to be safe given their low dose energy, particle size and rapid washout rate. Extensive testing has been conducted to determine the safety to health care workers. The amount of radiation exposure from the technique is very small and the cumulative effect is still well within acceptable levels (Eshima et al. 2000, Florica et al. 2001).

Sentinel nodes: pathologic examination

Traditionally, pathologic assessment of a lymphad-enectomy specimen entails teasing out individual lymph nodes from the surrounding fat pad, bisecting each and embedding them in paraffin for H&E staining. Typically, one slide from each side of the nodes is evaluated. From the pathologist’s point of view, each slide has an equal chance of containing metastatic disease. While standardized, the technique evaluates only an estimated 0.1% of the total nodal volume raising the possibility of a false-negative diagnosis. Sentinel node retrieval provides the opportunity for improved precision since the pathologist can focus his/her search for metastatic disease. In this manner, the sentinel node larger than 1 cm can be step-sectioned at 2–5 mm intervals and slides developed from each cut surface (Figure 9). Nodes smaller than this may be totally imbedded or bivalved for evaluation. In breast cancer patients, step-section processing has revealed underestimation of micrometastatic disease in 9–33% of node-negative cases (ILBCSG 1990). The expansion and availability of immunohistochemical techniques

Figure 7

Portable gamma probe for use in vulvar and laparotomy facilitates intraoperative lymphatic mapping

Figure 8

Local injection of radiocolloid may concentrate so highly as to obscure potential identification of proximally situated sentinel nodes. In this example of cervical injection it is easy to appreciate the difficulty of identifying a parametrial node

during the 1990s has afforded an additional measure of accuracy by allowing pathologists to evaluate the sentinel node tissue sections for specific markers. In the case of gynecologic epithelial tumors such as cervical and vulvar cancer, specific cytokeratins (AE1/AE3 and DF3) are made from pairs of step-sectioned nodal tissue and evaluated for micrometa-

Figure 9

Harvested sentinel nodes are serially sectioned (bread-loafed) to provide additional material for hematoxylin and eosin staining as well as immunohistochemistry

static deposits (Figure 10). The technique has been adapted to be available intraoperatively (Evdy et al. 2003, Munakata et al. 2003, Nahrig et al. 2003). The value immunohistochemisty adds to serial sectioning is debated, but individual series from gynecological lymphatic mapping procedures has reported unidentified micrometastatic disease in up to 4% of negative nodes (de Hullu et al. 2000). An increasingly important question will be how to manage patients with negative sentinel nodes on traditional H&E staining but positive by immunohistochemisty or other biochemical marker.
Van Trappen et al. (2001) used rapid polymerase chain reaction (PCR) testing for cytokeratin 19 in the lymph nodes of radical hysterectomy patients. Lymphatic mapping was not performed, however, it appears that the highest concentration of CK-19-positive nodes was found at the common sites of sentinel nodes. CK-19 was found in only one lymph node from nine patients with benign disease whereas 44% of the H&E-negative lymph nodes in the cervical cancer patients had CK-19 detected. A clearer understanding of micrometastatic disease and how the regional lymphatic process of these cells could form the basis of future molecular work.

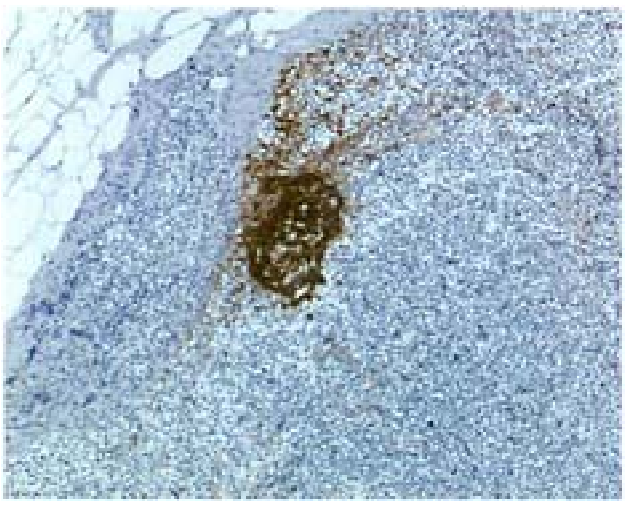

Figure 10

Micrometastasis of squamous cell carcinoma in an inguinofemoral sentinel lymph node. Small tumor deposits may be difficult to distinguish by hematoxylin and eosin staining in the background nodal architecture. In this example, cytokeratin AE1/AE3 is highlighted through immunohistochemistry. (Courtesy of Ate van der Zee)

Clinical experience

Vulvar cancer

Important contributions dating back to the mid 20th century have identified functional anatomic features, which particularly suit vulvar carcinoma patients with the lymphatic mapping concept. The most important are the clear identification of an ordered pathway from the vulva to the regional inguinofemoral lymphatics and the infrequency of 'in-flight' metastatic deposits in the skin bridge between the primary lesion and the regional basin. Parry-Jones (1963) demonstrated that the vulvar lymphatics did not cross the labiocrural folds as had been previously suggested. He demonstrated by lymphography that vulvar lymphatic flow drained predictably to the inguinofemoral basin. In the late 1970s, DiSaia and colleagues (1979) first attempted to apply these concepts in a treatment strategy directed to reducing the morbidity associated with standard radical vulvectomy and inguinofemoral lymphadenectomy. In a manner similar to that of Gould in 1960, these investigators designated the 8–10 anatomically situated superficial inguinal lymph nodes as the *sentinel nodes* of the vulva. They reasoned that if these nodes were histologically negative then the femoral nodes would be negative and one could forego deep inguinal dissection resulting in, among others, reduced wound breakdown. Unlike Cabanas (1977), there was no attempt to identify a solitary node directly draining the primary tumor. Several other groups have investigated the sentinel node concept proposed by DiSaia with mixed results. While Berman et al. (1989) reported no groin relapses in a group of 50 early-stage vulvar cancer patients undergoing superficial inguinal lymphadenectomy, Stehman et al. (1992) documented groin recurrences in 7.3% of the 121 patients with negative superficial inguinal nodes. This compared with a recurrence rate of less than 1% following formal inguinofemoral lymphadenectomy with negative nodes in a group of more than 300 patients participating in a Gynecologic Oncology Group (GOG) protocol (Homesley et al. 1986). On the basis of the GOG results, most gynecologic oncologists have abandoned superficial inguinal lymphadenectomy as it was initially purported. It is noteworthy, though, that despite even this manner of limited groin dissection, wound complications and chronic lymphedema were observed in 29% and 19%, respectively, highlighting the true 'carrot' of selective node evaluation, if validated.

The first report to utilize blue dye to identify a single sentinel node in vulvar carcinoma appeared in 1994 by Levenback and colleagues (1994). This group, following the growing experience of similar mapping techniques in malignant melanoma, identified sentinel nodes in 7 of 9 patients and in 7 of 12 groins. These authors concluded that the technique was feasible. Subsequent reports have vastly expanded and largely confirmed this experience.

Table 2 presents the available data from clinical trials evaluating one, either or both node-localizing techniques (blue dye, lymphoscintigraphy) in patients with operable vulvar carcinoma. Although the collective experience is comparatively small, interest is expanding and has attracted an international investigative audience. Currently, the GOG is evaluating the feasibility of lymphatic mapping in a multi-institutional setting.

Levenback and colleagues (2001) updated their collective experience on 52 patients undergoing blue dye localization. A sentinel node was identified in 46(88%) patients and in 57 of 76(75%) dissected groins. Independent effects hampering sentinel node identification were prior excisional biopsy, midline tumor location and operator experience. A median of one sentinel node was identified in each groin. The sentinel node was not found in 2 of the 12 groins that ultimately proved to have metastatic disease. Both events occurred in the first two years of the study. There were no false negative identified sentinel nodes. The authors demonstrated that following a short

Table 2 Literature summary of vulvar sentinel node trails

Author	*Date*	*No. patients*	*Blue dye*	*Tracer*	*Lymphoscintigraphy*	*ID rate*	*False negative SNL*
Levenback et al.	1994	9	Yes	No	No	58%	0
Levenback et al.	2001	21	yes	No	No	66%	0
DeCesare et al.	1999	10	No	Yes	Yes	100%	0
DeCicco et al.	1997	15	No	Yes	Yes	100%	0
De Hullu et al.	1998	10	yes	Yes	Yes	100%	0
Tavares et al.	2001	15	Yes	Yes	Yes	100%	0
Molpus et al.	2001	6	Yes	Yes	Yes	100%	0
Makar et al.	2001	6	Yes	Yes	Yes	100%	0
Sideri et al.	2000	44	No	Yes	Yes	100%	0
Ansink et al.	1999	51	Yes	No	No	56%	2(4%)
De Cicco et al.	1998	37	No	Yes	Yes	100%	0
De Hullu et al.	2000	59	Yes	Yes	Yes	100%	0
Levenback et al.	2001	52	Yes	No	No	88%	2(4%)
Sliutz et al.	2002	26	Yes[#]	Yes	Yes	100%	0
Moore et al.	2003	21	Yes	Yes	Yes	100%	0

ID, identification; SLN, sentinel node location.

learning curve and limiting the procedure to patients with clinically non-suspicious nodes and T1 or T2 squamous cell carcinoma lesions, virtually all patients (95%) were found with sentinel nodes.

A similar study by Ansink et al. (1999) had different results. In this multicenter study involving 51 patients undergoing blue dye lymphatic mapping, sentinel nodes were detected in just 56% of the 93 groins dissected. All tumors were squamous cell histology and had clinically non-suspicious groins. Nine groins were found with metastatic disease, 6(66%) of which the sentinel node was the only metastatic node. However, in 2 cases, a sentinel (blue) node was found and was histologically negative, yet metastatic disease was identified in non-sentinel nodes. The low sentinel identification rate and false-negative cases led these authors to conclude that the blue dye alone technique was not feasible and that combination with lymphoscintigraphy should be further studied. Feasibility concerns notwithstanding, the recommendation is of merit given the relative rarity of this tumor and the ability for lymphoscintigraphy to shorten learning curve proficiency. As seen in Table 2, sentinel node localization using lymphoscintigraphy alone or combined with blue dye is highly successful. De Cicco et al. (1998) studied 37 squamous T1 and T2 patients with preoperative and intraoperative lymphoscintigraphy alone. Bilateral groin dissection was performed if the primary lesion was within 2 cm of a midline structure. At least one sentinel lymph node was identified in each patient. Eight patients were identified with metastatic disease, including 5(63%) patients where the sentinel node was the only positive node. All 29 cases with negative sentinel nodes had negative groin histology. If lymphoscintigraphy did not identify a sentinel node in a groin, no metastases were found at surgery. Sideri et al. (2000) updated this group’s experience with 44 similarly staged and studied patients. A sentinel node was identified in each case. In 77 dissected groins, 13 cases demonstrated metastatic disease—all in sentinel nodes. In 10 cases, the sentinel node was the only positive node. These authors addressing the negative predictive value of an identified sentinel node concluded that if the technique was validated, less aggressive dissection of the groin could be entertained if the sentinel was histologically negative.

De Hullu and colleagues (2000) studied preoperative and intraoperative lymphoscintigraphy in combination with blue dye localization. In this study of 59 patients with T1 and T2 epidermoid cancers, sentinel nodes were identified in all patients with at least one of the techniques. Bilateral groin dissection was performed if the primary lesion was within 1 cm of a midline structure. Of the 107 groin dissections performed, a sentinel node was found in 95(89%). The authors noted that they relied primarily on the gamma probe to isolate sentinel lymph nodes, as blue sentinel nodes were observed in just 60% of cases. Metastatic disease was found in 20(34%) patients and in 27(25%) groins. In 15(54%) groins, the sentinel node was the only positive node. In this study immunohistochemical ultrastaging with cytokeratin staining was additionally performed. In 102 histologically negative sentinel nodes, 4(4%) were found with micrometastatic disease. The authors concluded that lymphatic mapping was feasible in this manner and that ultrastaging by step-sectioning and staining with immunohisto-chemical methodology may identify micrometastatic disease in some cases. A similar experience was reported by Moore and colleagues (2003) in 21 clinically node-negative stage I–IV vulvar cancer patients. Using a combined technique, all 9 patients with metastatic disease were identified by lymphoscintigraphy compared to just 3 of 9 patients with blue dye alone. However, in 2 of 31 dissected groins the sentinel node was described as blue only, not containing radio-colloid; similarly, just 29 of 89(33%) sentinel nodes retained characteristics of both tracers. It is not known which tumoral features impact the uptake of these individual components, thus making it prudent to use both at least early in the surgeon's experience. Overall, false-negative rates among series using lymphoscintigraphy, either alone or in combination with blue dye, have been very low but likely reflect the single institution experience of skilled surgeons.

Potential applications

One desirable outcome of sentinel node mapping investigation is to demonstrate the safety in perform-

Figure 11

A potential evolution of vulvar lymphatic mapping is limited and selective node sampling through a biopsy incision of 3 cm or less. A blue node with radiocolloid activity is depicted in this photograph

ing less than radical excision (even sentinel node-only biopsy) of the groin nodes and thereby reducing postoperative and long-term morbidity (Figure 11). This concept has been reported in two small series to date. Rodier et al. (1999) reported on 6 epidermoid and 2 melanoma vulvar cancer patients undergoing sentinel node biopsy alone. Both lymphoscintigraphy and blue dye were used for sentinel node localization. A sentinel node was identified in all patients. One case was found with metastatic disease. The authors report that the technique was successful in all but one case. This patient with a histologically negative sentinel node was found with a groin recurrence in a medial location 6 months postoperatively Cytokeratin ultra-staging was not utilized. In the second report by Terada et al. (2000), nine patients with epidermoid carcinoma underwent sentinel node biopsy after undergoing localization with lymphoscintigraphy and blue dye. A positive sentinel node was to be followed by a complete groin dissection. One patient was found with metastatic disease in the biopsied sentinel node. All of her non-sentinel nodes in that groin were negative. In her contralateral groin, a histologically negative sentinel node was found. This patient subsequently suffered a recurrence in the contralateral groin and immunohistochemical staining of the original negative sentinel node revealed micrometastatic disease. One additional patient in this series was found with micro-metastatic disease by cytokeratin staining. In all, two patients were found with three metastatic sentinel nodes, only one of which was found by routine specimen processing. The authors suggest ultrastaging techniques offer better accuracy, which may allow for sentinel node biopsy as a method of groin evaluation.

Future directions

Lymphatic mapping and sentinel node identification appear at this point to be clinically enticing for patients with vulvar carcinoma. Several issues, such as best candidate patients, most efficient preoperative and intra-operative tracers and techniques, the acceptable false-negative rate, best pathological evaluation strategy, role of molecular characterization, and the role of completed lymphadenectomy need resolution before the technique can be widely advocated. Indeed, in a survey of vulvar, cancer survivors—many of whom had suffered postoperative morbidity—60% reported that they would undergo the procedure again with its associated complications than accept a 5% false-negative rate from a sentinel node procedure (de Hullu et al. 2001). The reproducibility of the above clinical experience in the multi-institutional setting is currently underway and if validated, patients will have new options based on triage programs that could offer them improved precision of their disease status and reduced morbidity.

Cervical cancer

Cervical cancer is an excellent target for the lymphatic mapping strategy First and by design, most patients undergoing primary surgical treatment will not have metastatic disease. Second, the cervix is a midline

Table 3 Literature summary of cervical sentinel node trials

Author	*Date*	*No. cases*	*Dye*	*Tracer*	*Lymphoscintigraphy*	*ID rate*	*False negative SNL*
Echt et al.	1999	33	Yes	No	No	15%	0
Medl et al.	2000	3	Yes	Yes	Yes	100%	0
Verheijen et al.	2000	10	Yes	Yes	Yes	60%	0
O’Boyle et al.	2000	20	Yes	No	No	60%	0
Dargent et al.	2000	23	Yes	No	No	86%	0
Lantzsch et al.	2001	14	No	Yes	Yes	93%	0
Levenback et al.	2002	39	Yes	Yes	Yes	1(3%)*	
Rob et al.	2002	65	Yes	Yes	Yes	77%	0
Kamprath et al.	2000	18	No	Yes	No	89%	0
Malur et al.	2001	50	Yes	Yes	Yes	78%	1(2%)
Barranger et al.	2003	13	Yes	Yes	Yes	92%	0
Buist et al.	2003	25	Yes	Yes	Yes	88%	1(4%)*

* False-negative cases in these trials were parametrial nodes identified within the radical hysterectomy specimens. ID, identification; SLN, sentinel node location.

structure with numerous potential drainage basins, although, as demonstrated by Leveuf and Godard (1923), the preferred sites are generally at the obturator and external iliac locales. Third, the cervix is easily visible and accessible for injection both prior to and during surgery. Finally, since fertility-sparing options are now being described in highly selected, low-risk patients, developing a minimally invasive strategy to identify patients would be of benefit.

Clinical experience and data review

Limited clinical trials (summarized in Table 3) exploring the sentinel node concept in cervical cancer have been reported. Although mixed in early trials, the experience has generally supported the hypothesis that an identifiable, preferred lymphatic pathway from the cervix to the regional nodal basin exists. However, mapping in this disease site faces special challenges relating to the tumoral injection, high vascularity of the uterus and large number of potential pelvic and para-aortic lymphatic basins (Figure 12).

Blue dye. Echt and colleagues (1999) from the Moffitt Cancer Center were first to report an experience in attempting sentinel node identification among cervical cancer patients. In this 1999 series, 13 patients underwent peritumoral injection with lymphazurin 1% blue dye followed by laparotomy. In 12 of 13 patients, radical hysterectomy was

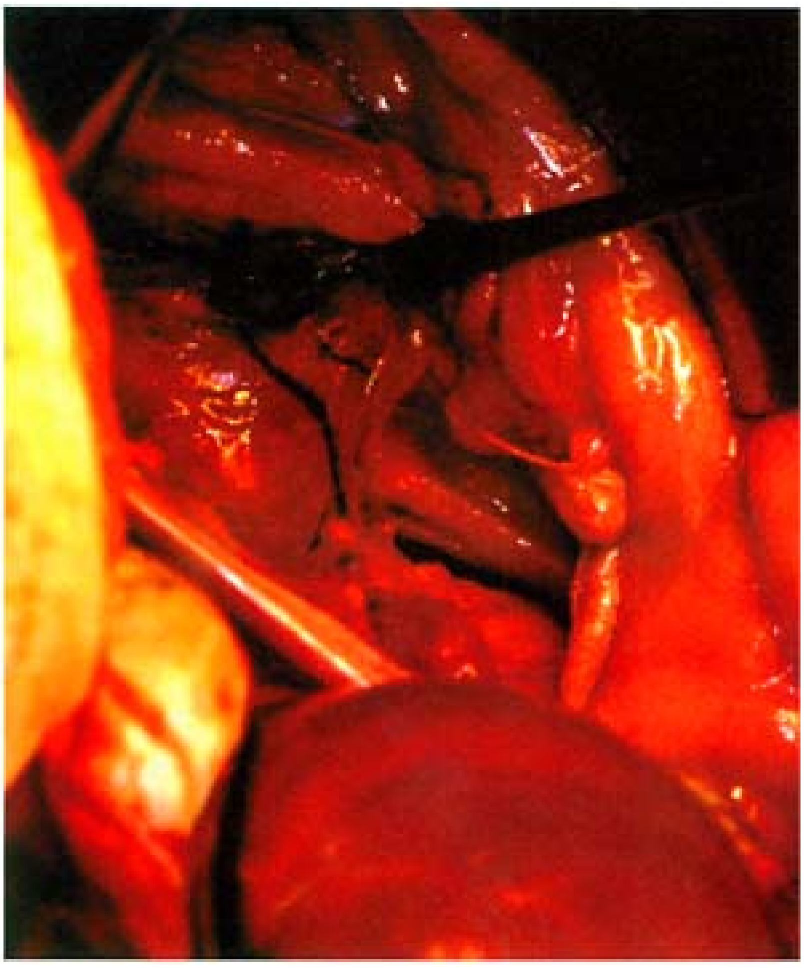

Figure 12

Sentinel node identification in a patient undergoing cervical cancer lymphatic mapping. In this example, the sentinel node, afferent and efferent lymph vasculature are visualized coming from the cervix

completed; one was aborted following identification of a metastatic para-aortic node. Collectively, just 2 patients (15%) were found with blue sentinel nodes. In these two cases, the sentinel nodes were found to contain metastatic disease along with positive undyed, non-sentinel nodes. The patient with metastatic para-aortic disease (a solitary node) and the remaining 10 patients did not have an identifiable sentinel node. It is not known if the quantity of dye used (2 ml in this series) or the timing for laparotomy contributed to the low rate of identification. The authors concluded that modification of their technique would be required for future study to accurately assess the concept.

In a similar report, Medl and colleagues (2000) reported on three stage IB–IIA patients they identified with metastatic nodal disease using blue dye alone. These patients underwent laparotomy following dye injection which was delivered into the lateral vaginal fornices, rather than cervical stroma. Although the authors voice support for the adaptation of this technology it is not stated what the total number of patients being studied was or if there were any false-negative determinations.

Technical and clinicopathologic features influencing sentinel node mapping success were detailed in a pilot project from O'Boyle et al. (2000). This group, injecting 5 mL of 1% lymphazurin dye intrastromally, reported sentinel node identification in 12 of 20(60%) patients undergoing laparotomy for early-stage cervical cancer (stage IB1–IIA). Tumor size (>4 cm) and prior conization were features associated with lack of sentinel node localization. The authors commented that temporal sequence of injection and laparotomy might be important, given the rapidity that blue dye is cleared from nodal tissues in the vascular pelvic basin. While the interiliac and external iliac nodal chains were the common location of the 23 sentinel nodes identified, 4 nodes were found in the common iliac basin and 4 were identified in parametrial tissues. Microscopic nodal metastases were found in 4(20%) patients, 3 of whom had disease in identified sentinel nodes. A fourth patient did not have an identifiable sentinel node. In addition, 2 of these 4 patients had bilateral nodal metastases, both of whom had only unilateral sentinel nodes (positive) found. Nonetheless, if patients were identified with a sentinel node, its histopathology reflected the nodal basin in each case.

Dargent and colleagues (2000) argued that this technology would be most important for patients undergoing minimally invasive procedures since its validation would limit the nodal dissection necessary and pave the way for total vaginal resection or even fertility-sparing procedures, such as radical trachelectomy In their report, 35 patients underwent laparoscopic mapping procedures and lymphadenectomy Defining ‘success’ as identifying a sentinel node on each pelvic side-wall, the authors reported that location (fornicies vs. stroma) and volume of dye (4 mL vs. less) were significant factors of a successful study. Overall, they identified sentinel nodes in 59 of 69(86%) lymphatic dissections (pelvic side-walls). Of these instances, 51 were associated with a single dyed node. Interestingly, blue dyed nodes were identified a median 52 min following injection with a range of 20–150 min. It is tempting to speculate that intra-abdominal pressure during laparoscopic procedures may reduce the rapid clearance of dye seen in laparotomy studies. Metastatic disease was seen in 11 nodes from 6 patients—all sentinels. No studies without false-negative results have been reported, although one patient had a metastatic node in a basin without a sentinel node identified. Details of sentinel node location in this study confirmed the importance of the lateral lymphatic trunks in cervical drainage. The interiliac, obturator and external iliac basins (so-called ‘Leveuf et Godard’ area) were the location of 53 sentinel nodes.

Rob and colleagues presented their experience of patent blue dye lymphatic mapping in 65 patients undergoing laparoscopy (*n*=12) and laparotomy

Table 4 Treatment cohorts in Rob et al. (2004)

Cohort	*No.*	*Technique*	*Stage*	*Detection*
A	12	Laparoscopy	IA2:2 IB2:10	11/12(92%)
B1	13	Laparotomy	IB1(<2 cm)	11/13(85%)
B2	20	Laparotomy	IB1(2–4 cm)	16/20(80%)
B3	20	NACT/Laparotomy	IB2	12/20(60%)

NACT, neoadjuvant chemotherapy.

(*n*=53) for early cervical cancer. Unique in this trial was the inclusion of 20 patients undergoing radical hysterectomy following neoadjuvant chemotherapy. Table 4 details the findings from this report. Three patients in the laparoscopy cohort were found with metastatic disease, all within identified nodes sent for intraoperative frozen section. There were no false-negative studies. The authors concluded that the technique was feasible in smaller tumors by both laparoscopy and laparotomy but limited in patients with larger tumors following neoadjuvant chemo-therapy. They further emphasized the importance of timing the dye infusion to follow port placement or laparotomy incision.

Lymphoscintigraphy. In an attempt to bolster the success of finding a sentinel node and to reduce the learning curve for these procedures, many investigators have turned to or added lymphoscintigraphy to their mapping technique. Verheijen and colleagues (2000) reported their experience with radiocolloid mapping in 10 women with cervical cancer. Focal uptake (‘hot’) was seen in 6 of 10 patients. Blue dye injection was also used in this study, showing localization in 4 patients and all within nodes previously identified as hot. A total of 18 sentinel nodes were detected at laparotomy, including the one patient with metastatic disease. Nodal localization was preferentially in the external and interiliac chains but sentinel nodes in the common iliac basin were seen in 3 cases. Bilateral sentinel nodes were seen in 4 cases.

Lantzsch et al. (2001) detailed their experience of sentinel node identification in 14 stage IB patients using preoperative and intraoperative lymphoscintigraphy alone. This group performed intraoperative localization with a hand-held gamma probe and then completed radical hysterectomy and pelvic lymph node dissection. Focal uptake of filtered radiocolloid

Table 5 Relationship of dye and radiaoactivity in 132 sentinel nodes (from Levenback et al. 2002)

	Radioactivity		
Dye	*Hot*	*Not hot*	*Total*
Blue	65	32	100
Not blue	32	0	32
Total	97	35	132

was seen in 13(93%) patients and it identified 26 sentinel nodes. Five patients were found with bilateral sentinel nodes and 8 patients had one or more unilateral sentinels retrieved. One patient was found with histologically positive sentinel nodes. There were no false-negative studies.

A larger, multi-institutional experience was published by Levenback and colleagues (2002), in which the combined technique was studied at laparotomy. In this series, 39 patients underwent either preoperative (*n*=23) or perioperative (*n*=16) radiocolloid cervical stromal injection. Localized uptake was seen in 33 patients from the lymphoscintigrams. All patients had at least one sentinel node identified and bilateral sentinel nodes were found in 37 of 39 patients. In contrast to other reports, sentinel nodes in this trial retained either or both characteristic of blue and hot. Table 5 demonstrates the relationship seen in this trial. Further, size and preoperative cervical conization did not negatively affect identification of a sentinel node. Metastatic disease was found in 25 nodes from 8 patients. In 7 of these patients at least one positive sentinel node was retrieved and in 5, the only positive node was the sentinel node. In one patient with negative bilateral sentinel nodes a positive parametrial node was identified in the hysterectomy specimen. The authors concluded that compared to their earlier trials with blue dye alone, lymphoscintigraphy added significantly to their sentinel node identification and that more work in this area was needed to validate the technique. The identification of blue, not hot sentinel nodes in this trial needs further explanation and may relate to altered injection sites or clearance of short half-life radiocolloid. The relatively high radioactivity observed near the cervix following injection limits precise localization of nodes in the parametrium (unless blue). The clinical relevance of these nodes to survival has been recently called into question (Winter et al. 2002).

Combined technique and laparoscopy

As was illustrated by Dargent and colleagues (2000), laparoscopic sentinel node mapping may provide the greatest measure of benefit for patients with early-stage disease. There has been limited experience reported utilizing the intraoperative gamma probe but the early reports would support its feasibility and importance in sentinel node localization. Kamprath and colleagues (2000), in a letter to the Editor, in the *American Journal of Obstetrics and Gynecology*, presented data on 18 patients undergoing laparoscopic lymphadenectomy following preoperative radiocolloid injection. Laparoscopic radical hysterectomy was performed in 15 patients and radical trachelectomy in 3 patients. Since no blue dye was used in this trial, resected nodes were secondarily scanned ex vivo for activity. 'Hot' nodes were labeled sentinel and were found in 16 of 18(89%) patients. Interestingly, a median 2.1 pelvic sentinel nodes were found, with a median 1.4 para-aortic sentinel nodes found among 5 patients. Their two non-diagnostic studies included the first two patients given one fifth and one half of the radiocolloid dose, respectively. One patient was found with metastatic disease. This patient had one sentinel and three non-sentinel positive nodes.

Similarly, Malur and colleagues (2001), from the same institution, later reported their experience with patent blue dye alone (*n*=9), radiocolloid alone (*n*=21), and the combination (*n*=20) in early-stage cervical cancer patients undergoing pelvic and paraaortic lymphadenectomy via laparoscopy (*n*=45) or laparotomy (*n*=5). Table 6 outlines the success of sentinel node identification and representation by technique. Detection rate was similar between laparotomy and laparoscopy (about 78%), although 6 patients in this series had stage IV disease and were undergoing extirpation by pelvic exenteration. Metastatic disease was documented in 10(20%) patients, 6 of whom had identifiable sentinel nodes. In all but one of these cases, the sentinel node had metastatic disease. In two, the sentinel node was the only positive node. One patient identified with blue-dyed, histologically negative sentinel nodes was found with a single, positive metastatic non-sentinel node—a false-negative study. This patient was evaluated by blue dye alone, prompting the authors to recommend the combined technique for further study. In this latter cohort, 18 of 20 patients were identified with sentinel nodes; 4 with metastatic disease and all within sentinel nodes.

Table 6 Characteristics and probability estimates for 50 patients undergoing lymphatic mapping (from Malur et al. 2001)

Variable	*Blue dye*	*Radiocolloid*	*Combined*	*Overall*
No. of patients	9	21	20	50
Detection rate(%)	56	76	90	78
Sensitivity(%)	50	0	100	83
Specificity(%)	100	100	100	100
Positive predictive value(%)	100	0	100	100
Negative predictive value(%)	75	100	100	97
Accuracy(%)	80	100	100	97
False negative(%)	50	0	0	17

Barranger et al. (2003) discussed their experience with laparoscopic sentinel node mapping following the combination of patent blue dye and radiocolloid cervical injection. In this limited series of 13 patients, 1–3 sentinel nodes were identified in 12 patients. No patients were found with metastatic disease on routine H&E staining. However, micrometastatic lesions were found in 4 sentinel nodes from 2 patients by immuno-histochemical analysis. None of these patients received adjuvant therapy. Interestingly, one patient was found with a sentinel node in the common iliac area. The authors concluded that sentinel node mapping could have a role in minimally invasive surgical procedures for patients with early-stage cervical cancer.

Buist et al. (2003) reported on 25 early-stage cervical cancer patients undergoing laparoscopic sentinel node assessment as a triage technique for subsequent abdominal radical hysterectomy. If metastatic disease was detected in the sentinel node, complete lymphadenectomy was performed laparoscopically and the uterus was left in situ. If no metastatic disease was identified, a laparoscopic pelvic lymphadenectomy was performed followed by an abdominal radical hysterectomy. One or more sentinel nodes were detected in all patients and bilateral sentinel nodes were found in 22 of 25(88%) patients. Metastatic disease was detected in 40% of the cohort. One patient with two negative obturator sentinel nodes was later found to have a metastatic parametrial node removed with the primary tumor. This represented the only false-negative study. Two additional patients were later identified by immunohistochemistry to have micrometastatic disease. Importantly, six patients underwent only laparoscopic lymphadenectomy and ovarian transposition following sentinel node identification averting exploration for radical hysterectomy. The authors concluded the procedure was feasible and triage in this manner could avert additional morbidity from transperitoneal exploration.

Future development

Surgical validity of this technology requires prospective investigation in more diverse cohorts, the multi-institutional environment, and with adaptation of newer and more specific pathologic/molecular techniques of nodal evaluation. Further, validation is required for the development of prospective, randomized trials where individual treatment triage is specified on the basis of the sentinel node. Such trials are currently under development. In this regard, it would seem that patients eligible for laparoscopic dissection would be ideal candidates for this technology, as focused dissection and potentially fertility-sparing operations (such as radical trachelectomy) could be offered (Covens et al. 1999). In addition, sparing of potential antigen-recognizing lymphoid cells could be critical to the successful adaptation of vaccine therapies. HPV-L1 virus-like particle (VLP) vaccine therapy is currently under phase I clinical development. The importance of such strategies on the prevention of viral infection has been documented in a randomized double-blind multicenter controlled clinical trial of a HPV-L1 VLP on healthy volunteers (Koutsky et al. 2002). At a median of 17.9 months follow-up the rate of persistent HPV infection was 3.9/100 woman-years in the control group compared to 0/100 woman-years in those receiving vaccine (p<0.001). All cases of HPV-16 related dysplasia occurred in the placebo cohort. Overall, however, more information of the clinical relationship between the primary tumor and its lymphatic basin is required to gain a deeper understanding of tumor biology and unravel the mysteries of clinical behavior.

Uterine cancer

Endometrial cancer is a difficult target for the mapping strategy. The primary tumor cannot be seen, imaged or palpated with standard clinical tools. However, endometrial cancer is an attractive disease site for lymphatic mapping given the complexity of the lymphatic drainage of the uterus. Sentinel nodes could, theoretically, be found anywhere from the obturator space to the renal vessels (Figure 13). In this largely experimental cohort, few clinical trials have been reported.

Lymphatic mapping studies

Echt et al. (1999) described their attempts at sentinel node identification in patients with endometrial cancer. Patent V blue dye was injected into the uterine fundus

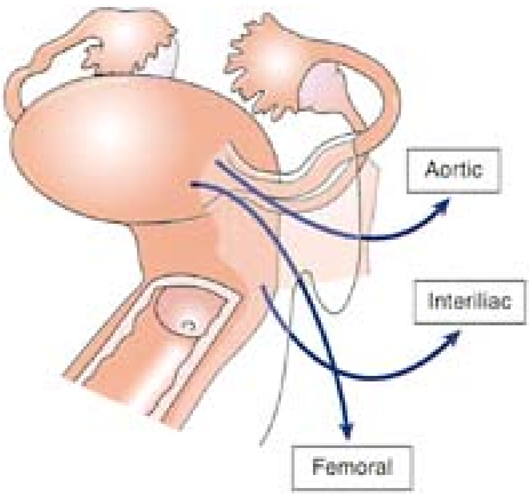

Figure 13

Lymphatics from the uterus may follow the vessels leading to the pelvic nodes or through the gonadal vessels to the para-aortic nodes. Rarely, they may follow the round ligament draining in the inguinofemoral basin

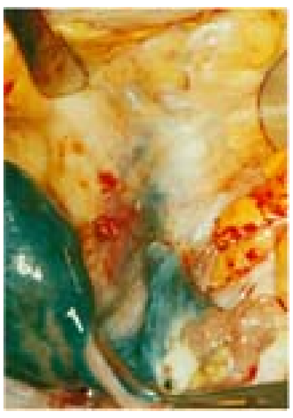

Figure 14

Blue dye in the uterine corpus, injected at the time of laparotomy, is seen traversing the gonadal lymphatics into the low paraotic region (seen transperitoneally). Although lymphatic mapping in this fashion may not accurately reflect the primary tumor’s specific drainage, one can appreciate the vast intrauterine lymphatic anastamotic network

at a depth of approximately half the thickness of the myometrium. The authors could not identify any sentinel nodes in eight patients. Burke et al. (1996) described intraoperative injection of isosulfan blue into the subserosal myometrium into 3 midline sites at the fundus, 2 cm anterior and 2 cm posterior to this site. These sites were chosen to mimic a fundal endometrial cancer. Dye uptake was seen in the lymphatic channels and lymph nodes within 10 minutes (Figure 14). Blue-stained nodes were identified and the location recorded and the nodes were sent to pathology as separate specimens. A selective pelvic and paraaortic lymphadenectomy was then performed. Blue dye was deposited in lymph nodes in 10 of 15 patients and blue nodes were found in the pelvic and para-aortic areas. No stained nodes were found between the bifurcation of the aorta and the origin of the inferior mesenteric artery. This confirms the observations of many anatomists that the lymphatic drainage of the uterus follows two paths, along the uterine vessels to the pelvis and the gonadal vessels to the para-aortics at the level of the renal vessels. Four patients had positive lymph nodes; two in sentinel nodes. One patient with bulky nodes had no dye uptake and one patient had a micrometastases to an unstained node in the obturator space.
Holub and colleagues (2001) described a laparoscopic-assisted technique for lymphatic mapping in patients with endometrial cancer. In this series, 8 patients underwent intraoperative injection of blue dye using the same locations as described by Burke

et al. using a 5 mm laparoscopic puncture needle. Blue nodes were found in the obturator, internal iliac and common iliac sites in 11 lymph nodes among 5 patients. Holub et al. expanded on their experience and reported two techniques for lymphatic mapping in endometrial cancer in 2002. In this study, 13 patients underwent subserosal injection as described in the first report and 12 patients underwent subserosal and cervical injections. The combined injection technique increased the rate of observation of blue-stained lymph nodes from 61.5% in the first group to 83.3% in the current report. The authors suggest that the combined approach is superior.

Pelosi et al. (2002) described using a combination of radioactive tracer and blue dye in 11 patients with early endometrial cancer during laparoscopic-assisted vaginal hysterectomy and bilateral salpingooophorectomy. The tracer and blue dye were injected into the cervix. Three sentinel nodes were identified that proved to be positive for micrometastases. Similarly, Gargiulo et al. (2003) reported on 11 patients with stage IB-IIA endometrial cancer who underwent preoperative cervical injection of radiocolloid and intraoperative cervical injection of blue dye prior to planned laparoscopic assisted vaginal hysterectomy, bilateral salpingo-oophorectomy and pelvic and paraaortic lymphadenectomy. Seventeen sentinel lymph nodes were identified, predominantly in the external iliac area—three with micrometastases. No para-aortic nodes were identified. While these studies are an interesting attempt at selective node identification for the laparoscopic approach, it is doubtful the cervical injection strategy would accurately reflect the more common fundal tumors.

At least one group has tried direct peritumoral injection of radiolabeled technetium-99m by hysteroscopy on the day prior to hysterectomy. When possible, injections were made in four locations around the tumor. In patients who had complete involvement of the endometrial cavity, five standard sites were injected. Lymphoscintigrams were performed following injection and then again the next morning prior to surgery. Intraoperative localization was performed with a hand-held gamma probe. At least one sentinel node was identified in 82% of patients. Results were best (21 out of 22) among the patients with invasion limited to the inner 50% of the myometrium. Six patients had invasion greater than 50%, in which sentinel nodes were identified in only 4 patients. Fifteen patients had sentinel nodes in both pelvic and paraaortic locations; 5 patients had pelvic locations only and, in a finding not described before, three patients had sentinel nodes in para-aortic sites only Only one patient of the 16 with sentinel nodes identified had metastases.

The use of this technique is an improvement over techniques that rely on injection into the uterine fundus or cervix without visualization of the actual tumor. In addition, this technique provides a preoperative lymphoscintigram that can help plan the operative procedure. The most cephalad sentinel node can be identified and perhaps a determination made about how long an incision it will take to reach it. Conversely, it requires another procedure and a two-day sequence. It remains to be seen if other groups can replicate these results. In addition, questions remain about the safety of hysteroscopy in patient with endometrial cancer and how much, if any, radioactive material finds its way into the pelvis and on to drapes and sponges during laparotomy.

Summary

Endometrial cancer is an excellent disease site for lymphatic mapping and sentinel node identification. Many technical challenges remain and the best method for sentinel node identification has not yet been described.

Future directions of lymphatic mapping

Continuing work to validate the concept of lymphatic mapping in gynecologic tumors is being conducted through multi-institutional clinical trials within the international community. Departure from ‘standard-of-care’ lymphatic resection paradigms in cancer management requires prudent and propitious decision-making through careful review of clinical outcomes in properly conducted and controlled clinical studies. Many challenges remain, not the least of which lie in the relative rarity of the diseases being studies. However, clear definition of the learning curve and establishment of an acceptable false-negative rate will need to accompany equally important advances in our understanding of the tumor physiology of the regional lymphatics. While selective resection of affected tissues remains the ‘holy grail’ of cancer surgery, treatment success defines the benchmark—a line which the pursuit of minimization cannot compromise. It is anticipated that better tracers and localizing agents, improved pathological processing and standardized operative techniques will measurably add to this growing body of challenging study.

References

Ansink AC, Sie-Go DM, van der Velden J, et al. (1999) Identification of sentinel lymph nodes in vulvar carcinoma patients with the aid of a patent blue V injection: a multi-center study. *Cancer* **86**:652–6.
Barranger E, Grahek D, Cortez A, et al. (2003) Laparoscopic sentinel lymph node procedure using a combination of patent blue and radioisotope in women with cervical carcinoma. *Cancer* **97**:3003–9.
Berman ML, Soper JT, Creasman WT, et al. (1989) Conservative surgical management of superficially invasive stage I vulvar carcinoma. *Gynecol Oncol* **35**:352–7.
Bostick PJ, Giuliano AE (2000) Vital dyes in sentinel node localization. *Semin Nucl Med* **30**:18–24.
Buist MR, Pijpers RJ, van Lingen A, et al. (2003) Laparoscopic detection of sentinel lymph nodes followed by lymph node dissection in patients with early stage cervical cancer. *Gynecol Oncol* **90**:290–6.
Burke TW, Levenback C, Tornos C, et al. (1996) Intraabdominal lymphatic mapping to direct selective pelvic and para-aortic lymphadenectomy in women with high-risk endometrial cancer: results of a pilot study. *Gynecol Oncol* **62**:169–73.
Cabanas RM (1977) An approach for the treatment of penile carcinoma. *Cancer* **39**:456–66.
Coleman RL, Whitten CW, O'Boyle J, et al. (1999) Unexplained decrease in measured oxygen saturation by pulse oximetry following injection of Lymphazurin 1% (isosulfan blue) during a lymphatic mapping procedure. *J Surg Oncol* **70**:126–9.
Covens A, Shaw P, Murphy J, et al. (1999) Is radical trach-electomy a safe alternative to radical hysterectomy for patients with stage IA-B carcinoma of the cervix? *Cancer* **86**:2273–9.
Dargent D, Martin X, Mathevet P (2000) Laparoscopic assessment of the sentinel lymph node in early stage cervical cancer. *Gynecol Oncol* **79**:411–15.
DeCesare SL, Fiorica JV, Roberts WS, et al. (1997) A pilot study utilizing intraoperative lymphoscintigraphy for identification of the sentinel lymph nodes in vulvar cancer. *Gynecol Oncol* **66**:425–8.
De Cicco C, Sideri M, Bartolomei M, et al. (1997) Sentinel node detection by lymphoscintigraphy and gamma detecting probe in patients with vulvar cancer. *J Nucl Med* **38**:33.
De Cicco C, Cremonesi M, Luini A, et al. (1998) Lymphoscintigraphy and radioguided biopsy of the sentinel axillary node in breast cancer. *J Nucl Med* **39**:2080–4.
de Hullu JA, Doting E, Piers DA, et al. (1998) Sentinel lymph node identification with technetium-99m-labeled nanocolloid in squamous cell cancer of the vulva. *J Nucl Med* **39**:1381–5.
de Hullu JA, Hollema H, Piers DA, et al. (2000) Sentinel lymph node procedure is highly accurate in squamous cell carcinoma of the vulva. *J Clin Oncol* **18**:2811–16.
de Hullu JA, Ansink AC, Tymstra T, et al. (2001) What doctors and patients think about false-negative sentinel lymph nodes in vulvar cancer. *J Psychosom Obstet Gynaecol* **22**:199–203.
DiSaia PJ, Creasman WT, Rich WM (1979) An alternate approach to early cancer of the vulva. *Am J Obstet Gynecol* **133**:825–32.
Echt ML, Finan MA, Hoffman MS, et al. (1999) Detection of sentinel lymph nodes with lymphazurin in cervical, uterine, and vulvar malignancies. *South Med J* **92**:204–8.
Ege GN (1976) Internal mammary lymphoscintigraphy. The rationale, technique, interpretation and clinical application: a review based on 848 cases. *Radiology* **118**:101–7.
Eshima D, Fauconnier T, Eshima L, et al. (2000) Radiopharmaceuticals for lymphoscintigraphy: including dosimetry and radiation considerations. *Semin Nucl Med* **30**:25–32.
Eudy GE, Carlson GW, Murray DR, et al. (2003) Rapid immunohistochemistry of sentinel lymph nodes for metastatic melanoma. *Hum Pathol* **34**:797–802.
Gargiulo T, Giusti M, Bottero A, et al. (2003) Sentinel Lymph Node (SLN) laparoscopic assessment early stage in endometrial cancer. *Minerva Gynecol* **55**:259–62.
Gould EA, Philbin WT, Hyland PH, et al. (1960) Observations on a 'sentinel node' in cancer of the parotid. *Cancer* **13**:77–8.
Halsted W (1997) The results of radical operations for the cure of carcinoma of the breast. *Ann Surg* **46**:1.
Henze E, Schelbert HR, Collins JD, et al. (1982) Lymphoscintigraphy with Tc-99m-labeled dextran. *J Nucl Med* **23**:923–9.
Holub Z, Kliment L, Lukac J, et al. (2001) Laparoscopically-assisted intraoperative lymphatic mapping in endometrial cancer: preliminary results. *Eur J Gynaecol Oncol* **22**:118–21.
Holub Z, Jabor A, Kliment L (2002) Comparison of two procedures for sentinel lymph node detection in patients with endometrial cancer: a pilot study. *Eur J Gynaecol Oncol* **23**:53–7.

Homesley HD, Bundy BN, Sedlis A, et al. (1986) Radiation therapy versus pelvic node resection for carcinoma of the vulva with positive groin nodes. *Obstet Gynecol* **68**:733–40.
International (Ludwig) Breast Cancer Study Group (1990) Prognostic importance of occult axillary lymph node micrometastases from breast cancers. *Lancet* **335**:1565–8.
Iversen T, Aas M (1983) Lymph drainage from the vulva. *Gynecol Oncol* **16**:179–89.
Kamprath S, Possover M, Schneider A (2000) Laparoscopic sentinel lymph node detection in patients with cervical cancer. *Am J Obstet Gynecol* **182**:1648.
Koutsky LA, Ault KA, Wheeler CM, et al. (2002) A controlled trial of a human papillomavirus type 16 vaccine. *N Engl J Med* **347**:1645–51.
Lantzsch T, Wolters M, Grimm J, et al. (2001) Sentinel node procedure in Ib cervical cancer: a preliminary series. *Br J Cancer* **85**:791–4.
Leong SP, Donegan E, Heffernon W, et al. (2000) Adverse reactions to isosulfan blue during selective sentinel lymph node dissection in melanoma. *Ann Surg Oncol* **7**:361–6.
Leveuf J, Godard H (1923) Les lymphatiques de l'uterus. *Revue de Chirurgie* 219–48.
Levenback C, Burke TW, Gershenson DM, et al. (1994) Intraoperative lymphatic mapping for vulvar cancer. *Obstet Gynecol* **84**:163–7.
Levenback C, Coleman RL, Burke TW, et al. (2001) Intraoperative lymphatic mapping and sentinel node identification with blue dye in patients with vulvar cancer. *Gynecol Oncol* **83**:276–81.
Levenback C, Coleman RL, Burke TW, et al. (2002) Lymphatic mapping and sentinel node identification in patients with cervix cancer undergoing radical hysterectomy and pelvic lymphadenectomy. *J Clin Oncol* **20**:688–93.
Malur S, Krause N, Kohler C, et al. (2001) Sentinel lymph node detection in patients with cervical cancer. *Gynecol Oncol* **80**:254–7.
Makar AP, Scheistroen M, van den Weyngaert D, et al. (2001) Surgical management of stage I and II vulvar cancer: the role of the sentinel node biopsy. Review of literature. *Int J Gynecol Cancer* **11**:255–62.
Medl M, Peters-Engl C, Schutz P, et al. (2000) First report of lymphatic mapping with isosulfan blue dye and sentinel node biopsy in cervical cancer. *Anticancer Res* **20**:1133–4.
Molpus KL, Kelley MC, Johnson JE, et al. (2001) Sentinel lymph node detection and microstaging in vulvar carcinoma. *J Reprod Med* **46**:863–9.
Moore RG, DePasquale SE, Steinhoff MM, et al. (2003) Sentinel node identification and the ability to detect metastatic tumor to inguinal lymph nodes in squamous cell cancer of the vulva. *Gynecol Oncol* **89**:475–9.
Morton DL, Wen DR, Wong JH, et al. (1992) Technical details of intraoperative lymphatic mapping for early stage melanoma. *Arch Surg* **127**:392–9.
Munakata S, Aihara T, Morino H, et al. (2003) Application of immunofluorescence for intraoperative evaluation of sentinel lymph nodes in patients with breast carcinoma. *Cancer* **98**:1562–8.
Nahrig JM, Richter T, Kuhn W, et al. (2003) Intraoperative examination of sentinel lymph nodes by ultrarapid immunohistochemistry. *Breast J* **9**:277–81.
O'Boyle JD, Coleman RL, Bernstein SG, et al. (2000) Intraoperative lymphatic mapping in cervix cancer patients undergoing radical hysterectomy: A pilot study. *Gynecol Oncol* **79**:238–43.
Parry-Jones E (1963) Lymphatics of the vulva. *J Obstet Gynaecol Br Commonw* **70**:751–65.
Pelosi E, Arena V, Baudino B, et al. (2002) Preliminary study of sentinel node identification with 99mTc colloid and blue dye in patients with endometrial cancer. *Tumori* **88**:S9–S10.
Plentl A, Friedman E, (1971) *Lymphatic system of the female genitalia.* Philadelphia: WB Saunders.
Rodier JF, Janser JC, Routiot T, et al. (1999) Sentinel node biopsy in vulvar malignancies: a preliminary feasibility study. *Oncol Rep* **6**:1249–52.
Rob L, Pluta M, Strnad P, et al. (2002) Sentinel node identification in uterine cervix cancer Stage I: A pilot study. *Gynecol Oncol 84:*521.
Rob L, Charvat M, Robova H, et al. (2004) Sentinel lymph node mapping in early-stage cervical cancer. *Ceska Gynekol* **69**:273–7.
Sadiq TS, Burns WW, 3rd, Taber DJ, et al. (2001) Blue urticaria: a previously unreported adverse event associated with isosulfan blue. *Arch Surg* **136**:1433–5.
Sherman A, Ter-Pogossian M (1953) Lymph node concentration of radioactive colloidal gold following interstitial injection. *Cancer* **6**:1238–40.

Sideri M, De Cicco C, Maggioni A, et al. (2000) Detection of sentinel nodes by lymphoscintigraphy and gamma probe guided surgery in vulvar neoplasia. *Tumori* **86**:359–63.
Sliutz G, Reinthaller A, Lantzsch T, et al. (2002) Lymphatic mapping of sentinel nodes in early vulvar cancer. *Gynecol Oncol* **84**:449–52.
Stehman FB, Bundy BN, Thomas G, et al. (1992) Groin dissection versus groin radiation in carcinoma of the vulva: a Gynecologic Oncology Group study. *Int J Radiat Oncol Biol Phys* **24**:389–96.
Tavares MG, Sapienza MT, Galeb NA, Jr, et al. (2001) The use of 99mTc-phytate for sentinel node mapping in melanoma, breast cancer and vulvar cancer: a study of 100 cases. *Eur J Nucl Med* **28**:1597–604.
Terada KY, Shimizu DM, Wong JH (2000) Sentinel node dissection and ultrastaging in squamous cell cancer of the vulva. *Gynecol Oncol* **76**:40–4.
Uren RF, Howman-Giles R (2002) The role of nuclear medicine. In: Cody HS, ed. *Sentinel lymph node biopsy*. London: Martin Dunitz: 19–43.
Van Trappen PO, Gyselman VG, Lowe DG, et al. (2001) Molecular quantification and mapping of lymph-node micrometastases in cervical cancer. *Lancet* **357**:15–20.
Verheijen RH, Pijpers R, van Diest PJ, et al. (2000) Sentinel node detection in cervical cancer. *Obstet Gynecol* **96**:135–8.
Way S (1951) Carcinoma of the vulva. *Malignant disease of the female genital tract.* Philadelphia: The Blakiston Co.
Wilhelm AJ, Mijnhout GS, Franssen EJ (1999) Radiopharmaceuticals in sentinel lymph-node detection—an overview. *Eur J Nucl Med* **26**:S36–S42.
Winter R, Haas J, Reich O, et al. (2002) Parametrial spread of cervical cancer in patients with negative pelvic lymph nodes. *Gynecol Oncol* **84**:252–7.
Wong JH, Cagle LA, Morton DL (1991) Lymphatic drainage of skin to a sentinel lymph node in a feline model. *Ann Surg* **214**:637–41.

8
Cone biopsy

Giuseppe Del Priore

Introduction

The cone biopsy—removal of a cone-shaped portion of the cervix—has been performed by gynecologists for decades. Several methods exist for obtaining this specimen. These include an electrosurgical technique, laser or scalpel method of excision. The electrosurgical technique referred to as the *loop electrosurgical excision procedure* (LEEP) or *loop excision of the transformation zone* (LETZ) has gained popularity. It has several advantages over the other methods. These include less immediate bleeding and discomfort. It is therefore possible to perform LEEP in the office without general anesthesia. Although the surgical margins are cauterized, it still provides a reasonable specimen for pathologic interpretation with no clinically significant limitations. The scalpel and LEEP techniques are also generally equivalent in their clinically significant outcomes (i.e. cure rates). However, the scalpel cone tends to be larger, which is of no particular advantage except perhaps when used in patients with adenocarcinoma of the endocervix. Since this histology tends to be more multifocal than squamous lesions, a larger specimen may be more likely to remove all of the lesions. As there may still be, on occasion, the need to perform a scalpel cone biopsy, all gynecologists should be familiar with both techniques.

Indications

Cone biopsy is indicated for the diagnosis or exclusion of microinvasive cervical cancer as suggested on a presurgical Papanicolaou (Pap) smear or colposcopic punch biopsy. It could also be used to exclude and possibly treat endocervical adenocarcinoma. As mentioned above, a large scalpel cone biopsy may be a better option for these women. Cone biopsy, preferably by LEEP, is also indicated for patients with high-grade squamous epithelial lesions on Pap smear but no identifiable colposcopic lesion.

Anatomic considerations

Vascular supply

A small descending branch of uterine artery supplies the cervix. It can usually be found laterally in the vaginal portion of the cervix at 3 and 9 o’clock. Despite its apparent accessible location, lateral stay sutures to occlude these vessels do so in less than half of all cases.

Innervation

The nerves of the cervix arise from the hypogastric plexus. Specific branches from this plexus to the cervix are sometimes known as the uterovaginal plexus that are found in the broad ligament. Even more distal, the uterine cervical ganglion may be identified in the paracervical tissue closest to the cervix. The autonomic sympathetic nerves arise from the sympathetic trunk originating in the nerve roots from T10 to L1. The parasympathetics arise from the roots of S2 to S4.

Muscles involved

The cervix sits above the urogenital diaphragm and, as such, does not have any direct muscle connection. Retaining the cervix during a supracervical hysterectomy or removing part of it during a cone biopsy does not have a significant effect on pelvic physiology.

Bony landmarks

The cervix lies roughly in the plane of the ischial spine, being slightly anterior and inferior to it. It is important to consider the bony pelvic outlet when contemplating operating transvaginally on the cervix. For cone biopsies, only the most contracted pelvis would present a significant limitation. Often, cases that seem impossible in the office are found to be feasible during general anesthesia with proper assistance and retraction.

Surgical procedure

Loop electrosurgical incision

The LEEP procedure begins with the proper positioning of the patient's legs. The standard office examination table with stirrups is usually sufficient. A speculum that is large enough to hold the vaginal wall away from the cervix should be inserted. An insulated speculum is not necessary. In fact, if the insulated speculum has an undetected break in its insulation, it may allow for a high-energy discharge and patient injury. Regardless of the speculum used, a suction apparatus for evacuating the copious amount of smoke produced is absolutely essential. This may either be built into the speculum or clipped on to a standard one. Hand-held wall suction is generally not adequate as it is usually too large to fit into the vagina simultaneously with the LEEP device. Immediately before the actual procedure, colposcopy is used to identify the lesion.

Local anesthesia should be administered circumferentially with a narrow gauge (e.g. 27-gauge reinforced Potocky needle). Larger needles will lead to significantly more bleeding. Any local anesthetic with adrenaline (epinephrine) 1:100000 will do. Since water dissipates the electrosurgical current, excess stromal injections may make the procedure difficult. Discomfort from the local injection can be minimized by having the patient cough simultaneously with placing the needle on the surface of the cervix. The movement

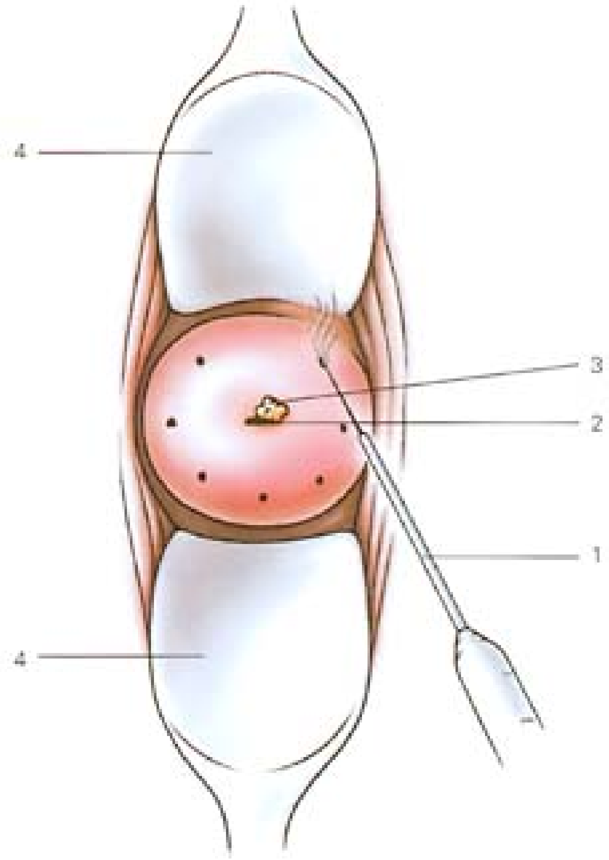

Figure 1

1 Reinforced shaft with thin needle
2 Squamocolumnar junction
3 Acetowhite epithelium
4 Speculum blades

inferiorly of the cervix during this Valsalva maneuver is usually all that is needed for the needle to painlessly enter the cervix. The anesthetic should be administered early to allow sufficient time for it to take effect (Figure 1).

Different electrosurgical units have various settings and power sources. The only important parameter is current density at the electrosurgical wire surface. This is the actual energy that the cervix receives and is dependent on the length of the wire loop in contact with the tissue, the diameter or gauge of the wire itself, and the current setting. The highest current density possible should be used to minimize drag through the tissue and, consequently, cautery artifact. However, too high a current density will result in the loop wire breaking much like an incandescent light bulb filament. If this should happen, completing the procedure will be more difficult as the operator will have to begin with a new wire loop in the middle of the specimen.

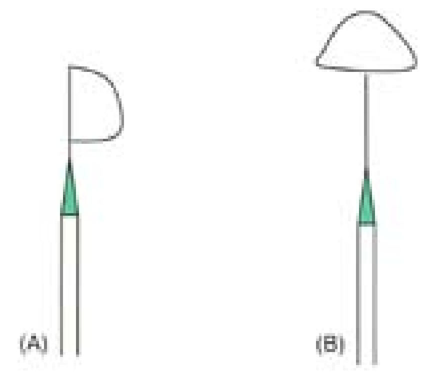

Figure 2

(A) The loop electrosurgical excision procedure (LEEP) tip.
(B) Standard tip

Trial and error using inanimate specimens may be needed to find the maximal power settings depending on the combination of generator and loop wires used.
After infiltration of the cervix, the operator should choose a loop size and shape that can remove the colposcopically identified acetowhite lesion with clear margins but no larger than necessary to avoid excessive cervical damage. However, if the cone is diagnostic, then the entire transformation zone should be removed. The operator should practice the hand motion to be used before actually turning on the current. Once a comfortable hand motion has been determined, the colposcope, used to identify the lesion and transformation zone, should be removed unless it has a very low magnification setting, since using the loop wire under colposcopic vision is unnecessarily difficult. Once everything has been rechecked, the operator applies the pure cutting current and smoothly passes the loop wire through the cervix being careful not to touch the vaginal wall. The specimen may be grasped with a forceps and sent to pathology. A sample of the endocervical canal may be obtained at this point using an endocervical curette followed by a brush and sent together to pathology. Alternatively, another smaller cone 'top hat' may be obtained with a smaller wire loop LEEP device (Figure 2). Although there is usually no immediate bleeding, late rebleeding can be reduced by prophylactically cauterizing the cone base. This should be done using a ball or spatula tip cautery attachment. The current should be set on coagulation at a sufficiently high current setting or 'spray' to exceed the capacitance of air. The ball or other suitable tip should then be held a few millimeters from the surface of the cone base to allow the current to arc across to the tissue for hemostasis. After the entire base is cauterized in this manner, ferric subsulfate (Monsel's) solution should also be applied. The patient should be instructed not to place anything in the vagina for at least 2 weeks. A routine postoperative visit is not necessary.

Scalpel 'cold knife' cone

Colposcopy should be used to identify the lesion. The scalpel cone biopsy does not require a special speculum with smoke evacuator. However, wall suction must be available since considerably more bleeding will be encountered. Because the procedure lasts longer than the LEEP and patient cooperation is necessary to deal with the intraoperative bleeding, either general or regional anesthesia is usually required. No thromboembolic or antibiotic prophylaxis is needed. After positioning of the speculum, two lateral stay sutures are placed at approximately 3 and 9 o'clock. The sutures are placed in a figure-of-eight manner to help hold the cervix and reduce the blood supply by ligation of the cervical branch of the uterine artery. An absorbable suture of 0 or 00 is sufficient. These are held with hemostats attached to the drapes to help draw the cervix down into the lower vagina (Figure 3). Starting posteriorly, using a large curved knife handle, the colposcopically identified acetowhite lesion is

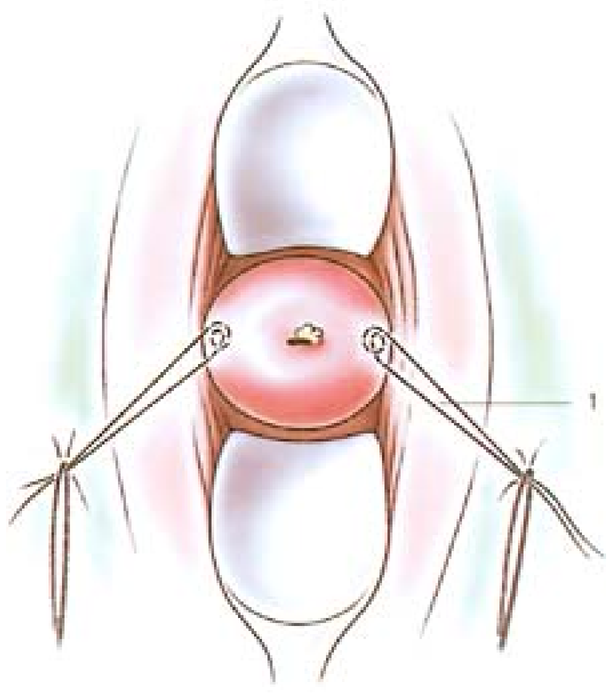

Figure 3

1 Hemostat on drape

excised. Again, for diagnostic cones, the entire transformation zone should be removed. The base of the cone may be difficult to separate completely with the scalpel. Instead, curved scissors may be used. A sample of the endocervical canal may be obtained at this point using an endocervical curette and brush. Active bleeding may be controlled with cautery or fine 000 absorbable sutures. Prophylactic cautery of the base reduces delayed bleeding better than the occluding 'Sturmdorf' sutures which turn the edge of the cervix over the excision base. Care must be taken not to occlude the os during any of these maneuvers. A cotton-tipped swab, placed in the os before any sutures, will help in avoiding this complication. Monsel's solution should be applied after hemostasis for prophylaxis against delayed bleeding. If hemostasis is still a problem, a commercial hemostatic agent, such as sheets of oxidized cellulose, may be used to tamponade the bleeding base and held in place by the lateral stay sutures. These sutures can be brought together over the midline and tied together (Figure 4).

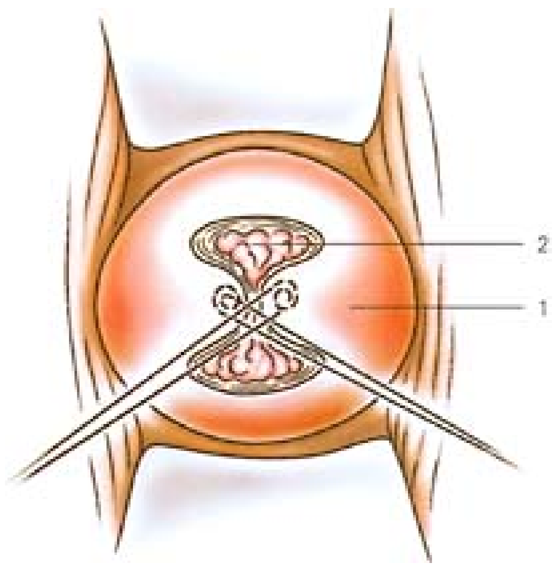

Figure 4

1 Ectocervix
2 Hemostatic absorbable packing filling cone base

9
Radical abdominal hysterectomy

J Richard Smith
Deborah CM Boyle
Giuseppe Del Priore

Introduction

Radical abdominal hysterectomy is designed to remove the uterus, cervix, upper third of the vagina, either part or the whole of the parametrium, and the uterosacral and vesicouterine ligaments. In addition, the common iliac, internal iliac, external iliac, obturator, hypogastric and presacral lymph nodes are also removed, as may be the para-aortic nodes.

This surgery is used for the management of stage IA2 and IB1 and IB2 tumors of the uterine cervix. It may be used by some surgeons for the management of stage IIA cervical tumors and occasionally in the management of vaginal cancer. It has been classified by Rutledge as radical abdominal hysterectomy types II and III (Piver et al. 1974). Staging of cervical cancer, carried out preoperatively, is not further discussed in this chapter. The choice of whether to perform this procedure or one of those described in Chapters 8, 9 and 10 depends on the surgeon's preference, with each operation tailored to the needs of the specific patient. The radicality of the planned procedure depends on the characteristics of the tumor. Prior to surgery, the patient's bowel should be prepared using standard protocol. Consent for the specific procedure, including oophorectomy if planned, should have been obtained.

Surgical procedure

A general anesthetic is administered with or without an epidural anesthetic. The addition of a regional anesthetic allows better pain control postoperatively and facilitates surgery by reducing intraoperative blood loss.

The patient is then placed supine on the operating table. The bladder is catheterized with an indwelling Foley catheter and the vagina packed with a roll of gauze. Some surgeons insert the Foley catheter postoperatively, whilst others prefer to insert a suprapubic catheter at the end of the procedure. The authors' practice depends on the radicality of the procedure. In cases of stage IIA cervical cancer the vagina may be marked with cutting diathermy 2–3 cm away from the vaginal lesion to assist in later ensuring good resection margins.

The abdomen is opened using either a subumbilical, vertical midline incision or a large lower transverse, rectus muscle-cutting incision, dependent on the patient's desire for cosmesis (Figure 1). It may be helpful to insert stay sutures to hold the peritoneum to the edges of the transverse skin incision.

After adequate exposure of the pelvis, the lymph nodes of the pelvis, the common iliac nodes and those above the bifurcation of the aorta are palpated, as is the liver.

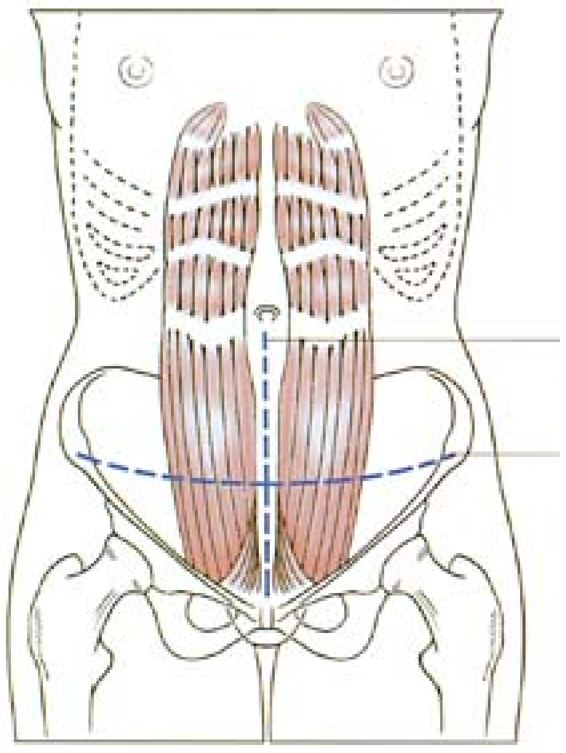

Figure 1

Opening the abdomen. (A) Low transverse rectus muscle-cutting incision. (B) Vertical subumbilical incision

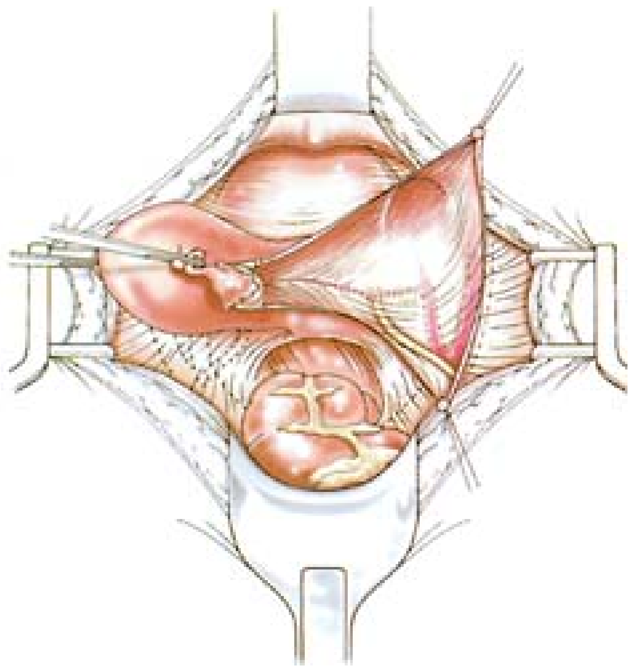

Figure 2

The round ligament is divided and the broad ligament opened

The round ligament is then grasped, divided and ligated close to the pelvic side-wall and the broad ligament opened to expose the retroperitoneal structures including the ureter attached to the medial aspect (Figure 2).

The paravesical space is the first of the potential spaces to be developed during surgery (Figure 3). This is achieved using blunt dissection with a combination of dissecting scissors and fingers or mounted pledgets. The dissection is commenced medial and slightly inferior to the external iliac vein. The paravesical space is bounded medially by the bladder and obliterated hypogastric artery and caudally by the ventral aspect of the cardinal ligament. The obturator muscle and fossa form the lateral border; this is dissected out later.

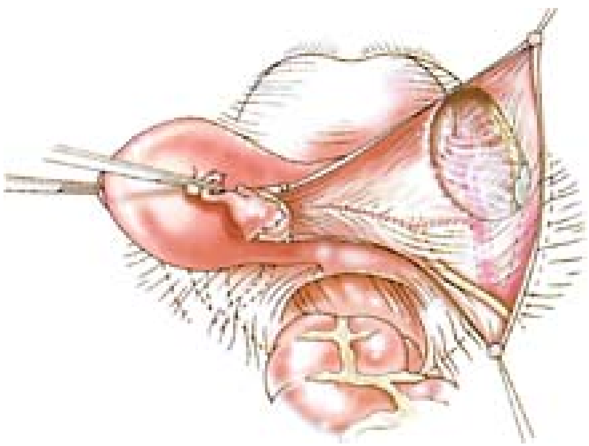

Figure 3

Developing the paravesical space

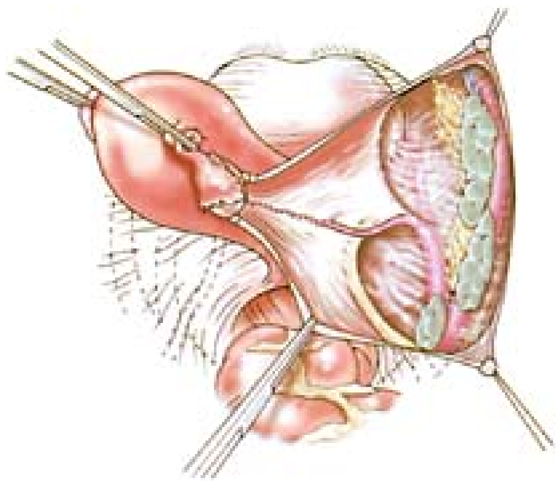

Figure 4

Developing the paravesical space

The pararectal space is then opened using a similar technique (Figure 4). This space is bounded by the rectum medially, the sacrum ventrally, the pelvic side-wall and internal iliac vessels laterally, and the cardinal ligament anteriorly This allows the cardinal ligament and parametrium to be directly assessed by placing one's fingers in the newly opened paravesical and rectal spaces (Figure 5).

The lymphadenectomy is commenced at the bifurcation of the common iliac vessels, excising the loose lymphatic tissue overlying the internal and external iliac arteries and veins (Figures 6 and 7). This is performed in

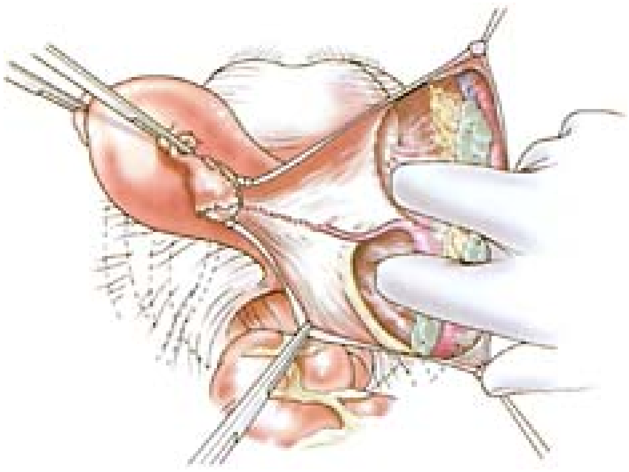

Figure 5

Boundaries of the paravesical space

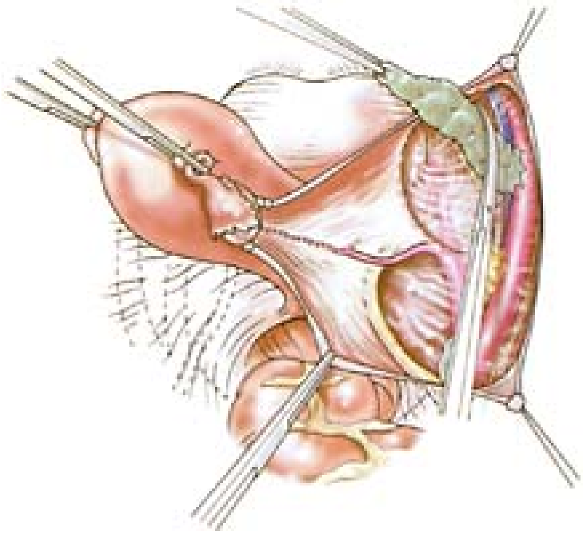

Figure 6

Pelvic lymphadenectomy

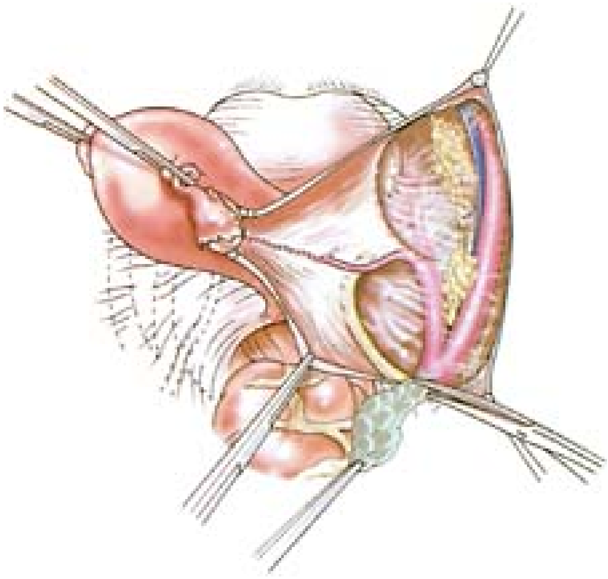

Figure 7

Pelvic lymphadenectomy: side-wall dissection

a caudal direction, having first identified psoas muscle and the genitofemoral and lateral cutaneous nerve of the thigh. The dissection of the external iliac vessels continues caudally until the circumflex iliac vessels are encountered. Dissection in a cephalad direction allows clearance of common iliac and para-aortic nodes. Presacral nodes are also removed (Figure 8).

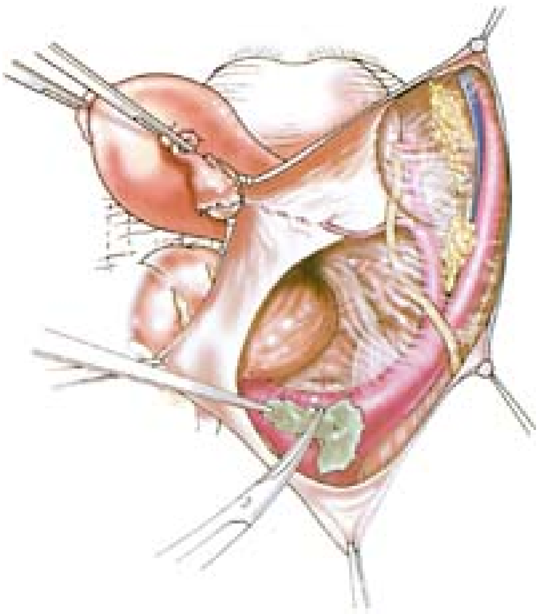

Figure 8

Presacral node removal

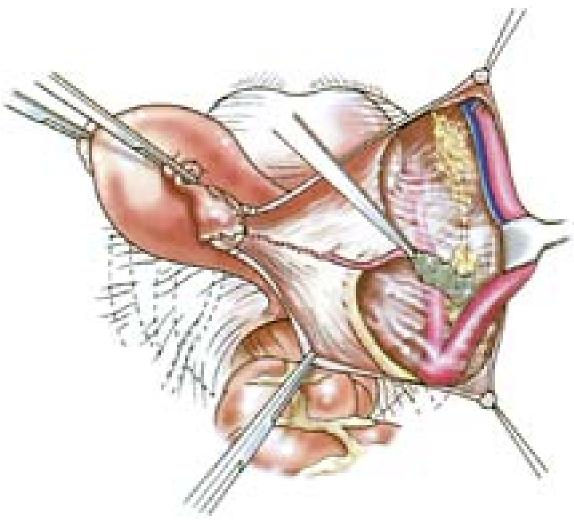

Figure 9

Exposure of the obturator fossa

Once the external iliac artery and vein are exposed they can be separated from the underlying tissue laterally. With gentle lateral (Figure 9) and/or medial (Figure 10) traction on the external iliac vessels the obturator fossa is now exposed. It is often helpful to sweep the external iliac vessels off the pelvic side-wall and approach the obturator fossa from the lateral side (Figure 11). Great care must be taken to preserve the obturator nerve, and the dissection always becomes much easier once this structure has been identified (Figures 12 and 13). Occasionally, the obturator artery and vein may require to be sacrificed to allow adequate dissection of the tissues posterior and lateral to

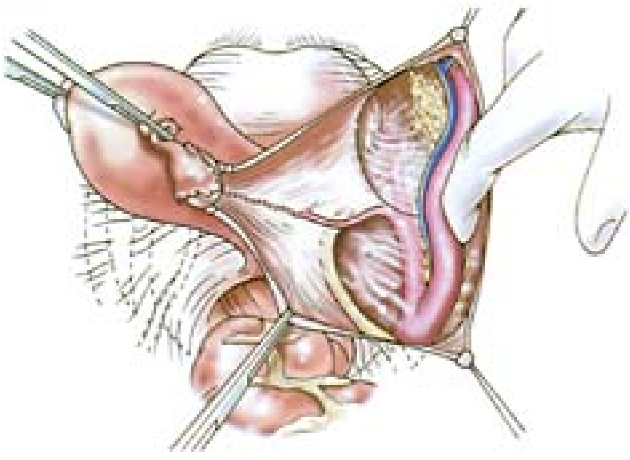

Figure 10

Exposure of the obturator fossa: lateral approach

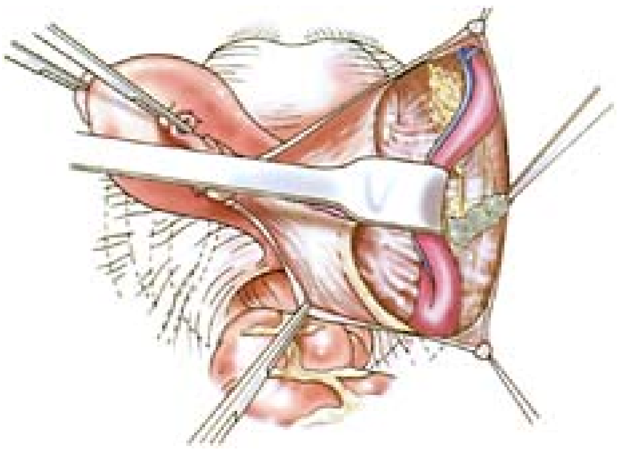

Figure 11

Exposure of the obturator fossa

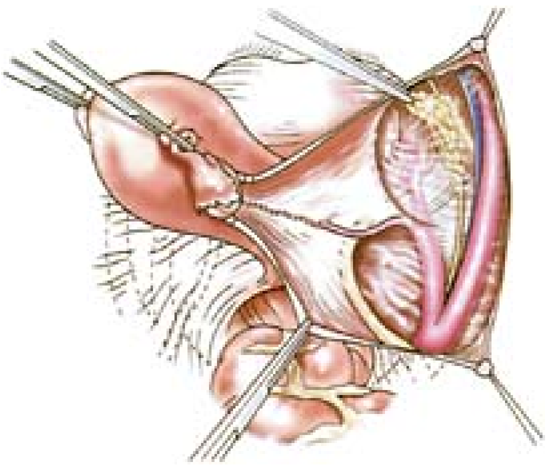

Figure 12

Exposure of the obturator fossa

the nerve. The ureter is further dissected from the peritoneum. Sharp dissection is employed to create the vesicouterine and vesicocervical spaces (Figure 14). It is important to find the correct tissue plane since this facilitates easier and bloodless dissection. The uterine arteries are clamped, divided and ligated close to their origins at the internal iliac arteries using either ligatures or hemoclips (Figure 15). The ureteric tunnels are then deroofed, allowing exposure of the ureters and their separation from parametrial tissue (Figure 16). This can be performed cephalad to caudal or vice versa. Roberts clamps or large hemoclips are helpful in minimizing hemorrhage. Whatever technique is used, bleeding tends to be brisk at this stage.

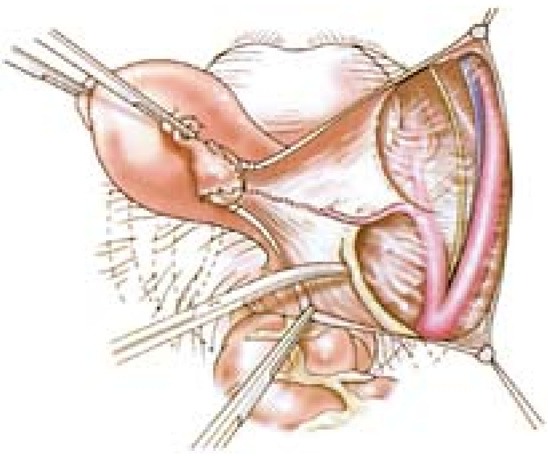

Figure 13

Exposure of the obturator fossa

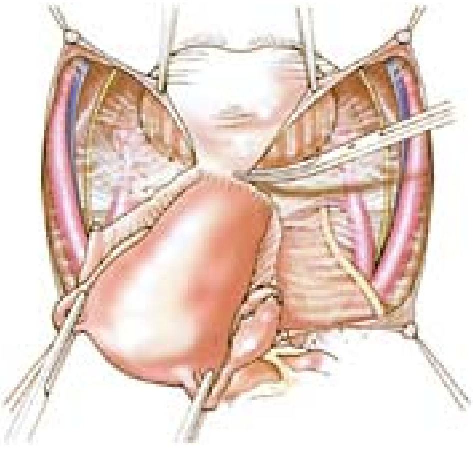

Figure 14

Developing the vesicouterine and vesicocervical spaces

The pararectal space is further developed from above from between the ureter medially and the internal iliac vessels laterally (Figure 17). The boundaries have been described above but the dissection now takes place to the level of the pelvic floor. The rectum is dissected away from the uterus, thus freeing it of its posterior visceral attachments (Figure 18). This is best achieved by grasping the rectum between the fingers and lifting it in a cephalad direction and then entering the rectovaginal space by sharp dissection. The rectum is often much higher on the uterus than is often at first suspected and this technique minimizes the possibility of inadvertent rectal injury.

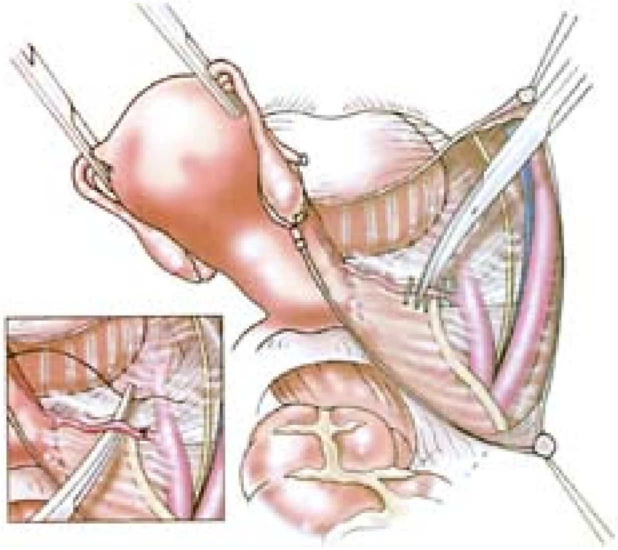

Figure 15

The uterine arteries are clamped and divided close to their origins

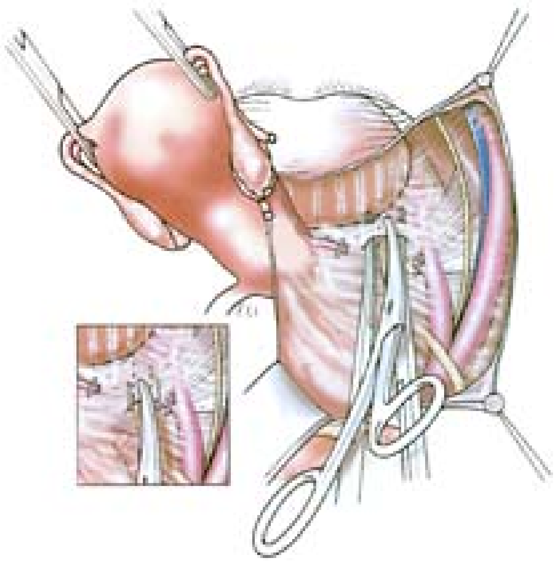

Figure 16

Deroofing of the ureteric tunnels

Clamping, division and ligation of the uterosacral ligament then takes place (Figures 19 and 20). These can either be performed midway along the ligaments or at the sacrum, depending on the size and nature of the tumor. The cardinal ligaments are then clamped, divided and ligated, again either halfway between the cervix and the pelvic side-wall or at the pelvic

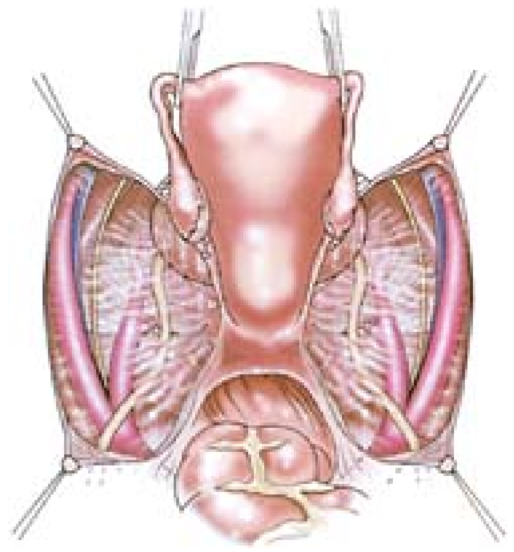

Figure 17

Further dissection of the pararectal space

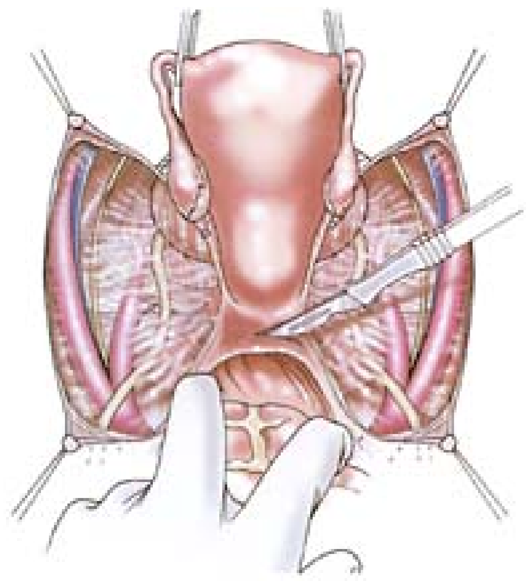

Figure 18

Dissection of the rectum from the uterus, opening the rectovaginal space

side-wall, using the same criteria as with the uterosacral ligaments (Figure 21). These differing levels of radicality have been classified by Rutledge and the procedures just described are Rutledge II and III procedures (Piver et al. 1974) (Figure 22).

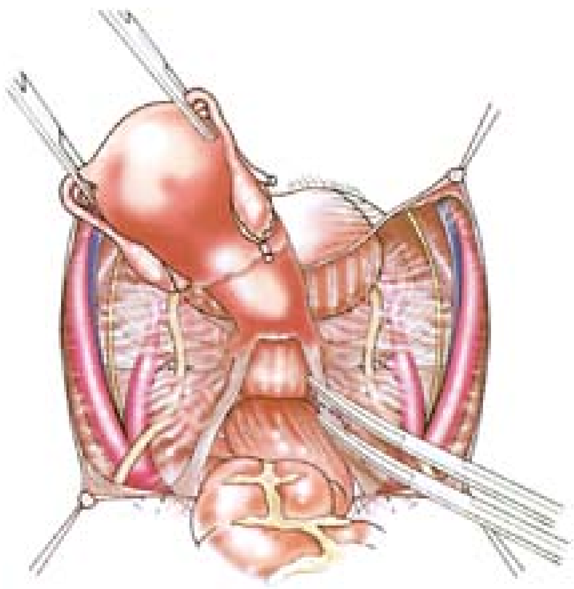

Figure 19

Division of the uterosacral ligaments

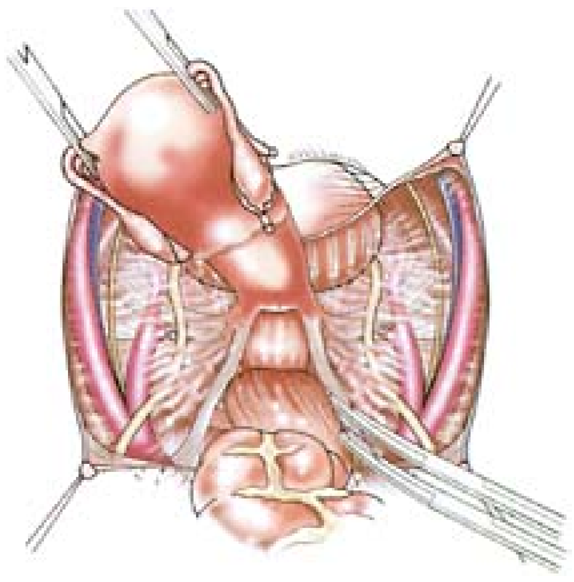

Figure 20

Division of the uterosacral ligaments

The division of these ligaments causes the para-vesical and pararectal spaces to be united (Figures 23 and 24).
Right-angle clamps are applied to the vagina far enough caudally to allow removal of the upper third of

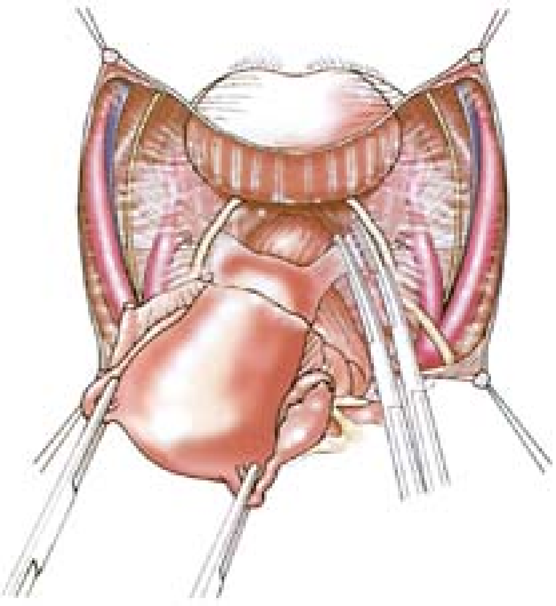

Figure 21

Division of the cardinal ligaments

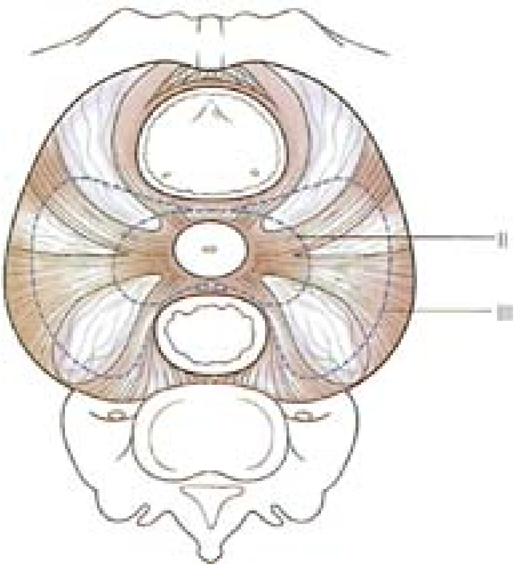

Figure 22

Rutledge II and III procedures Operative procedure

the vagina (Figure 25). As described above in cases of stage 2a tumor, the vagina may have been marked with diathermy at the start of the procedure to ensure adequate resection margins are obtained. The vagina is then incised and the uterus with parametrium and

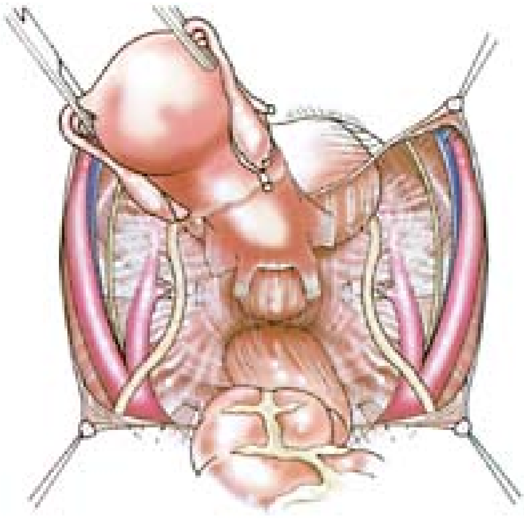

Figure 23

Pararectal spaces united

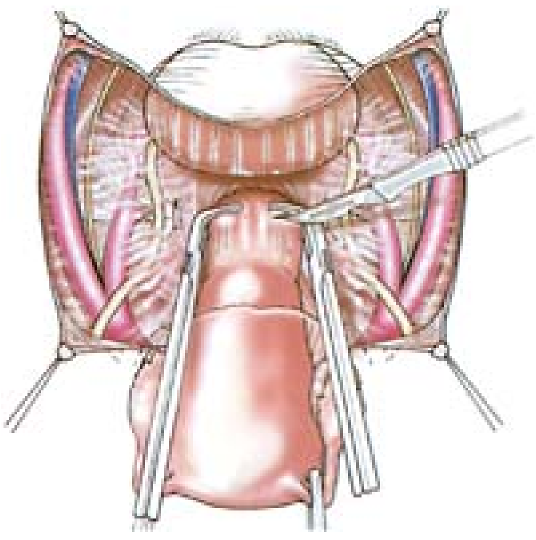

Figure 24

Paravesical spaces united

upper vagina is then removed. The upper edges of the vagina may be oversewn circumferentially with a locked-on suture to achieve hemostasis, while leaving the vagina open to act as a natural drain. It is also thought that this suturing allows the edges of the vagina to come together by direct apposition, thus minimizing the chances of vaginal mucosa being obscured from view during long-term follow-up. Direct closure of the vagina will inevitably leave some

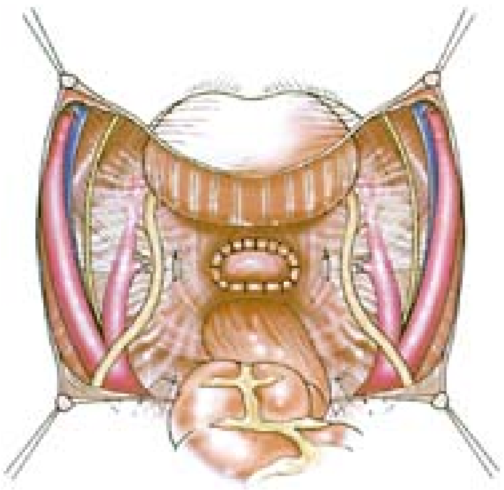

Figure 25

Division of the vagina

vagina above the suture line and thus out of sight when inspected at follow up.
At the end of the procedure, the skeletonized vessels, nerves and ureters can be clearly seen. The paravesical and pararectal spaces are joined and the rectum is exposed to the level of the pelvic floor. Many surgeons leave a silastic drain with gravity drainage in situ at the end of the procedure, although the need for this is questionable. This will probably not be required for more than 24 hours (Figure 26). Suction drainage has been shown not to reduce lymphocyst formation. A suprapubic catheter may be inserted at this point. It is the authors' practice to use one when a Rutledge III procedure has been performed, since these patients

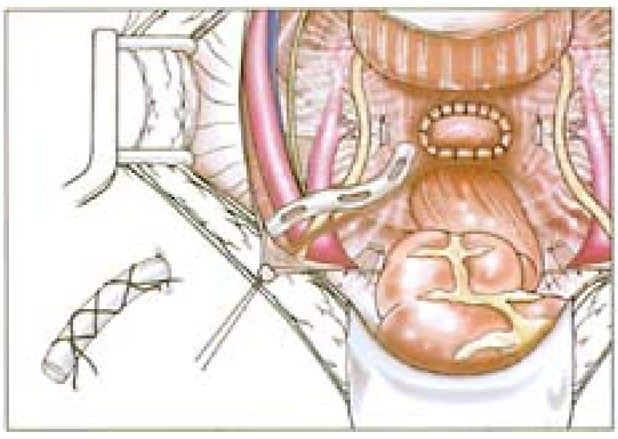

Figure 26

The completed procedure. A drain may be left in situ

are more likely to encounter urinary difficulties in the postoperative period.
The abdomen is then closed with mass closure for vertical incision using a looped PDS suture; a fat suture is not used and the authors use clips to skin. Transverse muscle cutting incisions are closed in layers, usually without attempting to repair the transected rectus muscles; again, clips to skin are used.

Reference

Piver MS, Rutledge FN, Smith JP (1974) Five classes of extended hysterectomy for women with cervical cancer. *Obstet Gynecol* **44**:265–72.

10
Radical vaginal hysterectomy

Daniel Dargent

Introduction

When surgeons considered treating cancers of the cervix in ways other than by cauterization or similar palliative tools, the vaginal hysterectomy was the first technique used (Recamier 1829). However, at the turn of the 19th century the abdominal approach became common, as a consequence of two developments. First, even if it was more risky than vaginal surgery, abdominal surgery was no longer a death sentence. Second, the concept of radical surgery, introduced by Halsted in the field of breast cancer, was also spreading to the management of all other malignancies. The first ‘radical hysterectomy’ performed by Clark in 1895 included, as a true Halstedian operation, an extirpation of the parauterine tissues and pelvic lymph nodes. Just before Clark devised the radical abdominal hysterectomy, Pavlik in Czechoslovakia (1889) and Schuchardt in Germany (1893) had described a method enabling the removal of the parauterine tissues at the same time as the uterus, while maintaining a vaginal approach. However, the removal of the pelvic lymph nodes could obviously not be included in this operation.

The abdominal and vaginal techniques were used concurrently in central Europe at the end of the 19th century. Wertheim became the champion of the first technique and Schauta the defender of the second. The long and hard fight between the two surgeons ceased when Wertheim’s book (1911) was published. Despite higher rates of per- and postoperative complications, the survival rates obtained by Wertheim were far higher than those noted by Schauta in his 1908 book. With Marie Curie’s subsequent discovery of radium in 1910 surgery was no longer a treatment option until the 1930s and 1940s.

Surgery found a new place in the management of cervical cancer as a tool to solve the problem of positive lymph nodes that were not managed by radiotherapy. Leveuf in France (1931) and Taussig in the United States (1935) proposed a combination of radiation therapy and pelvic lymphadenectomy in order to improve outcomes. This idea was the first step towards the reintroduction of radical surgery, whose official beginning was 1945, the year in which JV Meigs delivered his first paper about the new Wertheim operation. Since the highlight of the new radical surgery was systematic pelvic lymphadenectomy, the vaginal approach clearly could not benefit from the revival of such surgery.

The role of laparoscopy

Following an idea first expressed by Navratil, the Indian surgeon Suboth Mitra (1959) proposed a new combined approach and can be considered as the spiritual father of the new era of vaginal surgery in the management of cervical cancer. In the Suboth Mitra operation a systematic pelvic lymphadenectomy was first carried out through a bilateral abdominal extraperitoneal incision, then a vaginal radical hysterectomy (VRH) after Schauta. Despite two successive surgical interventions the operation remained less dangerous than abdominal radical hysterectomy (ARH) because it did not include a large and lengthy opening of the peritoneal cavity During the 1970s, postoperative morbidity was three times less after the Suboth Mitra operation than after the Meigs operation. We therefore used it (Dargent 1991) for high-risk patients, as does Massi today (Savino et al. 2001). However, we did not use the procedure on standard surgical risk patients.

In order to increase the area of application of the VRH it was proposed (Dargent 1987) to replace the bilateral abdominal incision by the laparoscopic tool for performing systematic pelvic dissection which has been part of radical hysterectomy since the Meigs publication. Thus was born the concept of 'Celio-Schauta' my (LAVRH), a concept derived from laparoscopically or laparoscopically assisted vaginal radical hysterecto-assisted vaginal hysterectomy (LAVH). LAVH has five variants. In variant 0, the laparoscopy is only used for assessing the peritoneal cavity before performing vaginal hysterectomy. In variant 1, the round ligaments and the infundibulopelvic ligaments (and the peritoneal adhesions if needed) are divided with the laparoscope. In variant 2, one pushes up to the level of the uterine arteries. In variant 3, the paracervical ligaments are also divided with the laparoscope. In variant 4, the entire operation is carried out with the laparoscope, including incision and closure of the vagina. A similar classification can be used for the LAVRH.

From 1986 to 1992, the LAVRH type 0 Celio-Schauta procedure was part of our daily practice. The laparoscope was used for assessing the pelvic cavity, the organs it contains and the lymph nodes along the pelvic side-walls in the retroperitoneal spaces. After performing the systematic pelvic lymphadenectomy the vaginal approach was used and the VRH was performed following the Celio-Schauta technique using either the German variant (Stoeckel 1928) whose radicality is like the Piver 2 ARH or the Austrian variant (Amreich 1924) whose radicality is like the Piver 3 ARH. The first operation was selected for the smallest tumors (less than 2 cm in size) and the second one was reserved for the largest (2 cm in size or more).

From 1992, a handful of papers (Dargent and Mathevet 1992, Kadar and Reich 1993, Roy et al. 1996) were published concerning variants of LAVRH which one could designate as type 3. This meant that the laparoscope was not only used for performing the indispensable systematic pelvic lymphadenectomy but also for dividing the uterine arteries and the paracervical ligaments. The common feature of these techniques was the quest for radicality which could be greatly increased thanks to the laparoscope. Indeed, one of the technical difficulties of the vaginal approach is clamping the parametrium close to the pelvic sidewall because the oblique angle of this is opposite to the angle of the following plane through which the vaginal surgeon naturally works. Conversely, arriving from above through an ipsilateral iliac laparoscopic port one arrives parallel to the plane of the pelvic side-wall and one can (using either endoscopic staplers, bipolar cauterization, argon beam or other devices) divide the parametrium at the very level of its lateral insertion. The procedure we describe in the following pages is a variant of LAVRH type 3.

Surgical procedure

The aim of the radical hysterectomy operation, whichever approach is chosen, is to retrieve part of the vagina and the parauterine tissues, together with the uterus itself. The ventral and dorsal surfaces of the vagina and of the tissues adjoining the uterus are in close proximity to the bladder floor (and the ureters) from the ventral surface of the specimen when opening the vesico-vaginal space on the midline and the paravesical spaces on either side in order to locate the bladder pillars and divide them after identification of the ureters. The dorsal aspect of the specimen is freed when the rectal pillars are divided (a much simpler step of the operation).

Laparoscopic surgery

The laparoscopic component of the LARVH can be done using either the classic transumbilical transperitoneal route, or a direct extraperitoneal approach: the latter is more appropriate because if the peritoneal cavity is not entered, there is less chance of inducing peritoneal adhesions, but it takes more time. The rate of adhesions after laparoscopic surgery, whatever the route, is low; the only situation where it is important to have no adhesions is the conservative variant of the LARVH where one intends to preserve fertility (see below).

A cutaneous incision is made along the inferior brim of the umbilicus. The abdominal fascia is opened under direct endoscopic guidance using a trocar with a transparent cutting tip (Visiport: Merlin Medical, Rhymney, UK; Optiview: Ethicon Endosurgery, Edinburgh, UK). Once the preperitoneal space is

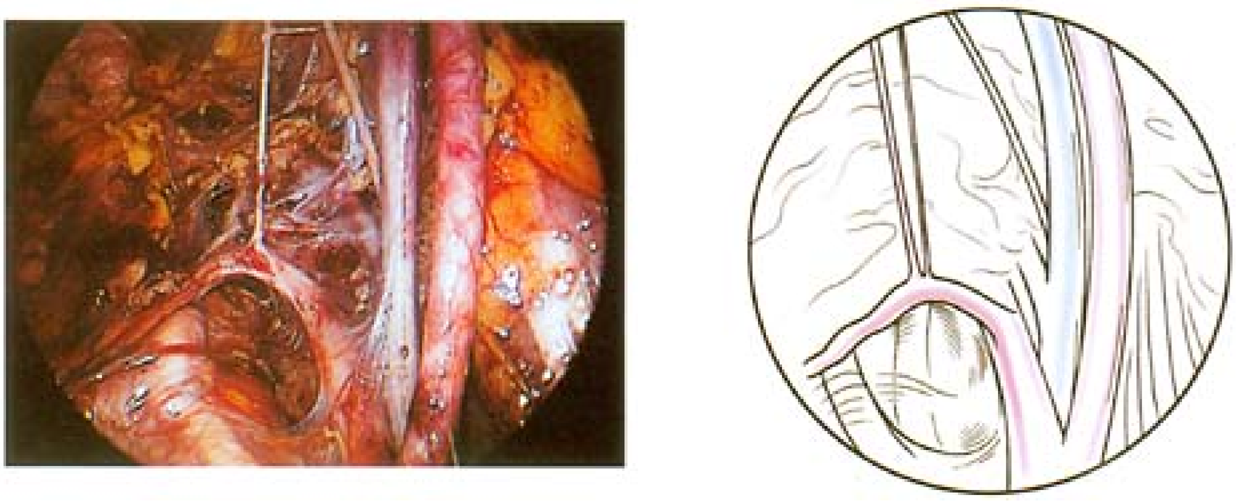

Figure 1

Laparoscopic view of the medial aspect of the common iliac bifurcation: laparoscopy has been performed using the preperitoneal approach. The superior vesical artery runs in a dorsal direction; the obturator artery runs in a ventral direction

entered the trocar is removed, the carbon dioxide insufflation is linked to the sheath and the laparoscope is introduced, pushing it vertically in a caudad direction until contact is made with the symphysis pubis. This creates a vertical tunnel, at the lower extremity of which an ancillary trocar is introduced. The trocar is pushed laterally to the McBurney area, at which level two more ancillary trocars are introduced, one on each side. Then, using three instruments (two forceps and one pair of scissors), the peritoneal sac is mobilized dorsally after the round ligaments have been cut at their most ventral, extraperitoneal, parts. The lymphadenectomy is performed in the same way as in transumbilical transperitoneal laparoscopy. The panoramic view is the same. The only differences are better 'baro' hemostasis and absence of intestinal problems.

The medial aspect of the iliac vessels is easily cleaned (Figure 1). The lateral aspect is a little more difficult. However, this can be achieved laparoscopically as effectively as it is at laparotomy—if not better. The iliac vessels are detached from the psoas muscle and pushed medially. The opened space is cleaned out until the obturator nerve is identified (Figure 2).

The last step of the laparoscopic procedure is dividing the uterine arteries and preparing the cardinal ligament (Figure 3). Rather than cutting the ligament laparoscopically, its lateral part is emptied of the lymph node-bearing tissues which are in the vascular network of the ligament. This emptying is done by gentle teasing of the adipose tissue between the vessels. Among the vessels handled are the uterine arteries which are accompanied by lymphatic channels. A superficial uterine vein can also accompany the artery (Figure 3).

Vaginal surgery

The Celio-Schauta operation starts with determining the vaginal margin (Figure 4). The separation is made roughly at the junction between the middle third and the upper third of the vagina. Traction is exerted on the forceps, creating a form of internal prolapse of the vagina. The inferior brim of the head of the prolapse is infiltrated using diluted synthetic vasopressin, primarily for prophylactic hemostasis but also to separate the two parts of the fold.

Dividing the vagina is done in four stages. The anterior aspect is treated first (Figure 5). It is the most difficult step, because the bladder floor is drawn inside the vaginal fold one pulls on. All the layers of the vaginal wall must be cut, without injury to the bladder wall. Treating the posterior aspect is easier because of the tissue present between the rectum and vagina. In the lateral aspects only the mucosa is cut (Figure 6) in order to keep the relationship between the vaginal cuff and the underlying structures (i.e. the paracervical ligaments). Compare this with the anterior and posterior surfaces, where the goal was separating the cuff from the underlying organs (i.e. the bladder and rectum).

Once the vaginal cuff is separated it is grasped using Chrobak forceps (Figure 7) and pulled downwards.

Figure 2

Laparoscopic view of the lateral aspect of the common iliac venous convergence: the obturator nerve crosses the gluteal vessels
1 Common iliac vein
2 Obturator nerve
3 Internal iliac vein
4 External iliac vein

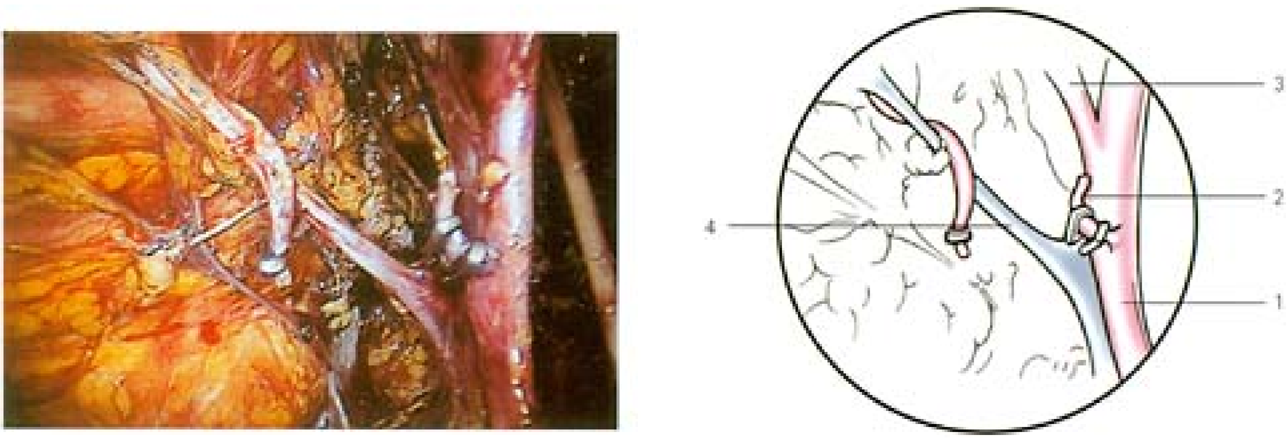

Figure 3

Laparoscopic view after transection of uterine artery: a superficial uterine vein will be cut next
1 Internal iliac artery
2 Uterine artery
3 Superior vesical artery
4 Uterine vein

Traction reveals the supravaginal septum, a pseudo-membrane made by condensation of the connective fibers joining the bladder floor to the vagina. This pseudo-aponeurosis has to be opened on the midline close to the base of the trigone (Figure 8). Once the aponeurosis has been opened (use the scissors perpendicularly to the vagina), the areolar tissue of the vesicovaginal space is visible and a tunnel can be made and enlarged up to the level of the vesicovaginal peritoneal fold (this is possible, using the scissors parallel to the vagina).
Next, the vesicovaginal space is opened, together with the paravesical space.
To open the paravesical spaces, two forceps are applied to the brim of the vagina (at positions 1 and 3 o’clock for the left side, 11 and 9 o’clock for the right side). Pulling on the forceps reveals a depression located close to the most lateral instrument (Figure 9).

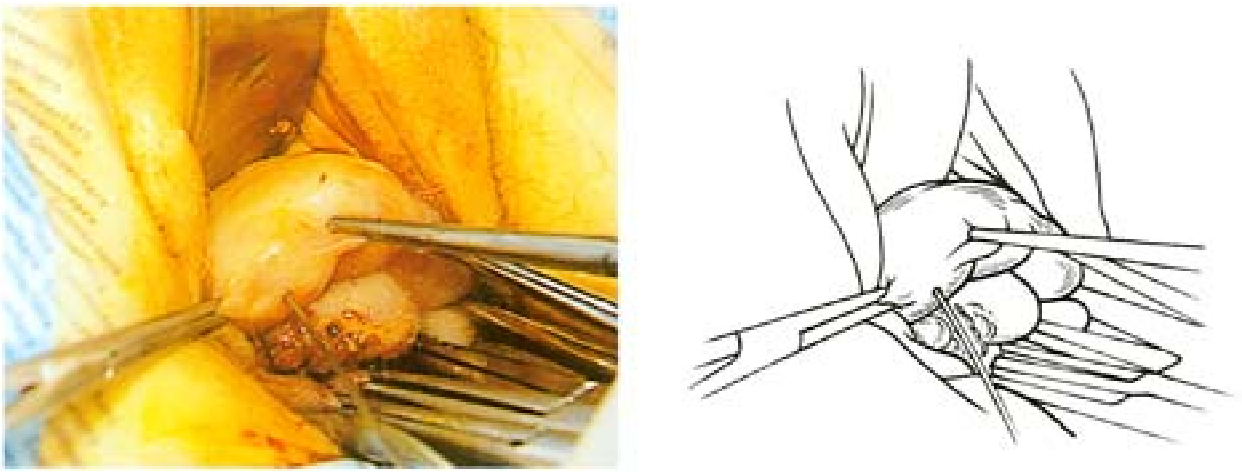

Figure 4

Infiltration of the vaginal margin

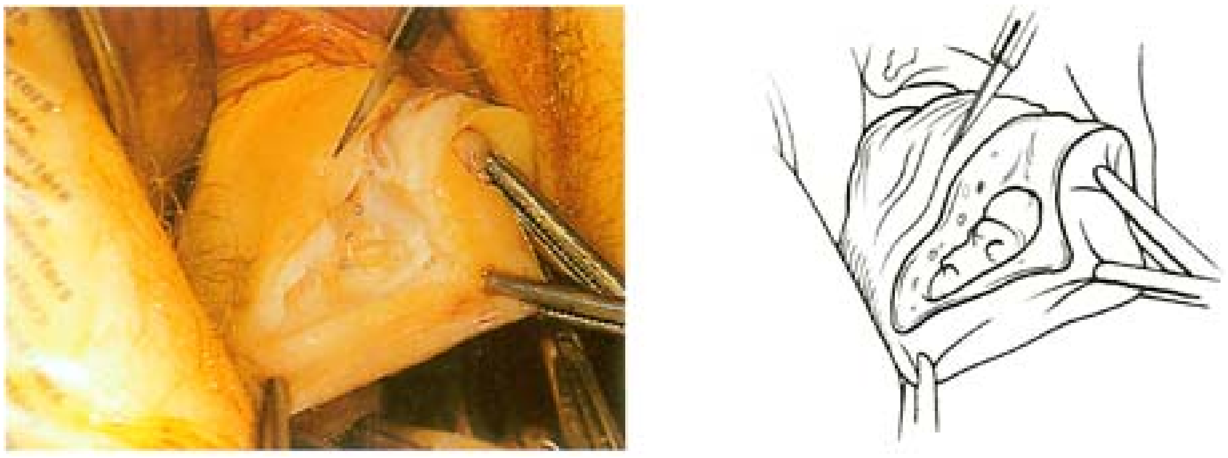

Figure 5

The Celio-Schauta operation: separation of the vaginal cuff on the ventral (anterior) aspect; the incision is full thickness

Deepening this depression by blunt use of Metzenbaum's scissors oriented laterally and ventrally (Figure 10) opens the paravesical space, into which is introduced a micro-Breiski retractor. The structure interposed between this retractor and the previously opened vesicovaginal space is the bladder pillar, inside which the contour of the ureter can be identified while palpating the pillar against the retractor. The characteristic 'snap' of the ureter is evinced (Figure 11).

While appropriate exposure is maintained with the retractors, the inferior brim of the pillar, which appears vertical, is opened with the tip of the scissors and its lateral fibers are separated using the same scissors (Figure 12). After a new palpatory assessment (make sure the ureter is located laterally to the isolated part of the pillar) the fibers of the pillar are cut (Figure 13). The paravesical space becomes wider, and a broader retractor is introduced. The lateral aspect of the 'knee' of the ureter becomes visible (Figure 14). The medial fibers of the pillar can then be cut to release the ventral aspect of the paracervical ligament (Figure 15): this enables location of the arch of the uterine artery in the paraisthmic window (a space whose inferior brim is the superior edge of the para-cervical ligament). The descending branch of the arch is tugged and the already divided artery arrives in the operative field with a staple at the cut end (Figure 16).

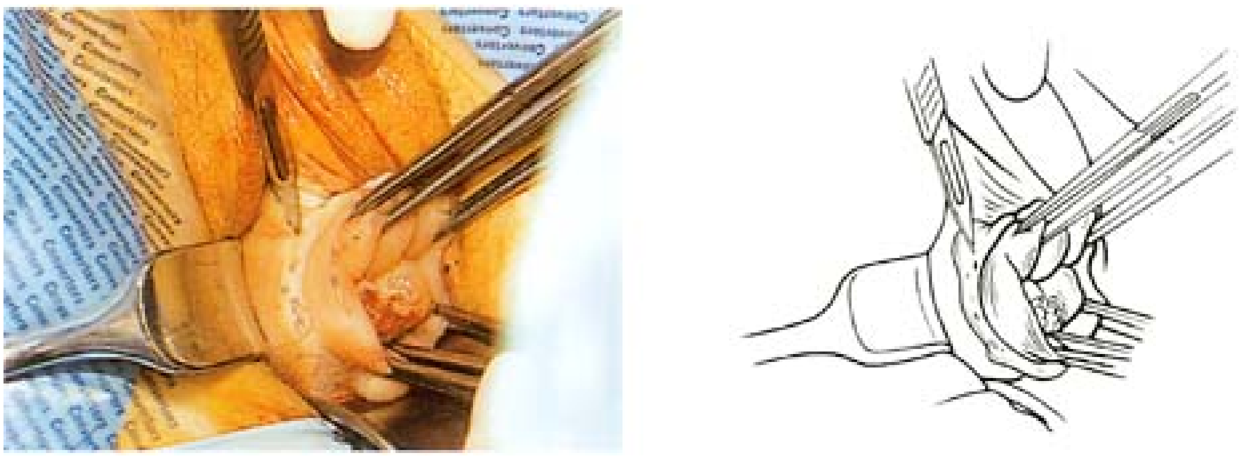

Figure 6

Separation of the vaginal cuff on the lateral aspect; the incision is only through the skin

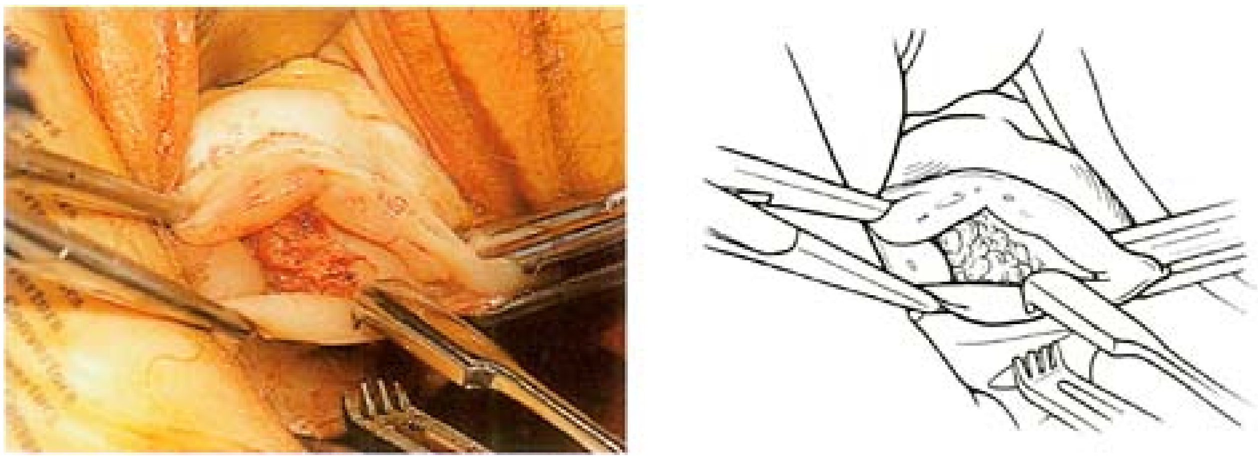

Figure 7

Grasping the vaginal cuff with the forceps

After freeing the ventral aspect of the specimen, the surgeon moves to the dorsal aspect. The first step is opening the pouch of Douglas (Figure 17). The rectouterine ligaments are then divided, at a point equidistant between the uterus and the intestine. Cutting at this level is easy (no preventive clamping is needed) and leads directly to the dorsal aspect of the paraisthmic window, the ventral aspect of which has been identified previously. The tip of a right angle forceps is pushed into the window from back to front.

Two clamps can be put on to the cardinal ligament. The first one is placed medially, and traction is exerted. The second clamp (which has a slightly greater curvature) is placed laterally; the convexity of its curvature lies in contact with the 'knee' of the ureter (Figure 18).

Following transection of the ligaments, the uterine body can be turned in a dorsal direction, and the adnexa can be left in place or removed, depending on the age of the patient (Figure 19). The subsequent steps are straightforward. The author's preference is for peritonization with two laterally angled stitches and a middle continuous suture, placing the stumps in an extraperitoneal position and joining the rectal peritoneum and the vesical peritoneum. Hemostasis is performed as necessary. The vagina is closed without a drain or gauze. A Foley catheter is left in place for 5 days.

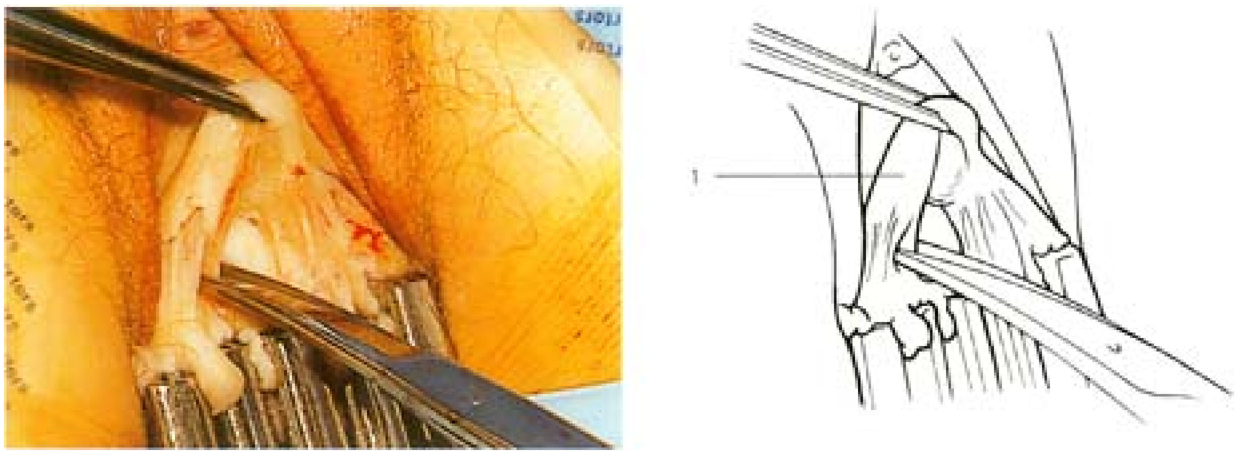

Figure 8

Opening the vesicovaginal space on the midline
1 Bladder

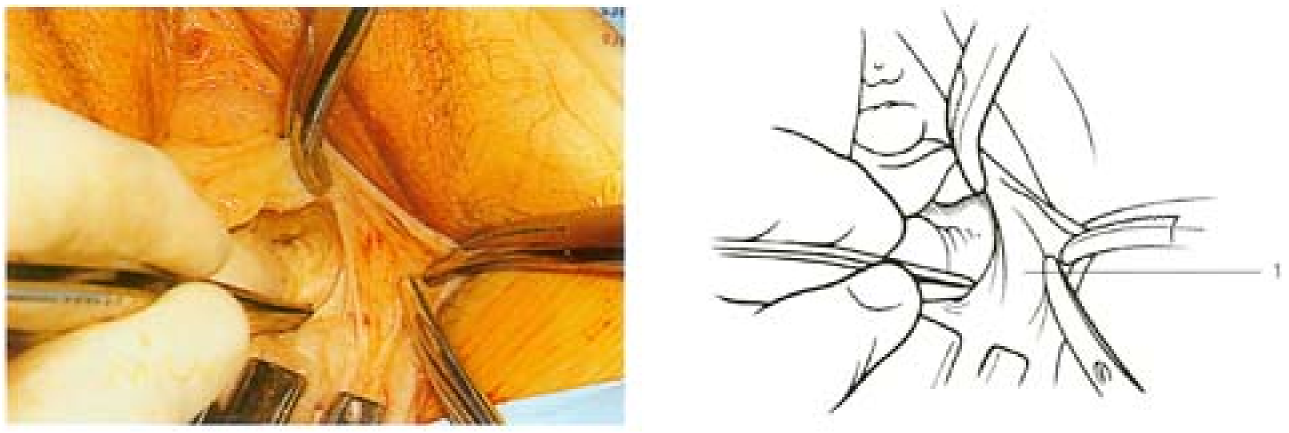

Figure 9

Opening the paravesical space
1 Bladder pillar

Postoperative complications

The LAVRH is performed over three hours, roughly divided two hours for the laparoscopic part and one hour for the vaginal part. Preservation of the bladder floor and ureters is the main concern. Injuries can occur and these are easily detected because of urine leakage. This can usually be corrected without having recourse to laparotomy. If the injury concerns the ureter(s) or the bladder floor close to the ureteric orifices do not omit to put stents into them. Other postoperative problems are nonspecific.
Postoperative progress is usually straightforward. The patient can and must get up the day after surgery. The return to normal diet should be rapid. However, resuming normal urinary bladder function can take time. We recommend leaving the bladder catheter in place for 5 days and removing it on day 6. If, after the end of day 6, the bladder volumes are incomplete (residue more than 100 mL), self-catheterization is taught to the patient who can then be discharged.
Postoperative complications are similar to those that can occur after any lengthy pelvic surgery.
Hemorrhage is usually the first complication. It often occurs during the first 48 hours postoperatively.
Postoperative pelvic contents of various types can be observed due to occult bleeding during initial postoperative days, or because of the accumulation of lymphatic fluid during the following weeks.
Fistulas are generally the consequence of undiagnosed injuries

Figure 10

Evincing the entry into the paravesical space on the left side
1 Bladder pillar

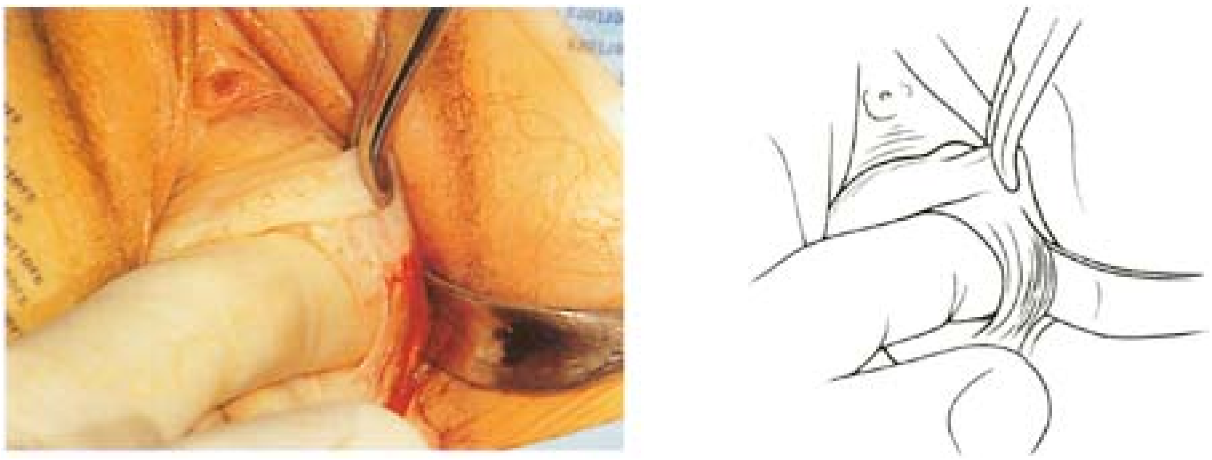

Figure 11

Palpation of the bladder pillar on the left side to elicit the ‘snap’ of the ureter

and symptoms appear in the first hours following surgery. Fistulas linked to tisssue necrosis and occurring later in the postoperative course are practically unknown after VRH, unlike ARH. Nevertheless it is mandatory to ask for an intravenous pyelogram if injury is suspected.
Urethrovesical, coloproctological and sexual sequelae can occur. The first is of most concern: the bladder-voiding difficulties observed in the immediate postoperative period can persist in the form of loss of feeling of the need to urinate, and taking a long time to void. At its worst, self-catheterization is the treatment. A urinary calender and biofeedback are usually enough. Constipation can be a consequence of neurogenic rectal atony. Non-irritant laxatives and biofeedback are the two pillars for management.
The complication rates of LAVRH depend essentially on the learning curve effect’. In the literature of the early 1990s, the rate of urinary injuries and/or fistulas was around 10%. In the literature of the early 2000s, the rates are much lower. In the Quebec City experience (Renaud 2000) seven complications were observed among 91 patients of which three were among the first 25 cases and four among the 77 following cases. In the Jena experience (Hertel et al. 2003), 65% of the complications occurred for the first 100 cases versus 35% for the 100 following cases. Other publications (Querleu et al. 2002) do not

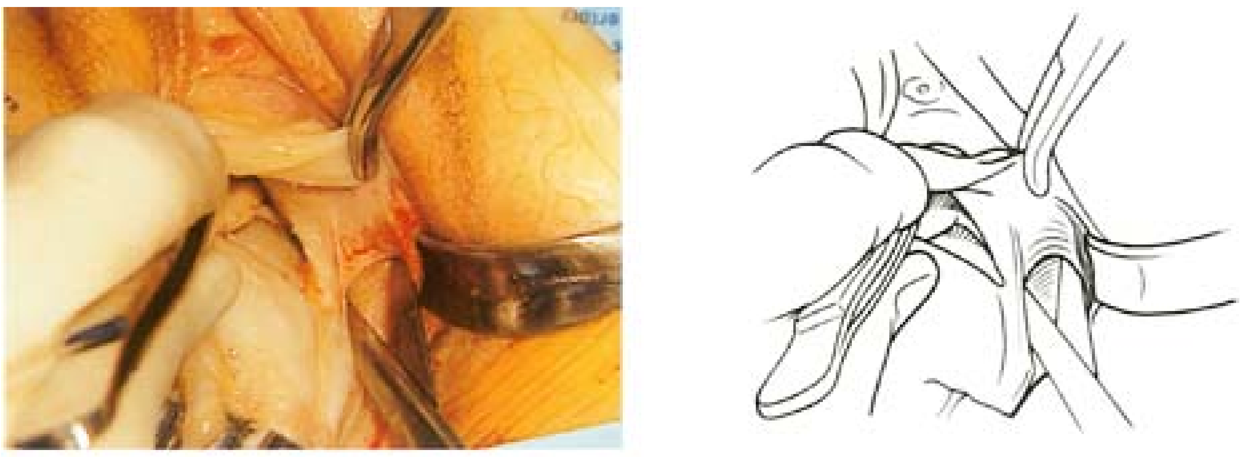

Figure 12

Separation of the lateral part of the bladder pillar on the left side

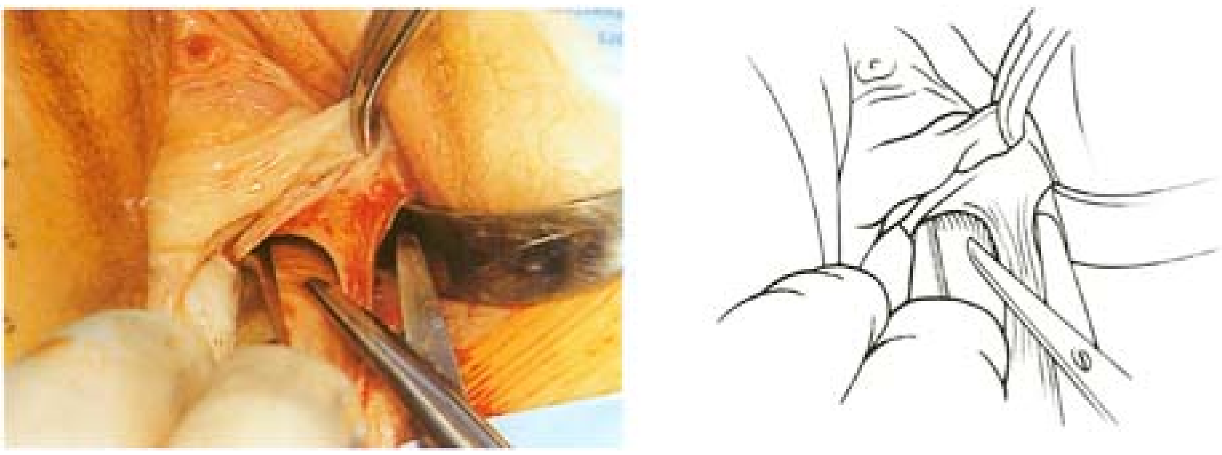

Figure 13

Cutting the lateral part of the bladder pillar

Figure 14

Further division of the lateral fibers of the bladder pillar on the left side: the knee of the ureter is visible

Figure 15

Division of the medial part of bladder pillar on the left side

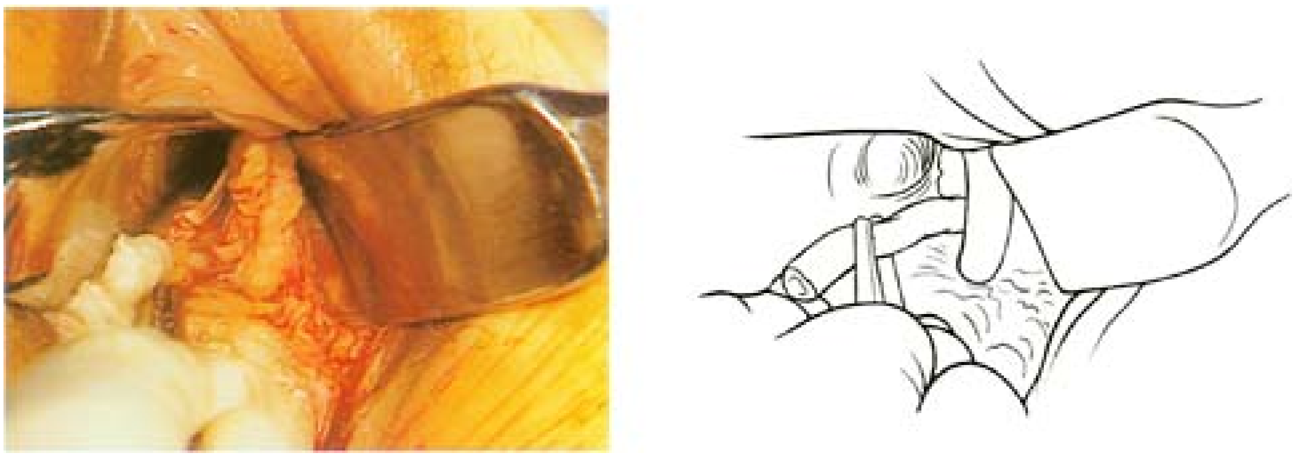

Figure 16

Pulling on the descending branch of the uterine artery arch on the left side

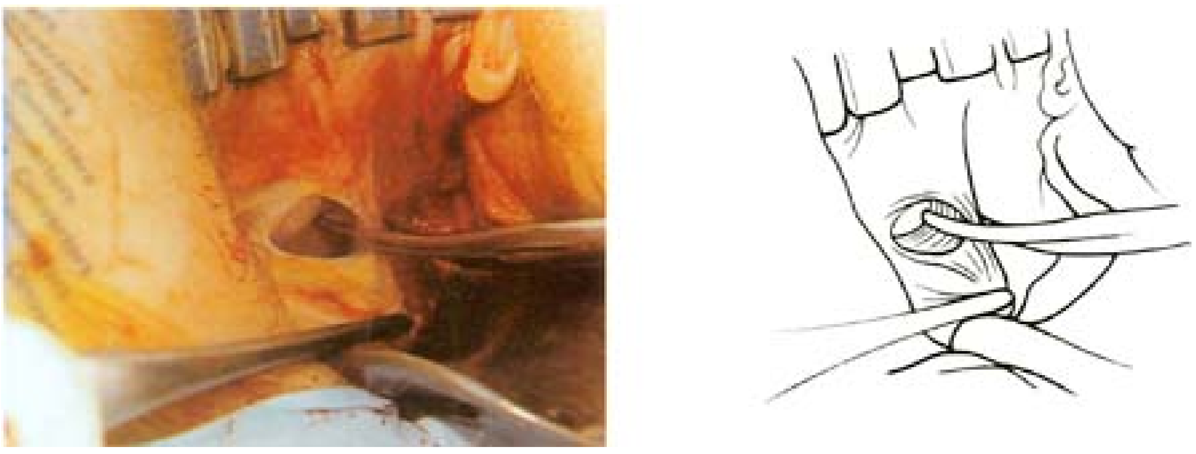

Figure 17

Opening the pouch of Douglas and the rectal pillar

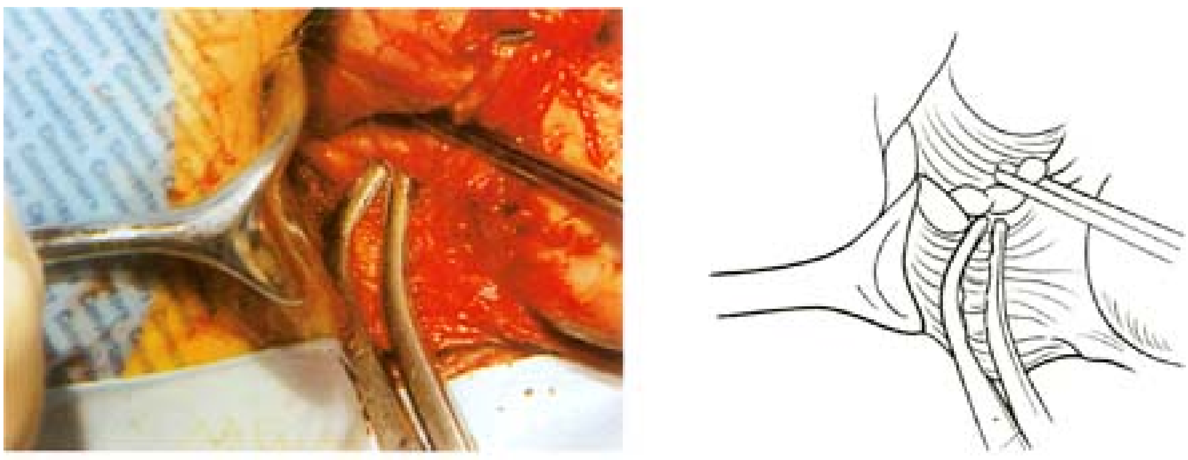

Figure 18

Paracervical ligament is clamped, the lateral clamp being put underneath the tip of the 'knee' of the ureter

Figure 19

Lateral portions of paracervical ligaments are lacking here, having been cleared out during the laparoscopic procedure

mention any severe complications, with the exception of one postradiotherapy ureteral stenosis in a series of 95 patients who had LAVRH.

Indications

Recent literature enables us to define the indications for the LAVRH. In our own series (unpublished data) the actuarial disease-free 5-year survival was 94.2% in a series of 216 patients with cervical cancer stage NO, pIA2 and pIB1 who had Celio-Schauta or LAVRH surgery between December 1986 and May 2002. However, in stage IB2 and higher, the results are less good. In the Jena series (Hertel et al. 2003) the actuarial disease-free 5-year survival was under 70% for stage IB2 and under 60% for stage IIA and IIB. In stage IB1, a clear cut-off exists between tumors less than 2 cm in size and the others. In our own experience (unpublished data), the disease-free 5-year survival was 100% for the 144 patients with tumors less than 2 cm in size versus 87.5% for the 72 patients with tumors 2 cm or more in size. Among patients with the largest tumors followed for 3 years or more, the number of recurrences was 4 out of 23 after VRH type Schauta-Amreich, 3 out of 11 after VRH type Schauta-Stoeckel, and 3 out of 19 after VRH type Schauta-Stoeckel preceded by paracervical lymphadenectomy carried out as a complement to laparoscopic pelvic lymphadenectomy which was performed in all cases.
Cancer stage IB2 and higher clearly cannot be treated with LAVRH. Clinical examination and magnetic resonance imaging (MRI) are key for this first selection. The team from Jena (Hertel et al. 2003) proposes going further and rejecting cases with lymphovascular space involvement and also pN1. The first risk factor is assessed on the initial large biopsy specimen. The second can be evidenced at the initial imaging. If not, frozen sections done on the nodes retrieved after laparoscopic dissection give the answer. Such a selection could provide a 98% rate of 5-year disease-free survival. Furthermore, this result can be obtained at the price of the least aggressive of the VRH techniques (i.e. that of Stoeckel). Our data seem to demonstrate that the parametrial lymphadenectomy performed during the laparoscopic part of the surgery significantly lower the chances of recurrence.

Conclusions

LAVRH, in the light of the published data, is likely to be equivalent to ARH in the management of early cervical cancer for the chances for cure. The evidence is level B (consistent retrospective and prospective surveys). Concerning postoperative comfort, LAVRH offers better than the ARH (level A). The minimally invasive surgery, at first sight, seems to be more ‘patient-friendly’. However, classic surgery has changed a lot since the time the LAVRH appeared and has been developed further: new incisions, instruments (Ligasure®, Biclamp®), wound closure techniques, and analgesic strategies, make postoperative progress much less painful than it was.

References

Amreich AI (1924) Zur Anatomic und Technik der erweiterten vaginalem Carzinom Operation. *Arch Gynäkol* **122**:497.

Clark JG (1895) A more radical method for performing hysterectomy for cancer of the uterus. *Bull Johns Hopkins Hosp* **6**:120.

Dargent D (1987) A new future for Schauta’s operation through presurgical retroperitoneal pelviscopy. *Eur J Gynaecol Oncol* **8**:292.

Dargent D (1991) Treatment of the cancers of the ectocervix and vagina with preservation of the uterus and adnexae. *Cah Oncol* **1**:21.

Dargent D (2001) Radical trachelectomy: an operation that preserves the fertility of young women with invasive cervical cancer. *Bull Acad Natl Med* **185**:1295.

Dargent D, Mathevet P (1992) Radical laparoscopic vaginal hysterectomy.*J Gynecol Obstet Biol Reprod (Paris)* 21:709.

Dargent D, Kouakou N, Adeleine P (1991) L’opération de Schauta 90 ans après. *Lyon Chir* **87**:324.

Hertel H, Kohler C, Michels W, et al. (2003) Laparoscopic-assisted radical vaginal hysterectomy (LARVH): prospective evaluation of 200 patients with cervical cancer. *Gynecol Oncol* **90**:505.

Kadar N, Reich H (1993) Laparoscopically assisted radical Schauta hysterectomy and bilateral laparoscopic pelvic lymphadenectomy for the treatment of bulky stage IB carcinoma of the cervix. *Gynaecol Endosc* **2**:135.

Leveuf J (1931) L’envahissement des ganglions lymphatiques dans le cancer du col de l’uterus. *Bull Mem Soc Nat l Chir* **57**:662.

Meigs JV (1945) Wertheim operation for carcinoma of the cervix. *Am J Obstet Gynecol* **49**:542.

Mitra S (1959) Extraperitoneal lymphadenectomy and radical vaginal hysterectomy for cancer of the cervix (Mitra technique). *Am J Obstet Gynecol* **78**:191.

Pavlik K (1889) O extirpaci cele dälohy a casti vaziva panvicniho. *Casopis Lekaru Ceskych* XVIII:28.

Pomel C, Atallah D, Le Bouedec G, et al. (2003) Laparoscopic radical hysterectomy for invasive cervical cancer: 8-year experience of a pilot study. *Gynecol Oncol* **91**:534.

Querleu D, Narducci F, Poulard V, et al. (2002) Modified radical vaginal hysterectomy with or without laparoscopic nerve-sparing dissection: a comparative study. *Gynecol Oncol* **85**:154.

Recamier JCA (1829) Ablation de l’uterus cancereux. In: *Recherche sur le traitement du cancer*. Paris: Gabon, 519–29.

Renaud MC, Plante M, Roy M (2000) Combined laparoscopic and vaginal radical surgery in cervical cancer. *Gynecol Oncol* **79**:59.

Roy M, Plante M, Renaud MC, Tetu B (1996) Vaginal radical hysterectomy versus abdominal radical hysterectomy in the treatment of early-stage cervical cancer. *Gynecol Oncol* **62**:336.

Savino L, Borruto F, Comparetto C, Massi GB (2001) Radical vaginal hysterectomy with extraperitoneal pelvic lymphadenectomy in cervical cancer. *Eur J Gynaecol Oncol* **22**(1):31–5.

Schauta F (1908) *Die erweiterte vaginale Totalextirpation des Uterus beim Kollumkarzinome.* Vienna: J.Safar.

Schneider A, Possover M, Kamprath S, et al. (1996) Laparoscopy-assisted radical vaginal hysterectomy modified according to Schauta-Stoeckel. *Obstet Gynecol* **88**:1057.

Schuchardt K (1893) Eine neue Methode der Gebärmutterexstirpation. *Zbl Chir* 1131.

Stoeckel W (1928) Die vaginale Radikaloperation des Collumkarzinomes. *Zbl Gynäkol* **52**:39.

Taussig FJ (1935) The removal of lymph nodes in cancer of the cervix. *Am J Roentgenol* **34**:354.

11
Radical vaginal trachelectomy

Marie Plante
Michel Roy

Introduction

Cervical cancer frequently affects young women in their reproductive years, often before they have had the chance to begin or complete their family plans. So, in terms of quality of life, fertility preservation has become a major issue in the management of young women with early-stage cervical cancer (Plante 2000).

Vaginal radical trachelectomy (VRT) is a new conservative fertility-preserving surgical procedure for the treatment of selected cases of early-stage cervical cancer. This procedure has the advantage of preserving the uterine body, which in turns allows preservation of childbearing potential. This surgery has been described and first published by Professor Daniel Dargent from Lyon, France (Dargent 1994). The procedure has been performed for over 15 years and several hundreds of women have undergone this procedure worldwide. More than 150 pregnancies have been reported and close to 100 healthy babies have been born so far. The majority of patients have delivered by elective cesarean section and approximately two thirds were at term. The main obstetrical problem is the risk of premature second trimester birth or miscarriage. Oncologic results are also reassuring as the risk of recurrences remains less than 5% (Plante 2003).

Indications

Currently, the indications for this procedure are not definitely established. The eligibility criteria have not changed significantly since first proposed (Roy and Plante 1998). As data accumulate, these criteria are subject to change in the future. These criteria are:

1. Desire to preserve fertility
2. No clinical evidence of impaired fertility
3. Lesion size less than 2.0–2.5 cm
4. International Federation of Obstetrics and Gynaecology (FIGO) stage IA1 with invasion of vascular space (VSI), stage IA2–IB1
5. Squamous cell or adenocarcinoma
6. No involvement of the upper endocervical canal as determined by colposcopy and/or magnetic resonance imaging (MRI)
7. No metastasis to regional lymph nodes.

Anatomic considerations

Vascular supply

The blood supply to the cervix is assured by the *cervical* (or descending) branch of the uterine artery, and by the *vaginal* artery which originates from either the hypogastric, the uterine or the superior vesical artery. At the level of the upper endocervix, these two arteries form a network of anastomosis and a rich vascular plexus. At the isthmus, the uterine artery also forms a loop often referred to as the *cross* of the uterine artery. This is an important landmark because all efforts should be made to preserve the uterine artery in order to assure a good vascular supply to the uterine body,

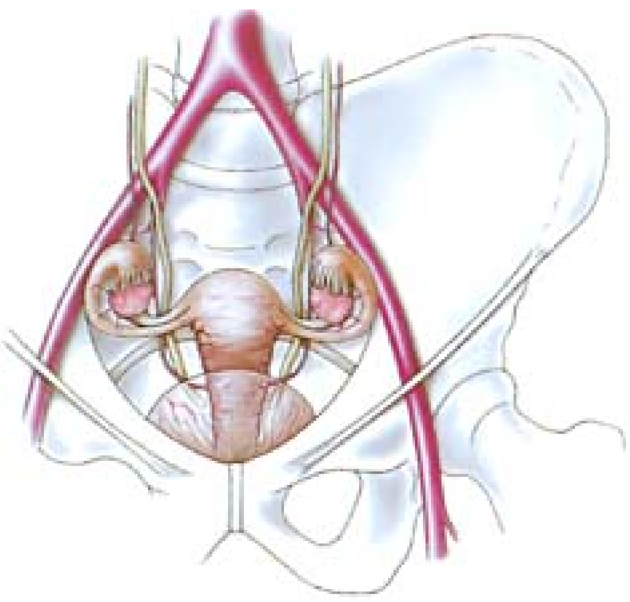

Figure 1

Cervical vascular supply

particularly in the event of a pregnancy. The venous supply follows the arterial one (Figure 1).

Uterovaginal endopelvic fascia

The endopelvic fascia refers to the reflections of the superior fascia of the pelvic diaphragm upon the pelvic

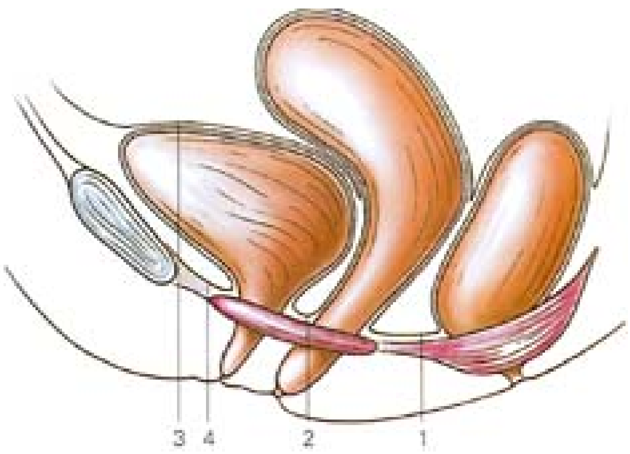

Figure 2

1 Rectal fascia
2 Uterovaginal fascia
3 Pelvic peritoneum
4 Urethrovesical fascia

viscera. This thin layer thus encases respectively the urethra and bladder (urethrovesical fascia), the vagina and lower uterus (uterovaginal fascia) and the rectum (rectal fascia). The uterovaginal endopelvic fascia is of particular importance as it lies in close proximity to the pelvic peritoneum. The former is an avascular space that should be defined when mobilizing the bladder base at the time of VRT, but the anterior pelvic peritoneum itself should not be entered (Figure 2).

Cardinal (Mackenrodt) ligament

The cardinal ligament is composed of condensed fibrous tissue and some smooth muscle fibers. It extends from the lateral aspect of the uterine isthmus toward the pelvic wall. This fibrous sheath contains the ureter, the uterine vessels and associated nerves, the lymphatic channels and lymph nodes draining the cervix and some fatty tissue. It is commonly referred to as the *parametrium*. The cardinal ligament is in continuity anteriorly to the uterovaginal endopelvic fascia and posteriorly, fibers are integrated with the uterosacral ligament. Since VRT is performed in patients with small lesions, only the medial part (i.e. approximately 2 cm) of the cardinal ligaments is usually taken at the time of a VRT (Figure 3).

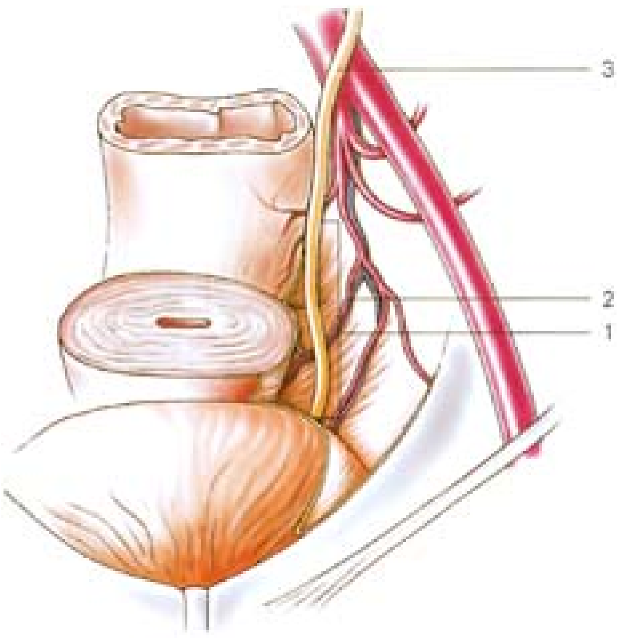

Figure 3

1 Cardinal ligament
2 Uterine artery
3 Ureter

Uterosacral ligaments

These ligaments are true ligaments of musculofascial consistency that run from the upper part of the cervix to the sides of the sacrum. They contribute to the uterine support together with the cardinal ligaments. Only the proximal part of the uterosacral ligaments are taken at the time of VRT so as to leave adequate uterine support (Figure 3).

Surgical procedure

Anatomic relationship

It is of paramount importance to understand the relationship between the ureter, the uterine artery and the cardinal ligament (parametrium), and picture the relationship between the bladder base and the lower uterine segment when performing radical vaginal surgery When a radical hysterectomy is done *abdominally*, the uterus is pulled upwards bringing with it the para-metrium and the uterine vessels, while the bladder base is mobilized downwards. Therefore, the uterine vessels lie *above* the concavity of the ureters as the ureters run into the parametrial tunnel to enter the bladder base. Thus, after mobilization, the ureters end up lateral and below the parametrium (Figure 4A). When the radical hysterectomy is done *vaginally*, the relationship between the structures is the complete opposite. The uterus is pulled downwards and the bladder base along with the ureter is mobilized upwards. As such, the uterine vessels end up *below* the concavity or the ‘knee’ of the ureter and after mobilization, the ureter courses above the parametrium (Figure 4B).

Vaginal cuff preparation

A rim of vaginal mucosa is delineated circumferentially clockwise using 8–10 straight Kocher clamps placed at regular intervals. For small lesions, 1–2 cm of vaginal mucosa is sufficient. To reduce bleeding from the edges of the vaginal mucosa, 20–30 cc of a xylocaine 1% solution mixed with adrenaline (epinephrine) 1:100000 is used to inject the vaginal mucosa between each Kocher clamp. A circumferential incision is then made with a scalpel just above the Kocher clamps (Figure 5). Finally, the edges of the vaginal mucosa are grasped with 5 or 6 Chrobak clamps in order to completely cover the exocervix and allow a good traction on to the specimen (Figure 6).

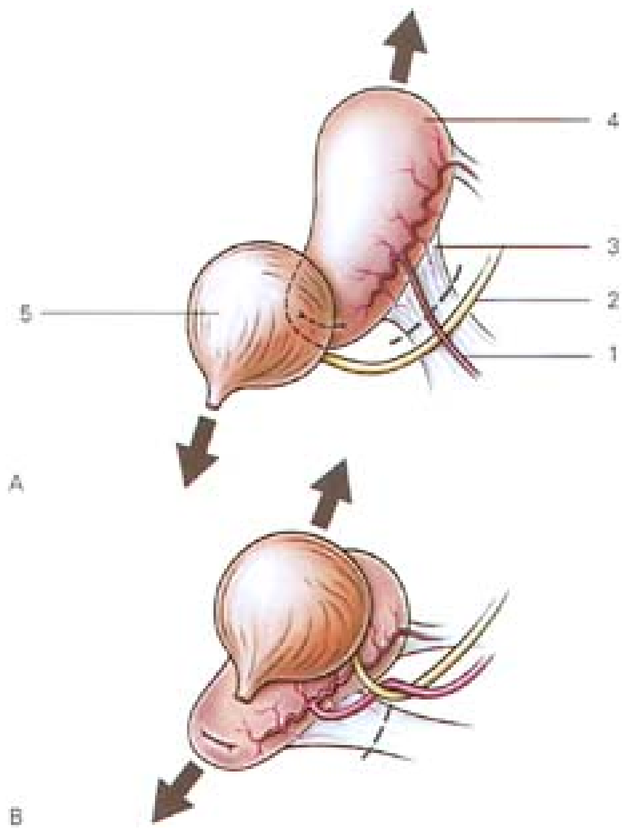

Figure 4

Comparison of (A) abdominal and (B) vaginal approaches to radical hysterectomy (after Dr Hélène Roy). The arrows indicate the direction of traction; the dotted line indicates the level of excision of the parametrium
1 Uterine artery
2 Ureter
3 Parametrium
4 Uterus
5 Bladder

Identification of the vesicouterine space

This space is opened by directing Metzenbaum scissors perpendicular to the cervix. Care is taken not to enter the peritoneum as in a simple vaginal hysterectomy. The space should be avascular and allows one to easily palpate the anterior surface of the endocervix and isthmus and see the whitish body of the uterus and the bladder base. When the space is stretched with a narrow Deaver, the anterior bladder pillars lie on each side of the space as vertical strands of tissue (Figure 7).

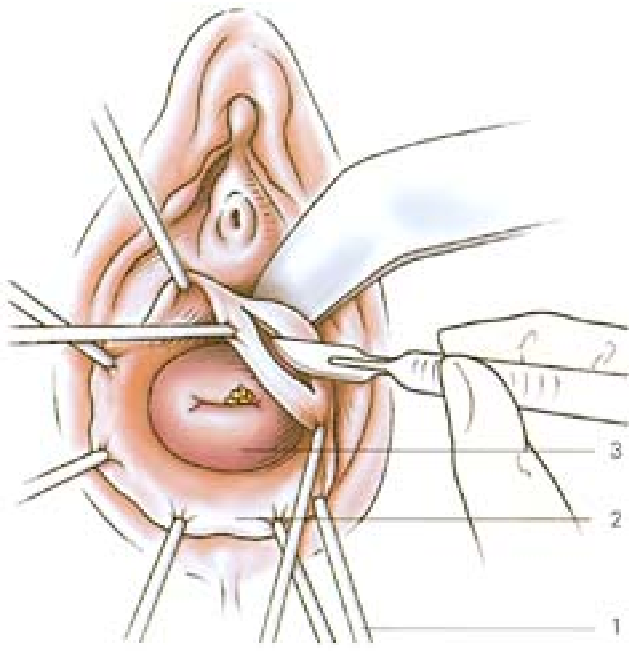

Figure 5

Vaginal cuff preparation: incision (after Dr Hélène Roy)
1 Straight Kocher clamps
2 Vaginal mucosa
3 Cervix

Opening of the paravesical space

This is a description for the patient's left side. The Chrobak clamps are pulled towards the patient's right side. Straight Kocher clamps are placed onto the vaginal mucosa at 1 and 3 o'clock and stretched out. An areolar opening is seen just medial and slightly anterior to the 3 o'clock clamp. The space is *blindly* entered using Metzenbaum scissors, with the tips pointing upwards and outwards. The space is widened by rotating the scissors under the pubic bone in a semicircular rotating motion to the patient's right side (Figure 8).

Identification and mobilization of the ureter

A small retractor is placed in the left paravesical space and rotated under the symphysis pubis pulling the

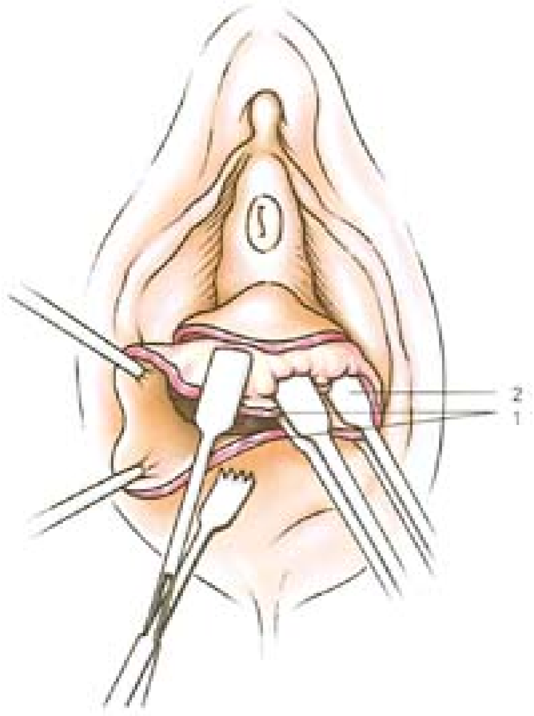

Figure 6

Vaginal cuff preparation: placing the clamps (after Dr Hélène Roy)
1 Anterior and posterior vaginal mucosa covering cervix
2 Chrobak clamps

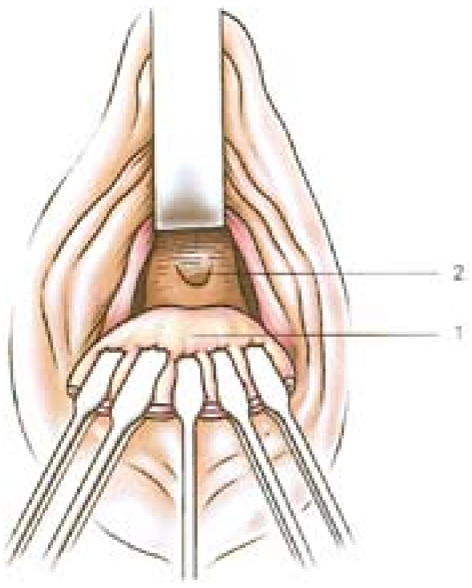

Figure 7

Opening the vesicouterine space (after Dr Hélène Roy)
1 Exocervix
2 Uterine isthmus

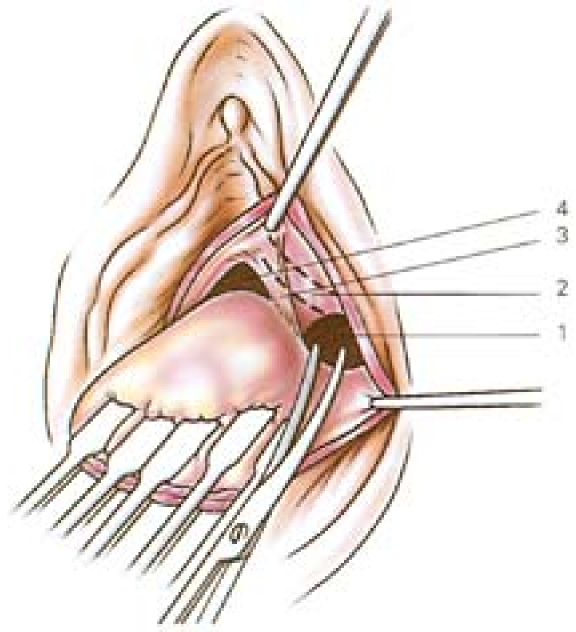

Figure 8

Opening the paravesical space (after Dr Hélène Roy)
1 Paravesical space
2 Ureter
3 Bladder pillars
4 Vesicouterine space

bladder pillars and the bladder medially. The knee of the ureter is located on the lateral aspect of the bladder pillars which act as pseudo-ligaments (Figure 9). Holding the Chrobak clamps between the palms of both hands, the surgeon's right index finger (or the back of a surgical instrument) is placed in the left paravesical space and the left index finger in the vesicouterine space. The surgeon's fingers are then pulled down gently until the 'click' is *heard* and the ureter is *felt* rolling under the fingers (Figure 10).

Section of the bladder pillars

To avoid damage, the ureter has to be seen and palpated unequivocally. With Metzenbaum scissors, the bladder pillars are stretched open and dissected carefully until the ureter is seen (Figure 11). Once the ureter has been safely mobilized upwards, the bladder pillars can be excised midway between the bladder base and the anterior aspect of the specimen (Figure 11). The ureter is then freed laterally from its posterior attachment to allow its mobilization upwards (Figure 11). Medial dissection of the ureter

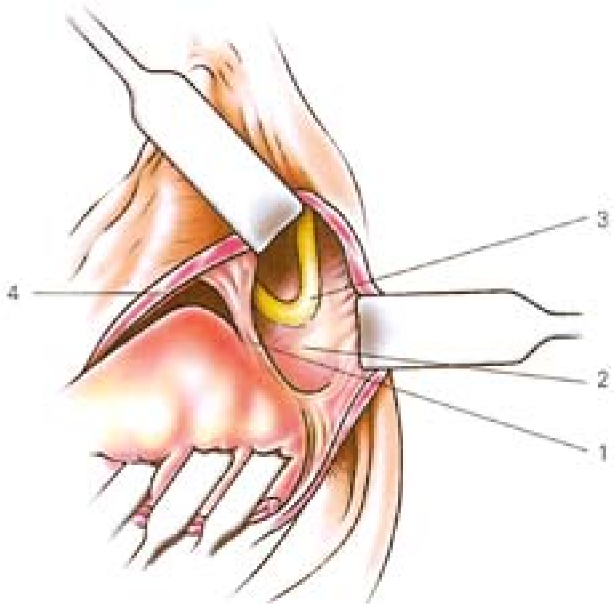

Figure 9

The 'knee' of the ureter is exposed on the lateral aspect of the bladder pillars (after Dr Hélène Roy)
1 Bladder pillars
2 Paravesical space
3 Knee of ureter
4 Vesicouterine space

should be avoided because of the risk of injury to the bladder base. This maneuver allows the ureter and the bladder base to be mobilized upwards as well.

Section of the cardinal ligament (proximal parametrium)

After opening the posterior cul-de-sac, the proximal aspect of the uterosacral ligament is excised. After careful re-identification of the ureter and the cross of the uterine artery, two curved Heaney clamps are used to secure the cardinal ligament or proximal parametrium. The first Heaney clamp is placed medially and with gentle traction the second Heaney is placed more distally to get wider parametrium, having the ureter safely mobilized upwards (Figure 12). The cervicovaginal branch of the uterine artery is then identified at the level of the isthmus, clamped, excised and ligated. Care should be taken to carefully identify and preserve the cross of the uterine artery (Figure 13).

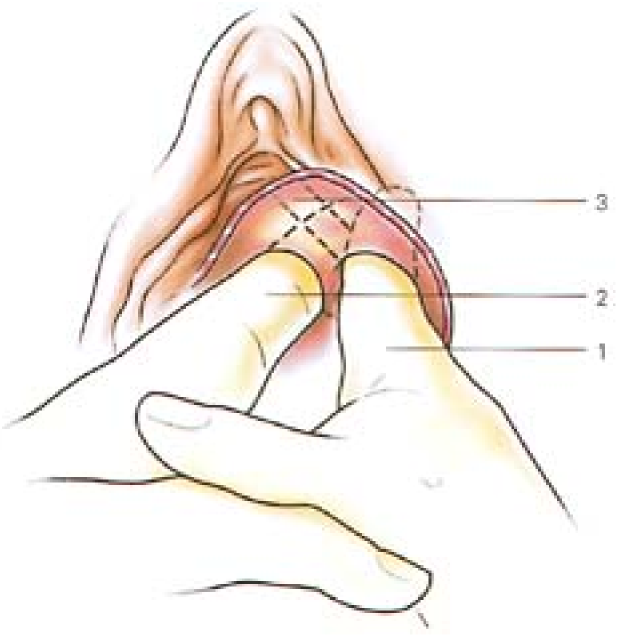

Figure 10

To avoid damage to the ureter, it must be clearly seen and palpated (after Dr Hélène Roy)
1 Right index in paravesical space
2 Ureter
3 Left index in vesicouterine space

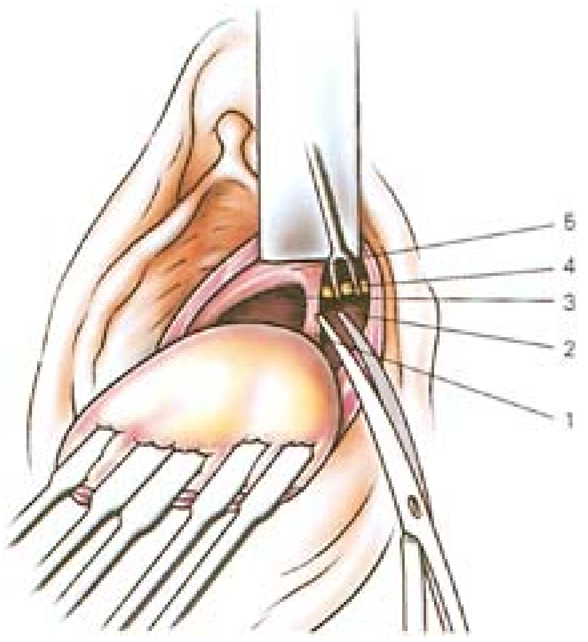

Figure 11

Excision of the bladder pillars (after Dr Hélène Roy)
1 Bladder pillars 4 Ureter
2 Paravesical space 5 Bladder base
3 Vesicouterine space

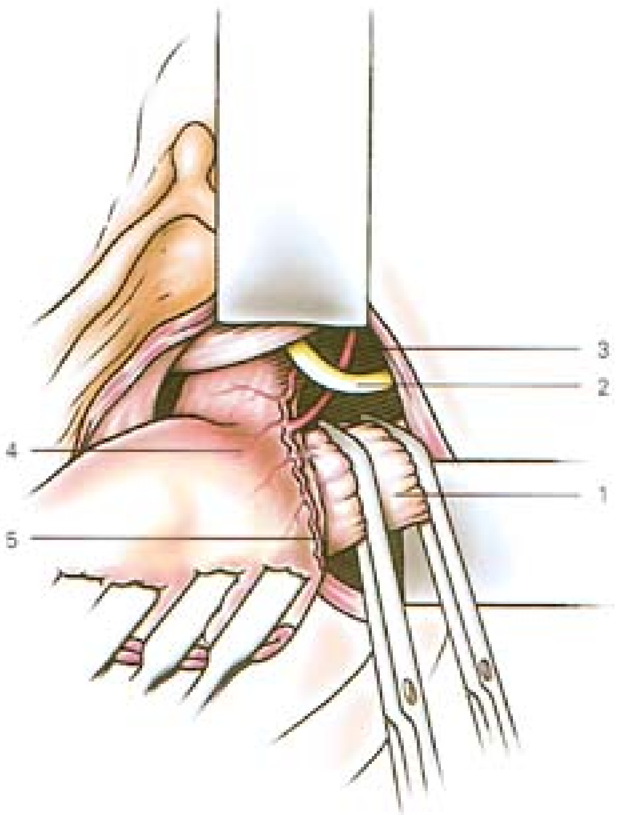

Figure 12

Excision of the parametrium (after Dr Hélène Roy)
1 Parametrium
2 Ureter
3 Uterine artery
4 Isthmus with cross of uterine artery
5 Descending branch of uterine artery

Excision of the specimen

Steps 5 to 8 are performed on the patient's right side. The cervix is then amputated with a scalpel held perpendicular to the specimen at about 1 cm from the isthmus (Figure 14). The new ectocervix appears gradually (Figure 15). An endocervical curettage (ECC) of the residual endocervical canal is done afterwards. The trachelectomy specimen is sent for immediate frozen section to assess the level of the tumor in relation to the endocervical resection margin. At least 8–10 mm of free endocervical canal should be obtained, otherwise additional endocervix should be removed, or the trachelectomy should be aborted and a radical vaginal hysterectomy (Schauta) completed instead.

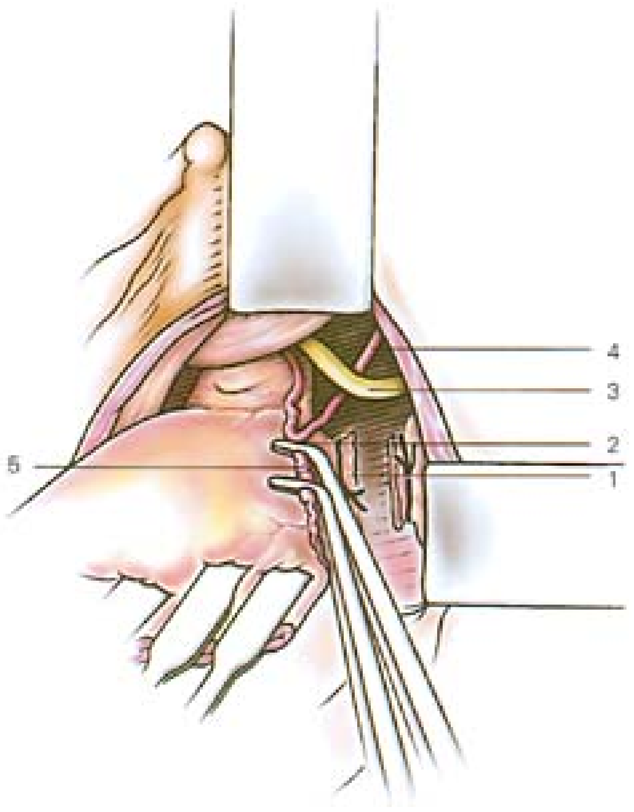

Figure 13

Care is needed to preserve the cross of the uterine artery (after Dr Hélène Roy)

1 Excised parametrium
2 Cross of the uterine artery
3 Ureter
4 Uterine artery
5 Descending branch of uterine artery

Prophylactic cervical cerclage and closure of the vaginal mucosa

The posterior cul-de-sac is first closed with a purse-string suture of Chromic 2–0 suture. A permanent cerclage is then placed using a non-resorbable Prolene-0 suture starting at 6 o'clock to have the knot lying posteriorly. Sutures are placed at the level of the internal os and not too deeply within the cervical stroma. When tying the knot, a uterine probe can be left in the cervical os to avoid tightening the knot too much as this may cause cervical stenosis (Figure 15). The edges of the vaginal mucosa are sutured to the residual exocervical stroma (and not to the endocervical tissue) with interrupted figure-of-eight. Sometimes, excess vaginal mucosa has to be excised to facilitate the closure. Sutures should not be placed too close to the

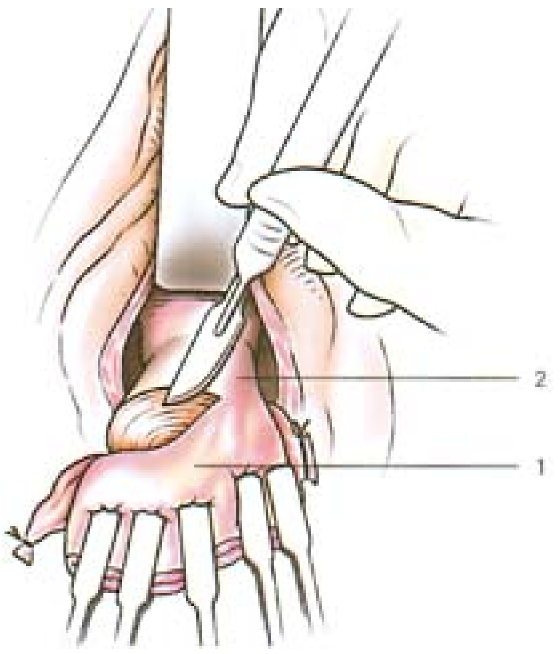

Figure 14

Excision of the cervix (after Dr Hélène Roy)
1 Trachelectomy specimen
2 Residual endocervix

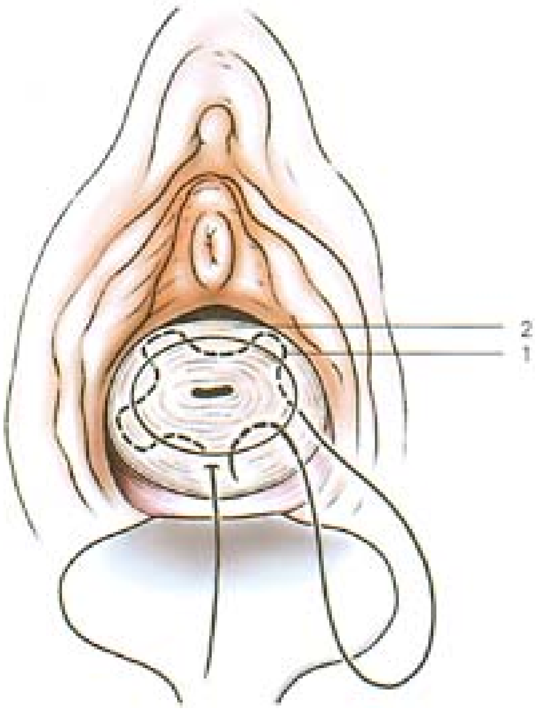

Figure 15

Placing the cervical cerclage (after Dr Hélène Roy)
1 Suture
2 New ectocervix

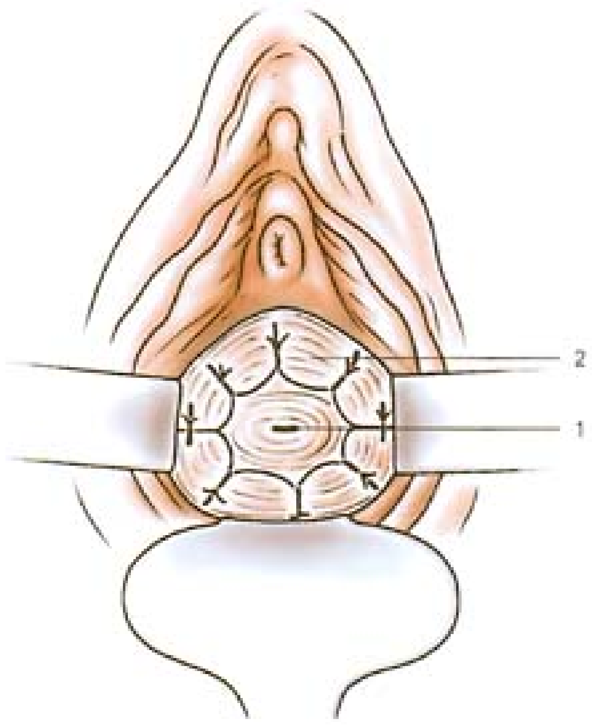

Figure 16

Closure of vaginal mucosa (after Dr Hélène Roy)
1 New external os
2 New ectocervix

new cervical os to avoid burying the cervix making follow-up examinations more difficult (Figure 16).

Trachelectomy specimen

Ideally, the cervical specimen should be at least 1 cm long, with 1 cm of vaginal mucosa and 1–2 cm of para-metrium. Figure 17A shows a cervix with a small exophytic lesion; Figure 17B shows a lateral view of the trachelectomy specimen demonstrating the endocervical cut margin, proximal parametria (stretched by the Debeaky instruments) and vaginal cuff (suture) covering the cervical lesion; Figure 17C shows the appearance of the cervix after suturing of the vaginal mucosa to the residual exocervix.

Cervical appearance after a trachelectomy procedure

With time, the new cervix gradually resumes an almost normal appearance except for its shorter length. It therefore remains accessible for monitoring with colposcopic examination, cytology and ECC. Figure 18A shows pictures of the cervix 6 months after a trach-electomy, and in the first trimester in a patient who became pregnant after the procedure (Figure 18B).

Saling procedure

Second trimester abortion and prematurity can be a major problem after a radical vaginal trachelectomy (Bernardini et al. 2003). The inevitable shortening of the cervix after this procedure seems to prevent the formation of an efficacious mucous plug. The mucous plug is thought to be a physiological barrier between the vaginal flora and the membranes to prevent ascending infections. In order to avoid chorioamnionitis, which is most likely responsible for premature rupture of membranes and premature labor following radical trachelectomy, Dargent (1999) has proposed a complete cervical closure of the cervix during pregnancy, a technique described by Saling in 1981 for patients with habitual abortions (Saling 1981).
The Saling technique of cervical closure is simple. The procedure is ideally performed at around 14 weeks of pregnancy under general anesthesia. The vaginal tissue just around the external os is superficially injected with a saline solution in order to separate the mucosa from the underlying mucosal layers. A 1.5 cm wide area of cervicovaginal mucosa is then removed 360 degrees around the external os. The defect is closed with a monofilament resorbable suture in two layers: the deep layer includes the cervical stroma, taking care not to go too deep in order to avoid rupturing the membranes, and the second layer includes the vaginal mucosa. Restoration of the permeability of the cervix is accomplished at the time of the planned cesarean section (at approximately 38 weeks), by digital perforation of this reversible vaginal closure.
According to Dargent’s data, the Saling procedure appears to significantly reduce the rate of premature deliveries after radical trachelectomy (Dargent 2001). Indeed, he reported 4 premature deliveries after cerclage alone in 18 patients (22%) versus 2 premature deliveries after a cerclage and a Saling procedure in 13 patients (15%). This potential benefit has to be weighted against the potential risks of the Saling procedure itself (infection, premature contractions and delivery and potential damage to the fetus). More data are needed before definitive recommendations can be made concerning its routine use.

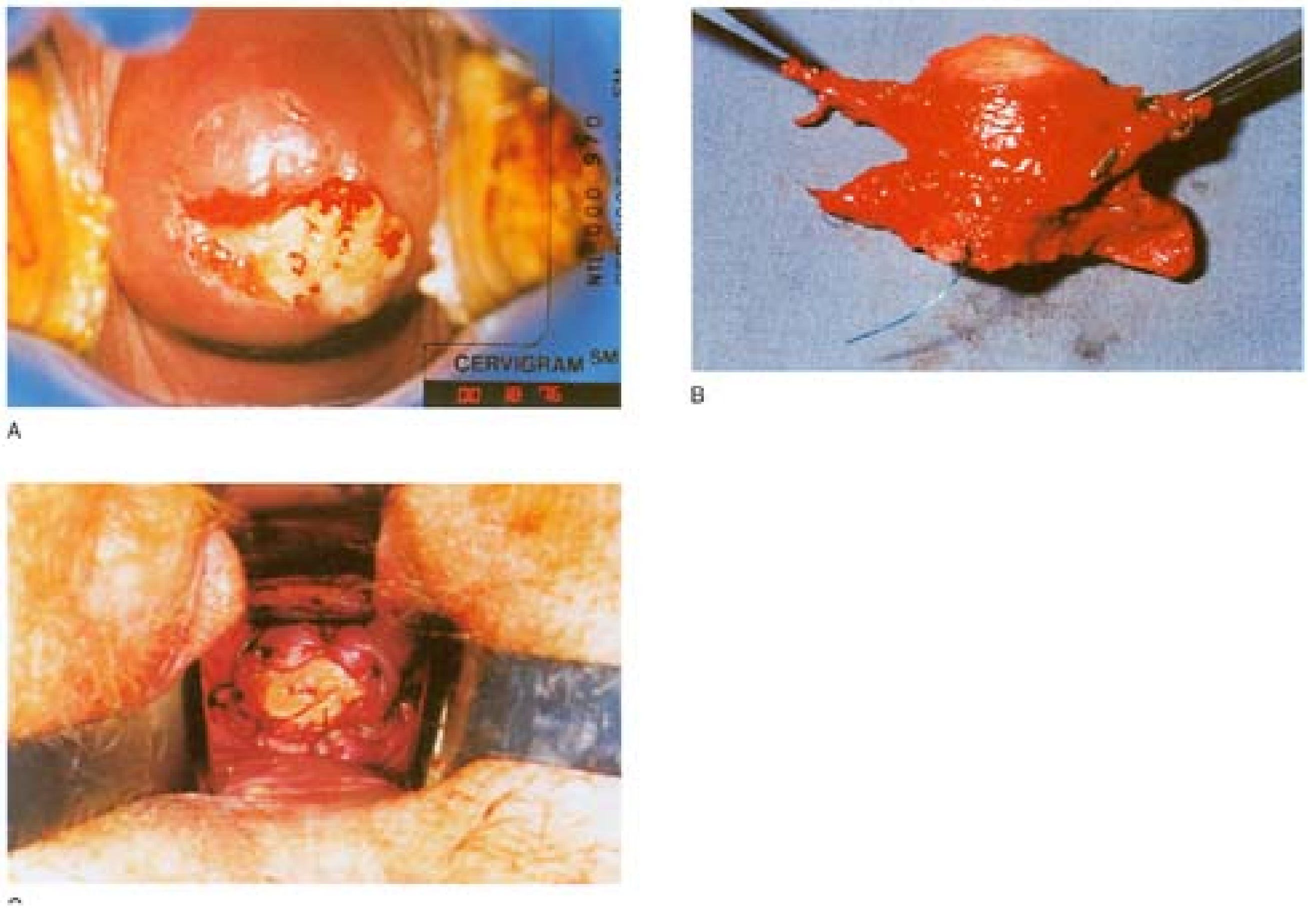

Figure 17

Example of trachelectomy specimen.
(A) Exophytic lesion. (B) Lateral view. (C) After closure

Results

The radical trachelectomy procedure has gained wider acceptance and recognition over the years. Several teams have begun to do the procedure and publish

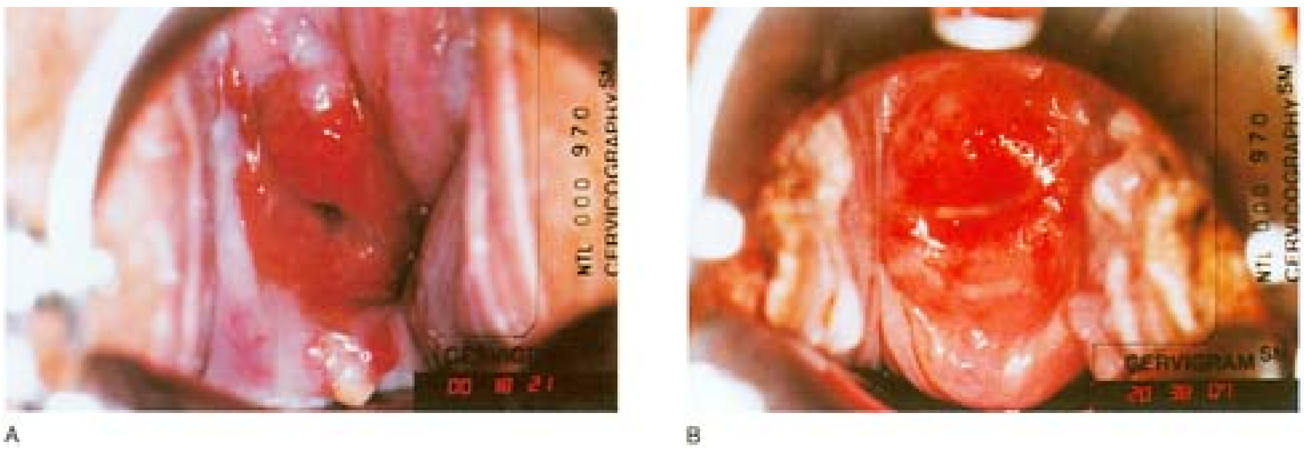

Figure 18

Postoperative appearance. (A) Six months after RVT. (B) First trimester of a subsequent pregnancy

their data so that physicians can get a better perspective with regards to the oncologic and obstetrical outcome. Data from six teams totaling over 300 cases has recently been summarized elsewhere and will be briefly reviewed here (Plante 2003).

Oncologic results

Over 300 cases of vaginal radical trachelectomies have been reported so far in the literature (Plante 2003). The recurrence rate has remained below 5% over the last decade and the death rate is in the range of 2–3%. This is comparable to the overall outcome following the standard radical hysterectomy for similar size lesions. In his analysis of 96 cases, Dargent has noted that the most important risk factor in terms of recurrence were the size of the lesion (>2 cm) and depth of stromal invasion (>1 cm). The presence of vascular space invasion and age <30 were almost statistically significantly associated with the risk of recurrence (Dargent et al. 2002).
Some of the recurrences reported have occurred in the lymph nodes, which probably represents a failure of the lymphadenectomy itself. Other recurrences have been reported in the parametrial area, which probably represents a failure of the trachelectomy and potentially an inadequate removal of parametrial tissue. Interestingly, there have been no recurrences reported on the residual cervix itself.

Obstetric results

Over 123 pregnancies have been reported (Plante 2003). The rate of first trimester loss is in the range of 17% which is comparable to the rate in the general population. However, the rate of second trimester loss is slightly over 10% which is clearly higher than in the general population. It is believed to be secondary to the short cervix and less effective mucous plug which normally acts as a natural barrier againsts ascending infection. Subacute chorioamnionitis probably eventually leads to premature contractions and premature labor and delivery. It is unknown at this point whether prophylactic cultures and antibiotic coverage are beneficial. Some authors suggest the routine injection of prophylactic steroids to hasten fetal lung maturation in case of premature delivery (Bernardini et al. 2003). Others have recommended the Saling procedure in the hope of reducing the rate of second trimester losses, although there is not a lot a data to support its routine use (cf section above on the Saling procedure).

Summary

The radical trachelectomy has now been performed for approximately 15 years. Data are slowly accumulating indicating that the procedure is oncologically safe in well-selected cases: young women, small lesions, limited endocervical extension and limited vascular space invasion. Obstetric data are also accumulating indicating that two thirds of patients can anticipate a normal pregnancy and delivery near term. However, the risk of premature second trimester loss or delivery is higher than in the general population and these pregnancies should probably be managed jointly with a high-risk consultant. Thus, this new fertility-preserving procedure truly offers a valuable alternative to young women with small lesions who wish to preserve their fertility potential.

References

Bernardini M, Barrett J, Seaward G, Covens A (2003) Pregnancy outcome in patients post radical trachelectomy. *Am J Obstet Gynecol* **189**:1378–82.

Dargent D (1999) The story of Mme M (videocassette). In: *Proceedings of the 30th Annual Meeting of the Society of Gynecologic Oncologists.* San Francisco.

Dargent D (2001) Radical trachelectomy: an operation that preserves the fertility of young women with invasive cervical cancer. *Bull Acad Natl Med* **185**:1295–304.

Dargent D, Brun J-L, Roy M, et al. (1994) La trachélectomie élargie (T.E.). Une alternative a l’hystérectomie radicale dans le traitement des cancers infiltrants développés sur la face externe du col utérin, *J Obstet Gynecol* **2**:285–292.

Dargent D, Franzosi F, Ansquer Y, et al. (2002) Extended trachelectomy relapse: plea for patient involvement in the medical decision. *Bull Cancer* **89**:1027–30.

Plante M (2000) Fertility preservation in the management of gynecologic cancers. *Curr Opin Oncol* **12**(5):497–507.

Plante M (2003) Fertility preservation in the management of cervical cancer. In: Bosze P and Roy M Guest, eds. *CME J Gynecol Oncol* **8**:128–38.

Roy M, Plante M (1998) Radical trachelectomy in the treatment of early stage cervical cancer. *Am J Obstet Gynecol* **179**:1491–6.

Saling E (1981) Der frühe totale Muttermundverschlufl zur Vermeidung habitueller Aborte und Frühgeburten. *Z Geburtshilfe Perinatol* **185**:259–61.

12
Radical abdominal trachelectomy

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FIGO staging

The traditional management of invasive cervical carcinoma has naturally depended on the stage of the tumor (Table 1). As outlined above, conization is suitable management for cervical intraepithelial neoplasia (CIN) and stage IA1 tumours. It is also probably adequate management for the majority of stage IA2 tumours. Table 2 shows the papers published relating to extracervical spread of microinvasive tumors, suggesting that the majority will be adequately managed by conization. Most gynecologic oncologists would qualify this, depending on whether lymphovascular permeation was present. If it was, they might proceed to a radical hysterectomy and pelvic lymphadenectomy. As can be seen from the table, this practice is not based strictly on evidence. It should be noted that, according to current FIGO definitions, some of the tumors referred to in the table would now be staged beyond IA2 by virtue of their lateral dimensions; however, this serves further to confirm that radical hysterectomy is overtreatment in many cases. Practice will also vary depending on the woman's desire to retain fertility. Traditionally, stage IB1, IB2 and IIA tumors have been managed by radical hysterectomy and pelvic lymphadenectomy, although many centers now utilize primary chemo-radiotherapy for stage IB2 and IIA tumors. Stage IIB, III and IV tumors are managed by radiotherapy, chemotherapy and surgery, either singly or in combination, and dependent upon the individual center and the individual patient. Units vary on their policy for commencing radiotherapy depending on the number of lymph nodes involved.

An increasing number of young women are being diagnosed with invasive cervical cancer. This is probably a result of the cervical smear program, which enables women to be detected both at an earlier stage in their malignancy and at an earlier age. The increasing number of young patients has made many wonder whether a less radical treatment than a radical hysterectomy and pelvic lymphadenectomy could be offered, while still maintaining a high cure rate and allowing preservation of fertility.

Daniel Dargent describes in Chapter 10 the radical vaginal hysterectomy. Expertise in this procedure is the prerequisite to having the skill required for a new technique he has described for removal of exophytic tumors—stages IA2 to IIA—which were unsuitable for treatment by conization; he called this procedure 'radical vaginal trachelectomy'. It involves removal of the cervix, parametrium and upper vagina via the vaginal route. Patients also undergo a pelvic lymphadenectomy performed laparoscopically prior to the trachelectomy (this operation is fully described by Plante and Roy in Chapter 11). This procedure requires considerable skill in both vaginal and laparoscopic

Table 1 The International Federation of Obstetrics and Gynaecology (FIGO) staging of cervical cancer

Stage	*Extent*
0	Intraepithelial neoplasia
1	The carcinoma is strictly confined to the cervix; extension to the uterine corpus should be disregarded
IA	Preclinical carcinomas of the cervix (i.e. those diagnosed by microscopy only). All gross lesions even with superficial invasion are stage IB. Invasion is limited to measured stromal invasion with a maximum depth of 5 mm and no wider than 7 mm. Measurement of the depth of invasion should be from the base of the epithelium, either surface or glandular, from which it originates. Vascular space involvement, either venous or lymphatic, should not alter the staging
IA1	Minimal microscopically evident stromal invasion. The stromal invasion is no more than 3 mm deep and no more than 7 mm in diameter
IA2	Lesions detected microscopically that can be measured. The measured invasion of the stroma is deeper than 3 mm but no greater than 5 mm, and the diameter is no wider than 7 mm
IB	Clinical lesions confined to the cervix, or preclinical lesions greater than stage IA
IB1	Clinical lesions not greater than 4 cm in size
IB2	Clinical lesions greater than 4 cm in size
II	Involvement of the vagina except the lower third, or infiltration of the parametrium. No involvement of the pelvic side-wall
IIA	Involvement of the upper two thirds of the vagina, but not out to the side-wall
IIB	Infiltration of the parametrium, but not out to the side-wall
III	Involvement of the lower third of the vagina. Extension to the pelvic side-wall. On rectal examination there is no cancer-free space between the tumor and the pelvic side-wall. All cases with a hydronephrosis or non-functioning kidney should be included, unless this is known to be attributable to another cause
IIIA	Involvement of the lower third of the vagina, but not out to the pelvic side-wall if the parametrium is involved
IIIB	Extension on to the pelvic side-wall and/or hydronephrosis or non-functional kidney
IV	Extension of the carcinoma beyond the reproductive tract
IVA	Involvement of the mucosa of the bladder or rectum
IVB	Distant metastasis or disease outside the true pelvis

techniques. Many gynecological oncologists have acquired laparoscopic skills to complement their open surgical skills, but few have been trained to perform Schauta’s radical vaginal hysterectomy For these rea sons, we have been involved in developing an abdominal approach to radical trachelectomy which is technically similar to a traditional radical hysterectomy, but still offers prospects for future fertility.

Table 2 Results of pelvic lymphadenectomy in microinvasive carcinomas (adapted from Burghardt 1993) (65 mm invasion, early stromal invasion excluded)

Author	*Year*	*No. depth (%)*	*Maximal she (%)*	*CLS involvement (%)*	*Confluent pattern (%)*	*Lymph-node involvement*	*Died of disease*
Roche and Norris	1975	30	5 mm	57	37	0	–
Sedlis et al.	1979	74	5×3>8 mm	NS	22.5 (of 133 cases)	0	–
Lohe et al.	1978	37	5×10 mm	NS	NS	0	–
Taki et al.	1979	55	3 mm	0	0	0	–
Hasumi et al.	1980	29	3.1–5 mm	11.1	100	4	–
van Nagell et al.	1983	52	3.1–5 mm			3	–
Creasman et al.	1985	32	5 mm	15.6 (of 95 cases)	20 (of 96 cases)	0	–
Simon et al.	1986	69	5×12 mm	6.6 (of 105 cases)	NS	1	–
Maiman et al.	1988	30	3.1–5 mm				
Kolstad	1989	63	5 mm	16.1 (of 411 cases)	NS	1	–
Burghardt et al.	1991	39	5×10 mm	NS	NS	0	–
Creasman et al.	1998	51	5 mm	25	NS	0	–

CLS, capillary-like space; NS, Not stated.

When considering more conservative surgery than has previously been the norm for a given condition, one has to consider both the pathology of the disease and its mode of metastasis. The spread of squamous cervical carcinoma is predominantly lateral; it may be continuous, where the tumor spreads in a confluent manner towards the pelvic side-wall, or discontinuous, with vessel or parametrial node involvement.

Vertical spread of cervical cancer is much less common than lateral spread. In Burghardt's series of 395 women (1991) there were no cases of vertical spread in any stage IB or IIA tumors. In the case of stage IIB tumors, there were 11 out of 220 cases (20%) of spread to the uterine corpus, while other workers quote figures of 26% (Mitani et al. 1964) and 24% (Ferrari et al. 1988). Age may be an important factor in spread to the uterine body. Balzer (1978) found that in women under the age of 50 the vertical spread of stage IIB tumors was 9.5%, whereas in women over 50 years old the figure rose to 32%.

Anatomical considerations

Fertility

To retain fertility without the need for assisted conception techniques, a woman must retain her ovaries, fallopian tubes, uterus, a residuum of cervix with a patent cervical os and a functioning vagina. With the use of assisted conception and ovum donation techniques, a woman requires as an absolute minimum to have retained her uterus and perhaps a tiny slither of cervix to retain a cervical cerclage suture.

Vascular considerations

The uterus is supplied by three pairs of arteries: the uterine, ovarian and vaginal arteries, the latter two via collaterals. Viability of the uterus can certainly be maintained in the absence of uterine arteries,and it used to be thought only if there is no interruption of the ovarian or vaginal arterial supply. At the Society of Gynaecologic Oncologists Meeting in New Orleans in February 1996, the membership in an interactive session were asked to vote on how many vessels they felt were required for uterine preservation: the majority felt that the uterus required three of its six supplying vessels to remain viable. Interestingly, we now know that uterine viability may be maintained by the ovarian arteries alone, as demonstrated in 33 cases of radical abdominal trachelectomy already undertaken.

Oncological considerations

Any form of radical surgery for treatment of cervical carcinoma requires the removal of at least the cervix, some of or all the parametrium and upper vagina coupled with pelvic lymphadenectomy The extent of parametrial resection required is still a subject of controversy (Hagen et al 2000). Pelvic lymphadenectomy should involve removal of the paracervical obturator, internal, external and common iliac nodes and possibly also the para-aortic nodes. A full description of Dargent's vaginal radical hysterectomy technique is given in Chapter 10. Plante and Roy describe the vaginal approach to radical trachelectomy in Chapter 11. Laparoscopic lymphadenectomy techniques are described in chapters 10 and 18.

Figure 1 demonstrates the tumor requiring to be removed and the vascular supply to the uterus. In our technique for performing a radical abdominal trachelec-

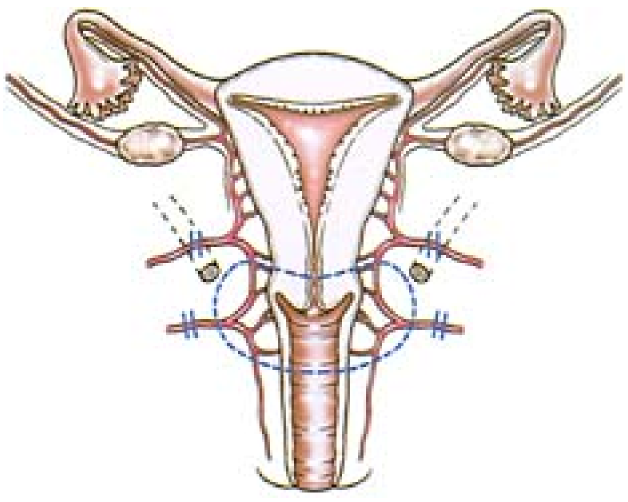

Figure 1

The area to be removed during the procedure

tomy the abdomen is opened in standard fashion, through either a midline incision or a modified Cherney's incision, and the operation proceeds initially like a standard radical abdominal hysterectomy. The dissection commences by dividing the round ligaments, opening the broad ligament, paravesical and pararectal spaces (Figure 2). The external iliac, common iliac, internal iliac and obturator nodes are removed (Figure 3). The ureter is dissected from its entry into the pelvis

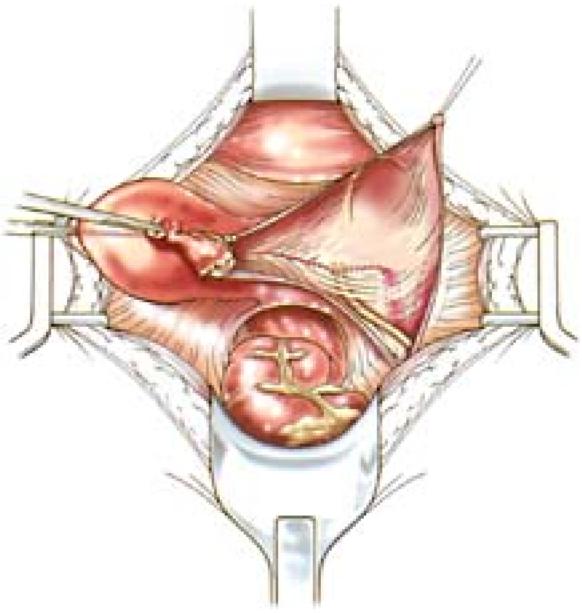

Figure 2

The round ligaments are divided and the broad ligament opened onto the pelvic sidewall

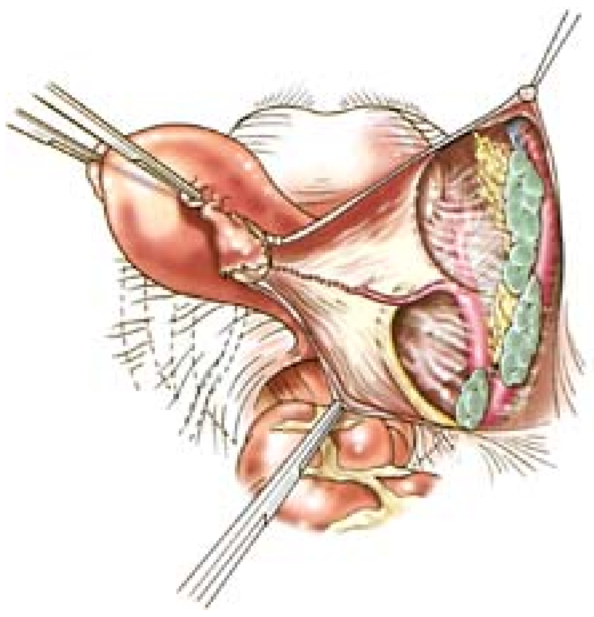

Figure 3

The internal iliac and uterine arteries are skeletonized

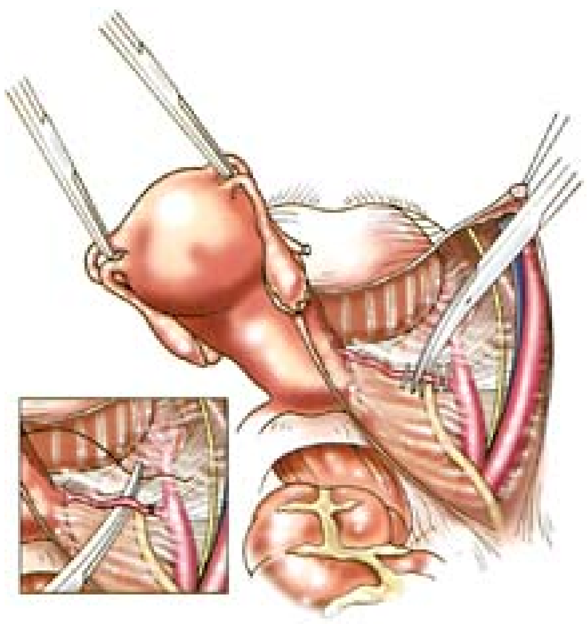

Figure 4

The uterine artery is divided close to its origin following application of hemoclips or ligation (see inset)

until it runs under the uterine artery. The dissection of the anterior division of the internal iliac artery into the superior vesical and uterine vessels is continued with skeletonization of the proximal part of these vessels (Figure 4). The uterine artery is ligated at its origin. The ureteric tunnels are then opened and dissected and the bladder deflected anteriorly (Figure 5). In method 1 the

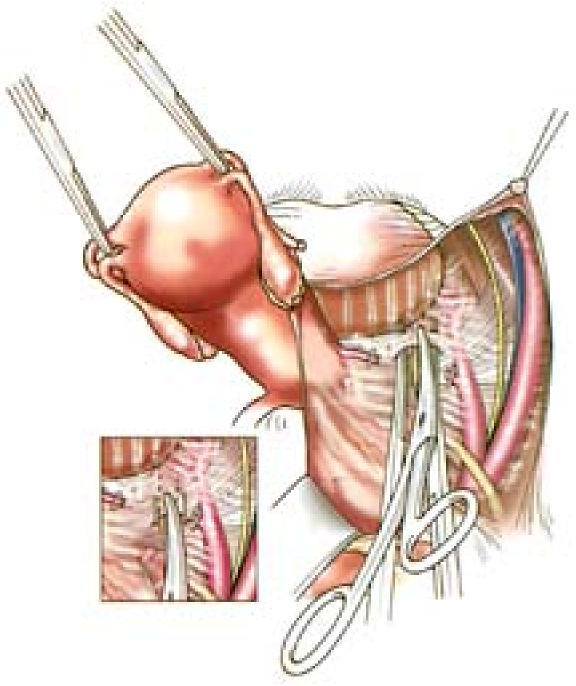

Figure 5

The ureteric tunnel is opened. Bleeding can be profuse at this point and the application of hemoclips or the use of Lotus harmonic scissors may be helpful. (Lotus company address is S. R.A. Developments Ltd., Bremridge House, Ashburton, South Devon TQ13 7 JK)

rectovaginal septum is opened to the level of the pelvic floor. The uterosacral ligaments are divided close to the sacrum and the vagina and parametrium are then incised. The uterus, cervix, upper third of vagina and parametrium are then swung superiorly, still attached to the ovarian pedicle (Figure 6). This allows excision of the cervix, parametrium and upper vagina (Figure 7). A small residuum of cervix may be left as the site for inserting a cervical cerclage suture. In method 2 it is also possible to cut across the cervix/cervicouterine junction (Figure 8), and to place the uterus still attached to the ovarian vessels into the abdomen (Figure 9). One can then undertake the opening of the rectovaginal septum and radical removal of cervix, parametrium and vagina without the danger of damaging the uterus (Figure 10); the authors have utilized both methods. Whichever method is used frozen section histological examination is performed on tissue from the upper surface of the cervix, to ensure adequate resection margins, and also from the lymph nodes. If the cervix demonstrates inadequate resection margins or the pelvic lymph nodes contain tumor, the procedure is abandoned and a full radical hysterectomy performed. Assuming the margins to be acceptable, if a thin plate of cervix has been retained a cervical cerclage

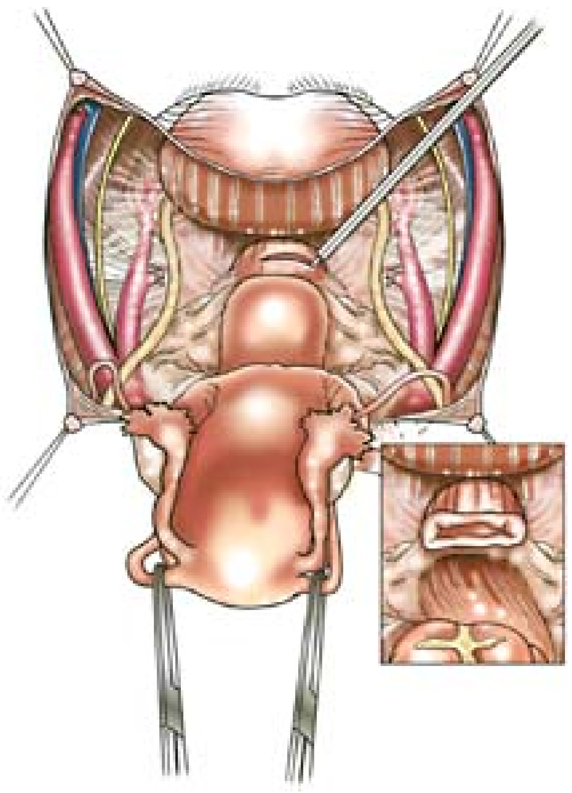

Figure 6

The vagina has been incised. Arterial supply at this point is via the ovarian vessels alone

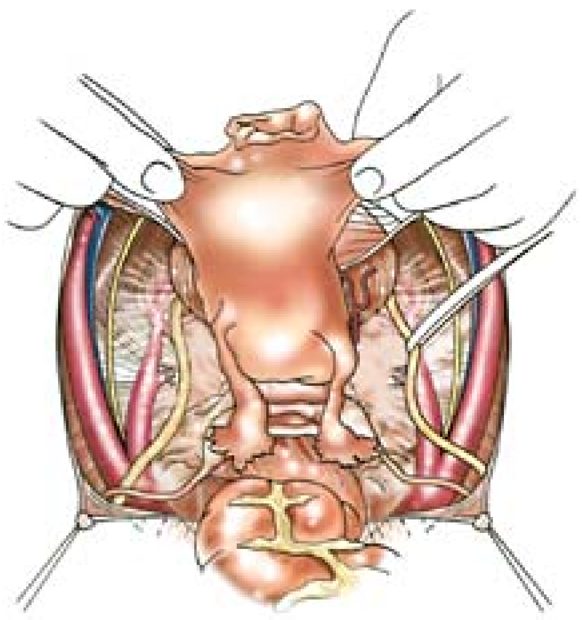

Figure 7

The uterus, cervix and parametrium are shown here, swung superiorly with the ovaries and uterine tubes attached

suture may be inserted. Prolene (Ethicon) can be used with the knot tied so as to lie posteriorly (Figure 11). This allows for the possibility of easy removal by a vaginal route via the Pouch of Douglas, should this ever be required. In addition it prevents potential bladder irritation by the knot. The vast majority of cases have been performed without use of a cerclage suture, even though in many of the cases the cervix has been removed in its entirety. The next step is to reanastomose the cervical plate/lower part of the uterus to the vagina. The authors have utilized two methods, one being insertion of a circumferential single layer running suture between uterus and vaginal cuff (Figures 12 and 13), the other being insertion of 6 interrupted sutures running from the outside of the vagina to the inside, then through the cervical plate from inside to outside. If this method is used it is made easier by moistening the vicryl sutures with lubricating jelly. After the 6 sutures are inserted, the uterus is 'parachuted' into position and the sutures ligated (Figures 14 and 15). Figure 16 shows the end result.
The abdomen is then closed in the standard fashion.

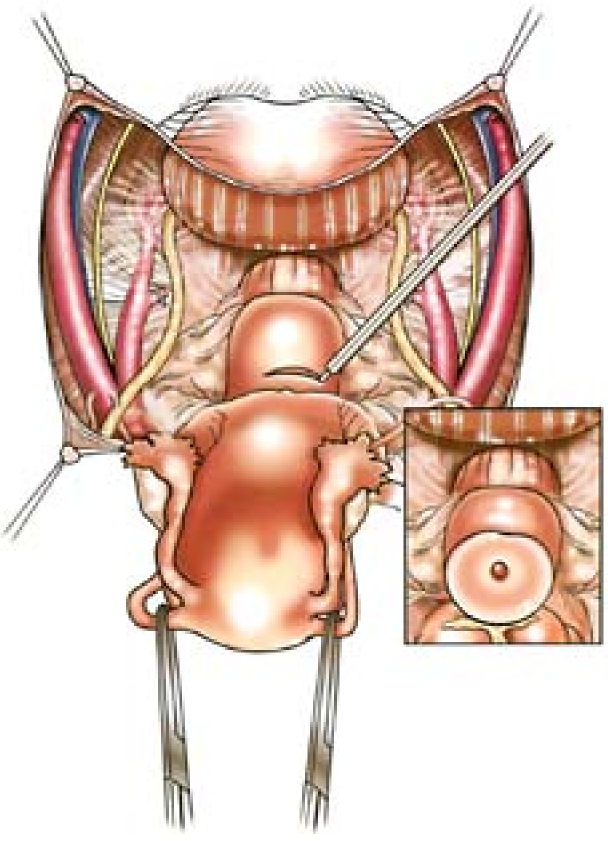

Figure 8

The uterocervico junction is transected

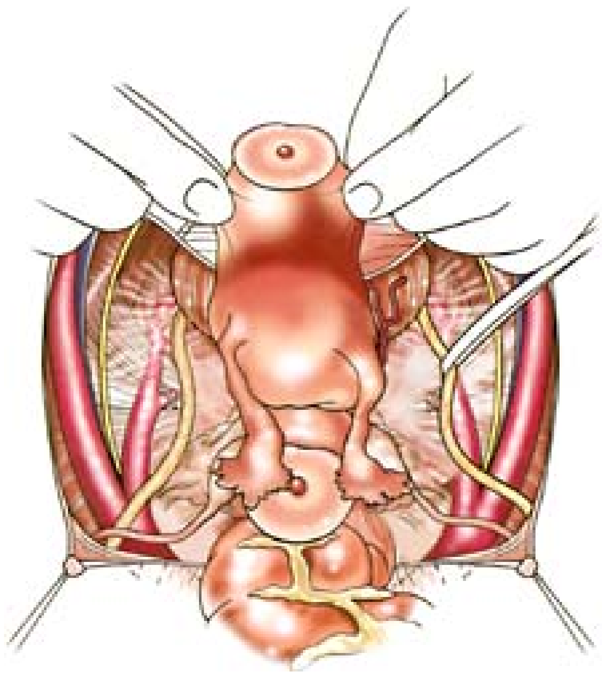

Figure 9

This allows the uterus to be placed in the abdomen prior to completion of the trachelectomy

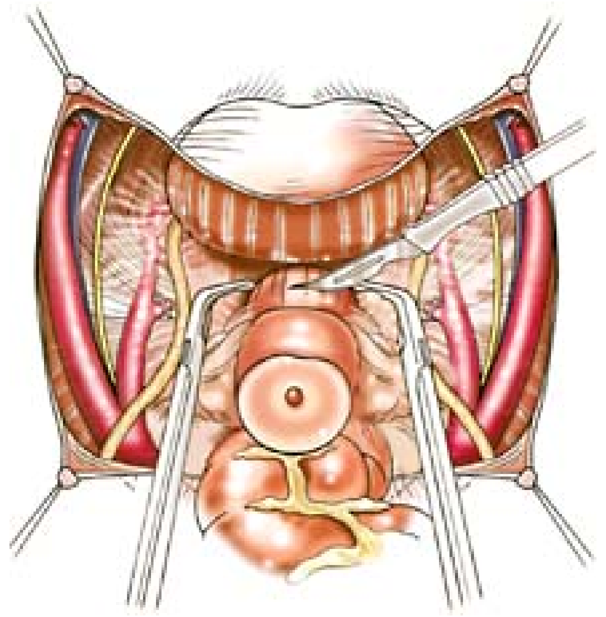

Figure 10

The parametrium is clamped, divided and ligated. Alternatively Lotus harmonic scissors may be used

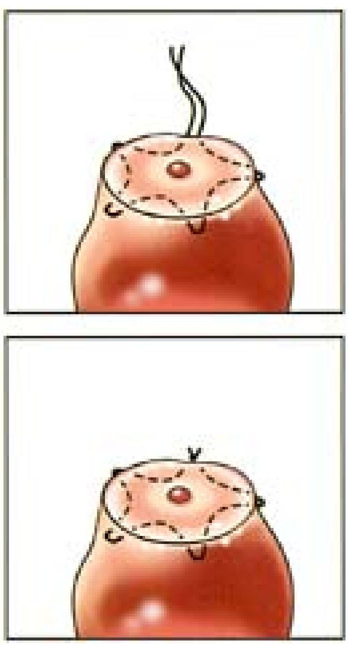

Figure 11

Insertion of the cervical suture with the knot placed posteriorly

Criticism of our procedure is not oncological, since our operation, in terms of clearance, is virtually the same as a radical hysterectomy and, we believe, has equal capacity to deliver clearance of tumor. Either a proportion of or all the parametrium can be removed, depending upon the tumor being excised.
The authors have now performed the operation in 33 cases (Ungar et al. 2005). Three procedures were abandoned after positive pelvic nodes (2 patients) and involvement of the cervical uterine margin in 1 patient. All our patients had FIGO stage I disease: 10 had IA2, 15 had stage IB1 and 5 had IB2 disease. During follow up one patient subsequently underwent a hysterectomy owing to an abnormal Papanicolaou smear result (the histology in this case was negative); the remaining 32 are well with no recurrences to date with a mean follow up of 42.8 months (range 14–75 months). A normal menstrual pattern resumed within 8 weeks of surgery in all but two patients. In these two women ultasound examination showed obliteration of the endometrial cavity.
Five of the 30 patients have tried to conceive resulting in 2 spontaneous and one IVF pregnancy. One pregnancy ended in miscarriage at 5 weeks' gestation. Two women in the authors' series have been delivered of live, healthy babies by cesarean section with no

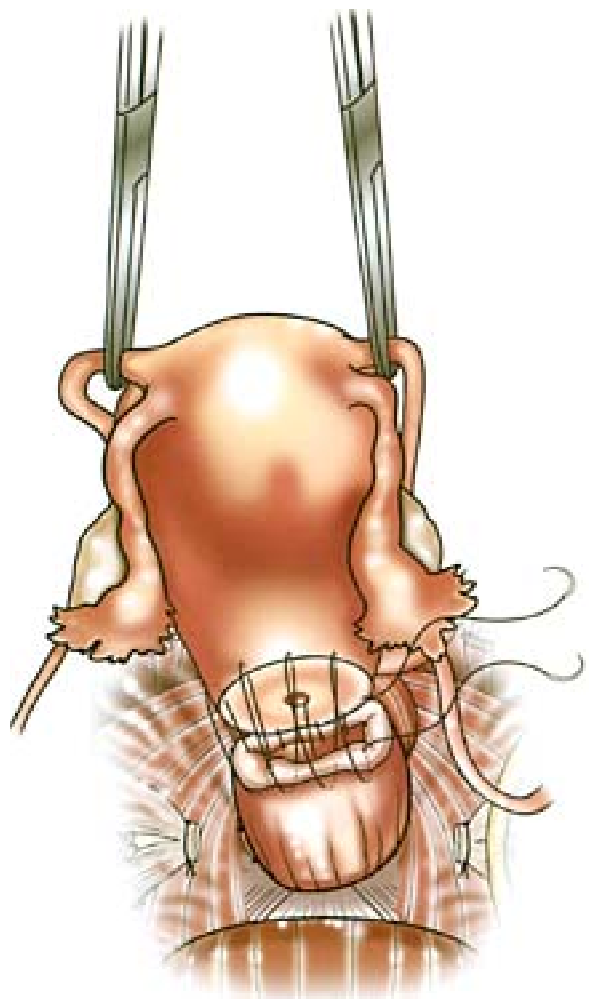

Figure 12

Insertion of the circumferential single layer running suture to achieve final end result

complications (Palfalvi et al 2003). The babies weighed 3200 and 3350 g despite the reliance on ovarian vessels alone. Doppler flow studies in pregnancy not surprisingly showed massively increased flow via these vessels. In a further report of three cases of radical abdominal trachelectomy one other baby has been delivered and that baby's mother was reported as being pregnant again (Rodriguez et al. 2001).
In summary, radical abdominal hysterectomy offers an oncologically sound procedure with a good chance of cure, but fertility is not preserved. It is this operation which is most commonly performed and has the best follow-up data. Radical vaginal trach

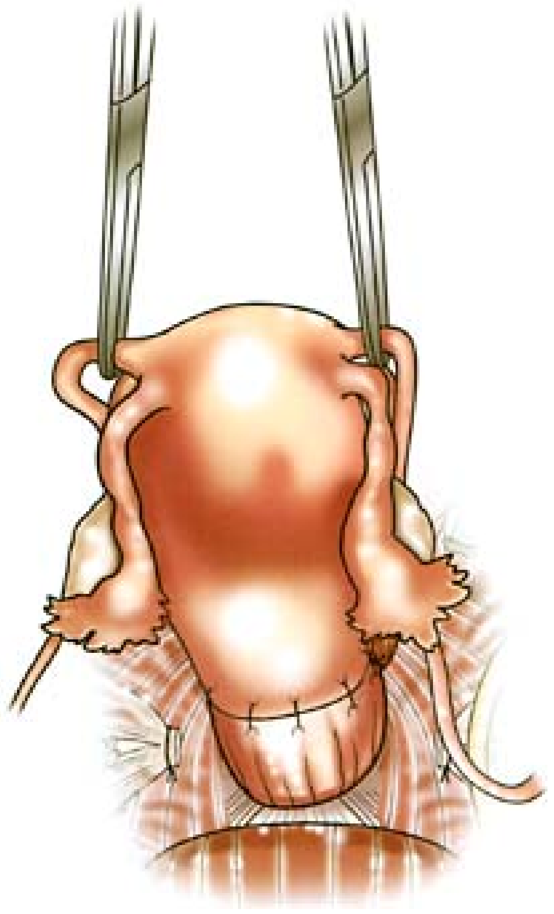

Figure 13

Insertion of the circumferential single layer running suture to achieve final end result

electomy requires advanced vaginal and laparoscopic surgical skills. It has, however, been proved that fertility follows such surgery, and so far, at least for tumors of less than 2 cm diameter the long-term survival data look impressive. In larger tumors recurrences have occurred (Dargent et al. 2000). Radical abdominal trachelectomy appears to be oncologically sound, and is perhaps more accessible in technical terms than radical vaginal trach-electomy. Fertility is preserved and despite limited follow-up data, we believe long-term survival rates should be similar to those in radical abdominal hysterectomy.

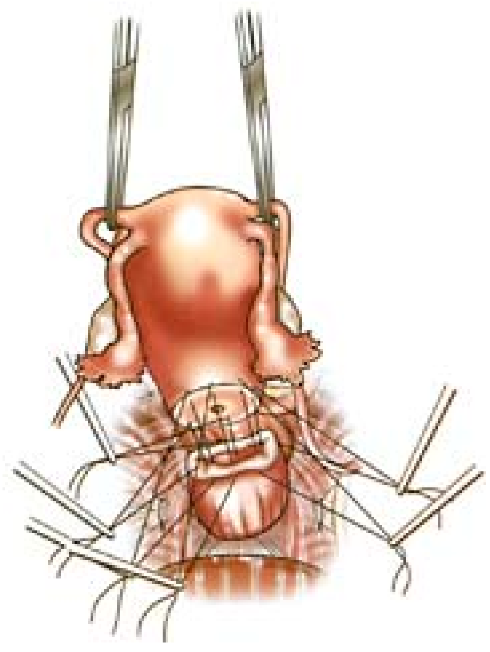

Figure 14

Insertion of six interrupted sutures to allow the uterus to be parachuted back into position to achieve the final end result

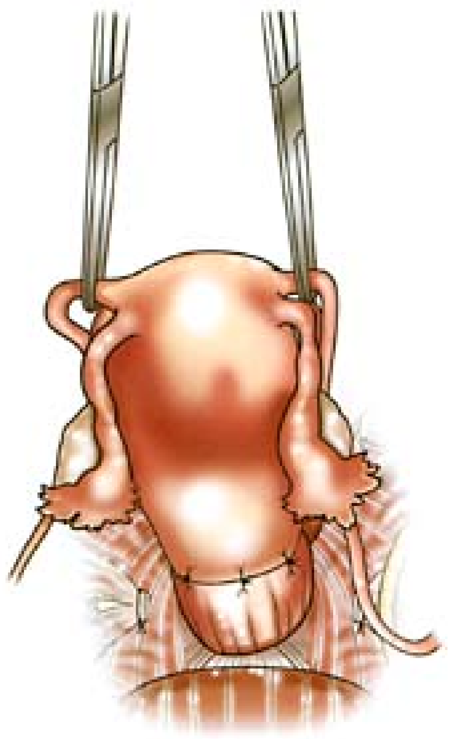

Figure 15

Insertion of six interrupted sutures to allow the uterus to be parachuted back into position to achieve the final end result

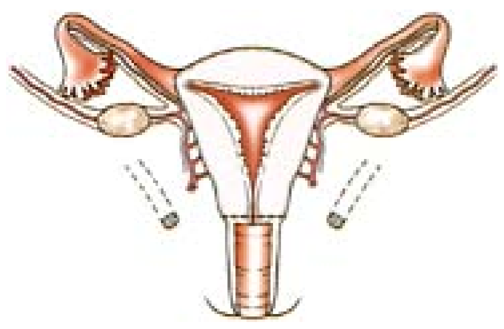

Figure 16

Shows an overview of the final result

References

Baltzer J (1978) *Die operative Behandlung des Zervixcarcinoms. Klinische, histologische und tumormetrische U Intersuchungsergebnisse einer kooperativen Studie an vier Universitätsfrauenkliniken bei 1092 Patientinnen mit Zervixcarcinom* (dissertation). Munich: University of Munich.
Burghardt E (1993) Cervical cancer. In: Burghardt E, Webb MJ, Monaghan JM and Kindermann G, eds. *Surgical gynecologic oncology*. New York: Thieme, 306.
Burghardt E, Girardi F, Lahousen M, et al. (1991) Microinvasive carcinoma of the uterine cervix. *Cancer* **67**:1037–45.
Creasman WT, Fetter BF, Clarke-Paterson DL, et al. (1985) Management of stage 1A carcinoma of the cervix. *Am J Obstet Gynecol* **153**:164–72.
Creasman WT, Zaino RJ, Major FJ, et al. (1998) Early invasive carcinoma of the cervix (3–5 mm invasion): Risk factors and prognosis. *Am J Obstet Gynecol* **178**:62–5.
Dargent D, Martin X, Sacchetoni A, Mathevet P (2000) Laparoscopic radical vaginal trachelectomy: a treatment to preserve the fertility of cervical carcinoma patients. *Cancer* **88**:1877–82.
Ferraris G, Lanza A, Re A, et al. (1988) The significance of lymph node status at pelvic, common iliac and para-aortic levels. *Bailliere's Clin Obstet Gynaecol* **2**:913–20.
Hagen B, Shepherd JH, Jacobs IJ (2000) Parametrial resection for invasive cancer. *Int J Gynecol Cancer* 10:1–6.
Hasumi K, Sakamoto A, Sugano H (1980) Microinvasive carcinoma of the uterine cervix. *Cancer* **45**:928–31.
Kolstad P (1989) Follow-up study of 232 patients with stage Ia1 and 411 patients with Ia2 squamous cell carcinoma of the cervix (microinvasive carcinoma). *Gynecol Oncol* **33**:265–72.

Lohe KJ, Burghardt E, Hillemans HG, et al. (1978) Early squamous cell carcinoma of the uterine cervix: clinical results of a cooperative study in the management of 419 patients with early stromal invasion and microcarcinoma. *Gynecol Oncol* **6**:31–5.
Maiman MA, Fruchter RG, DiMaio TM, et al. (1988) Superficially invasive squamous cell carcinoma of the cervix. *Obstet Gynecol* **72**:399–403.
Mitani Y, Jimi S, Iwasaki H (1964) Carcinomatous infiltration into the uterine body in carcinoma of the uterine cervix. *Am J Obstet Gynecol* **89**:984.
Palfalvi L, Ungar L, Boyle DCM, et al. (2003) Announcement of healthy baby boy born following abdominal radical trachelectomy. *Int J Gynecol Cancer* **13**:249.
Rodriguez M, Guimares O, Rose PG (2001) Radical abdominal trachelectomy and pelvic lymphadenectomy with uterine conservation and subsequent pregnancy in the treatment of early invasive cervical cancer. *Am J Obstet Gynecol* **185**:370–4.
Roche WD, Norris HJ (1975) Microinvasive carcinoma of the cervix: the significance of lymphatic invasion and confluent patterns of stromal growth. *Cancer* **36**:180–6.
Schauta R (1908) *Die erweiterte vaginale Totalextirpation des Uterus beim Kollumkarzinom* Vienna: Safar.
Sedlis A, Sall S, Tsukada Y, et al. (1979) Microinvasive carcinoma of the uterine cervix: a clinical—pathologic study. *Am J Obstet Gynecol* **133**:64–74.
Simon NL, Gore H, Shingleton HM, et al. (1986) Study of superficially invasive carcinoma of the cervix. *Obstet Gynecol* **68**:19–24.
Smith JR, Boyle D, Corless D, et al. (1997) Abdominal radical trachelectomy: a new approach to the management of early cervical cancer. *Br J Obstet Gyn* **104**:1196–1200.
Taki I, Sugimori M, Matsuyami T, et al. (1979) Treatment of microinvasive carcinoma. *Obstet Gynecol Surv* **34**:839–43.
Van Nagell JR Jr, Greenwell N, Powell DF, et al. (1983) Microinvasive carcinoma of the cervix. *Am J Obstet Gynecol* **145**:981–91.
Ungar L, Palfalvi L, Siklos P, et al. (2005) Abdominal radical trachelectomy: fertility sparing surgery for cervical cancer. BJOG **112**:366–9.

13
Central recurrent cervical cancer: the role of exenterative surgery

John Monaghan

Introduction

The procedure of pelvic exenteration was first described in its present form by Brunschwig in 1948. Over the years it has been used mainly in the treatment of advanced and recurrent carcinoma of the cervix. Its primary role at the present time is the management of the numerous patients who develop recurrent cancer of the cervix following primary radiotherapeutic treatment. It has been estimated that between one third and one half of patients with invasive carcinoma of the cervix will have residual or recurrent disease after treatment. Approximately one quarter of these cases will develop a central recurrence which may be amenable to exenterative surgery. However, pelvic exenteration as a therapy for recurrent cancer of the cervix has not been widely accepted and many patients will succumb to their disease having been through the process of radiotherapy followed by chemotherapy and other experimental treatments without being given the formal opportunity of a curative procedure. The published results of exenterative procedures show an acceptable primary mortality of approximately 3–4% and an overall survival/cure rate of 30–60%. The procedure is also applicable to a wide range of other pelvic cancers including cancer of the vagina, vulva and rectum, both for primary and secondary disease. It is less often applicable to ovarian epithelial cancers and melanomas and sarcomas because of their tendency for widespread metastases.

The surgery involved is extensive and postoperative care is complex; as a consequence, the operation has become part of the repertoire of the advanced gynecological oncologist working in a center with a wide experience of radical surgery. The procedure does demand of the surgeon considerable expertise and flexibility: virtually no two exenterations are identical, and considerable judgment and ingenuity are required during the procedure in order to achieve a comprehensive removal of all tumor. With small recurrences, more limited procedures may be carried out with a degree of conservation of structures in and around the pelvis. With extensive procedures and particularly following extensive radiotherapy, complete clearance of all organs from the pelvis (total exenteration) together with widespread lymphadenectomy may be essential in order to achieve a cure. There is now considerable evidence that even in patients with node metastases at the time of exenteration a significant survival rate can be achieved.

Selection of the patient for exenterative surgery

Exenterative surgery should be considered for both advanced primary pelvic carcinoma and recurrent disease. Many patients will be eliminated from the possibility of surgery at an early stage because of complete fixity of the tumor mass to the bony structures of the pelvis. The only exception to this rule is the rare circumstance in which a vulval or vaginal cancer is attached to one of the pubic rami: the ramus can be resected and a clear margin around the cancer obtained. In general terms exenterative surgery should not be used as a palliative, except perhaps in the presence of malignant fistulas in the pelvis when it may significantly improve the quality of the patient's life without any significant extension to her life. It is important that the surgical team including nurses and ancillary workers are confident in their ability to manage not only the extensive surgery involved but also the difficult, testing and sometimes bizarre complications that can sometimes occur after exenteration. The average age of patients who are subject to exenteration is 50–60 years, but the age range is wide—from early childhood through to the eighth or ninth decade.

Patient assessment

It is frequently difficult following radiotherapeutic treatment to be certain that the mass palpable in the pelvis is due to recurrent disease and not to radiation reaction or persistent scarring associated with infection or the effects of adhesion of bowel to the irradiated areas.
In recent years both computed tomography (CT) and more recently magnetic resonance imaging (MRI) have been used extensively in the preoperative assessment of patients for many oncological procedures. The considerable difficulties of assessing CT scans in patients who have had preceding surgery or radiotherapy are a particular problem in patients being assessed for exenteration. Some clinicians feel that CT scanning is useful, whereas the author has not found the level of reliability to be acceptable. There will be many individual variations from center to center depending upon the skills available to the clinician. A tissue diagnosis is essential prior to embarking on exenterative surgery, and needle biopsy, aspiration cytology or even open biopsy at laparotomy will be required. As distant metastases tend to occur with recurrent and residual disease, it is sometimes helpful to perform scalene node biopsies and radiological assessments of the pelvic and para-aortic lymph nodes together with fine-needle aspiration, in order to assist with the assessment. The mental state of the patient is also important, but should not in itself be a bar to the performance of such surgery.

Absolute contraindications

If there are metastases in extrapelvic lymph nodes, abdominal viscera, lungs or bones there appears to be little value in performing such major surgery. However, there is evidence that patients with pelvic lymph node metastases may well survive, and a good quality of life is reported in a small but significant percentage of such patients.

Relative contraindications

- Pelvic side-wall spread: if the tumor has extended to the pelvic side-wall either in the form of direct extension or nodal metastases the prospects of a cure are extremely small and the surgeon must decide whether the procedure will materially improve the patient's quality of life. The triad of unilateral uropathy, renal non-function or ureteric obstruction together with unilateral leg edema and sciatic leg pain is an ominous sign. The prospects of a cure are poor; readers are, however, referred to Chapter 14 for possible combination therapies. Perineural lymphatic spread is not visible on CT and can be a major source of pain and eventual death.
- Obesity is a problem with all surgical procedures, producing many technical difficulties as well as postoperative respiratory and mobilization problems. The more massive the surgery the greater are these problems.

Type of exenteration

In North America the majority of exenterations performed are total; in the author's series approximately half of his exenterations have been of the anterior type, removing the bladder, uterus, cervix and vagina, but preserving the rectum (Figure 1). For very small, high lesions around the cervix and lower uterus and bladder it may be possible to carry out a more limited procedure (a supralevator exenteration) retaining considerable parts of the pelvic floor. Posterior exenteration (abdominal perineal procedure) is rarely performed by gynecological oncologists as this procedure tends to be the province of the general surgeon.

Preoperative preparation

Probably the most important part of the preoperative preparation is the extensive counselling needed to make certain that the patient and her relatives, particularly her partner, understand fully the extent of the surgery and the marked effect it will have upon normal lifestyle, in particular the loss of normal sexual function when the vagina has been taken out. The transference of urinary and bowel function to the chosen type of diversionary procedure should be discussed, as should the possibility of reconstructive surgery of the vagina and bladder, and the significant risks of such extensive surgery must be honestly explained. During the course of this counselling the patient should be seen by a stoma therapist. The author finds it ideal for the patient to meet others who have had the procedure, to discuss on a woman-to-

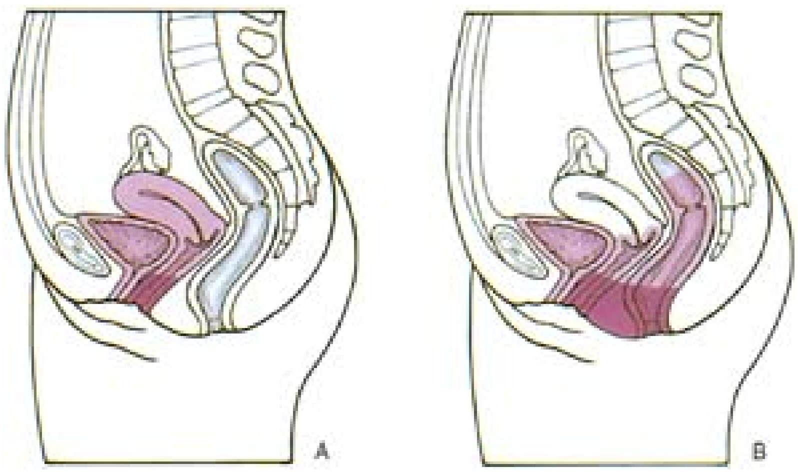

Figure 1

The limits of resection for (A) anterior and (B) total exenteration

woman basis the real problems and feelings about exenteration.

The patient is usually admitted to hospital 2–3 days prior to the planned procedure to undergo high-quality bowel preparation. With the modern alternative liquid diets and antibiotic therapy, complete cleaning of the small and large bowel can be achieved very rapidly. The anesthesiologist responsible for the patient's care will see the patient and explain the process of anesthesia. The author prefers to carry out all radical surgery under a combination of epidural or spinal analgesia together with general anesthesia. Cardiac and blood gas monitoring is essential. Although the majority of patients do not require intensive care therapy, its availability must be ensured prior to the surgical procedure. Prophylaxis against deep venous thrombosis is usually organized by the ward team utilizing a combination of modern elastic stockings and low-dose heparin which is initiated immediately following surgery.

The final intraoperative assessment

The final decision to proceed with exenteration will not be made until the abdomen has been opened and assessment of the pelvic side-wall and posterior abdominal wall has been made, utilizing frozen sections where necessary. In the author's practice the procedure is performed by a single team. If plastic surgical procedures such as the formation of a neovagina are planned then a second plastic surgical team will carry out the necessary operation at the same time as the diversionary procedures are being performed by the primary team.

Operative procedure

Once the patient has been anesthetized and placed in the supine position in the operating theater the abdomen is opened using either a longitudinal midline incision extending above the umbilicus, or a high transverse (Maylard) incision (Figure 2) cutting through muscles at the interspinous level. Exploration of the abdomen will confirm the mobility of the central tumor mass; thereafter the para-aortic lymph nodes and pelvic side-wall nodes are dissected (Figure 3) and sent for frozen section examination. Once the frozen sections show no extension of tumor the procedure of total exenteration can begin. At the same time as this initial intraoperative assessment the experienced exenterative surgeon will have opened tissue planes, including the paravesical, pararectal and presacral spaces to a deep level (Figures 4, 5) in the pelvis in order to become familiar with the full extent of the tumor. The dissection is achieved by opening the broad ligament:

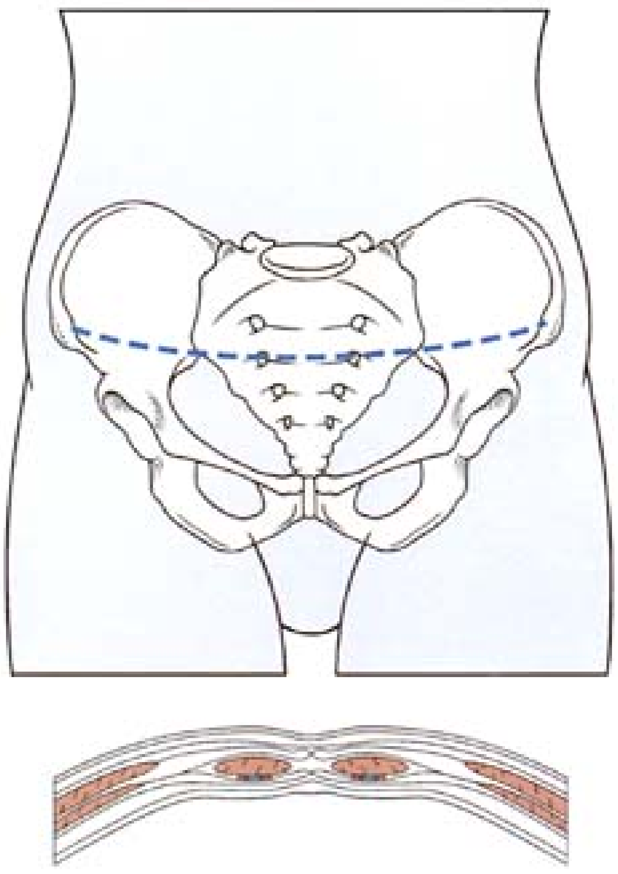

Figure 2

A Maylard or high transverse incision

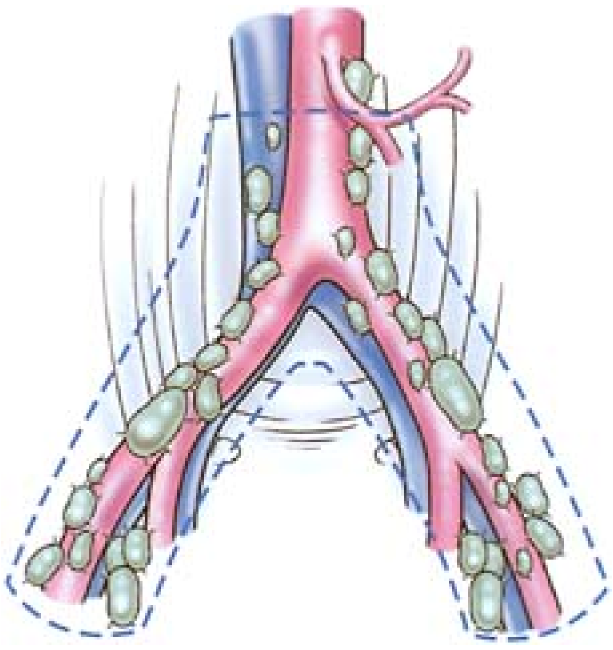

Figure 3

Pelvic and para-aortic node assessment

this can be done directly or the round ligament can be ligated and divided first. These dissections can be carried out without any significant blood loss and will yield considerable information. If it is not possible to proceed with the operation the abdomen may be closed at this stage as no significant trauma has been inflicted by the surgeon. Considerable experience and judgment are required in order to make this decision. Often the most difficult decision is to stop operating. Very occasionally, for example with some vulval cancers, resection of pubic bones may be attempted, but in general terms if there is bony involvement of tumor the procedure should be abandoned.

Total and anterior exenteration

After the comprehensive manual and visual assessment of the pelvis and the abdominal cavity, the surgeon proceeds by dividing the round ligament (if it is not already divided), drawing back the infundibulopelvic ligament and opening up the pelvic side-wall (Figure 6). The line of incision for removal of the entire pelvic organs begins at the pelvic side-wall, over the internal iliac artery, and will pass forward through the peritoneum of the upper part of the bladder, meeting with the similar lateral pelvic side-wall incision at the

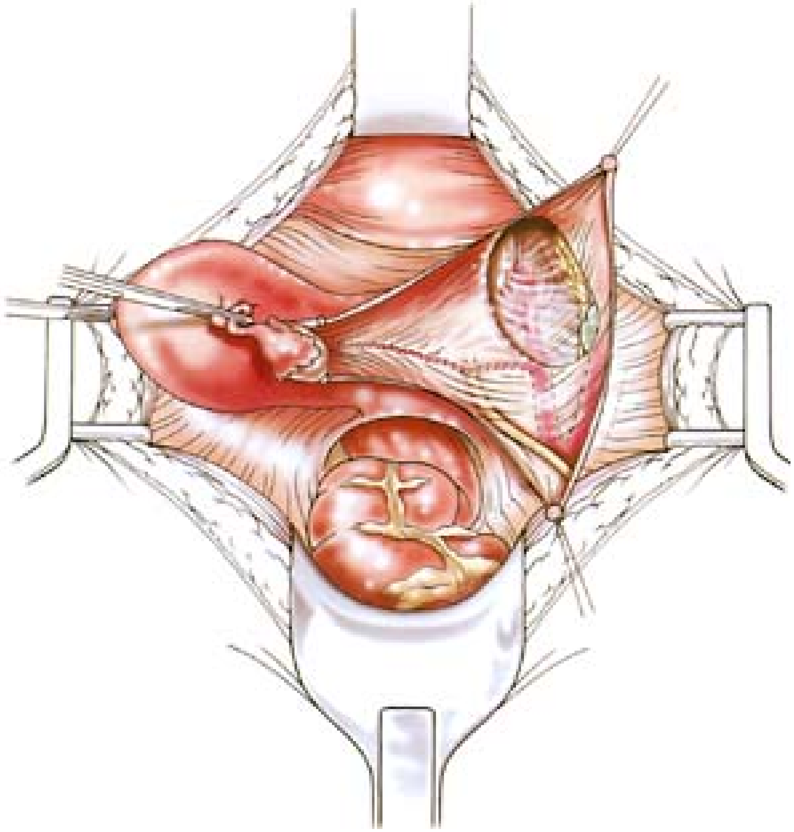

Figure 4

Division of the round and infundibulopelvic ligaments and the beginning of the lateral pelvic dissection

opposite side. The sigmoid colon will be elevated and at a suitable point will be transected, the peritoneal incision will be continued around the brim of the pelvis—with identification of the ureter as it passes over the common iliac artery—and will meet up with the similar incision on the opposite side. After the round ligaments have been divided and tied and the pelvic side-wall space opened, the infundibulopelvic ligament can also be identified, divided and tied. The incision is continued posteriorly and the ureters are separated and identified. If an anterior exenteration is to be performed the peritoneal dissection will be brought down into the pelvis to run across the anterior part of the rectum, just above the pouch of Douglas; this will allow a dissection from the anterior part of the rectum passing posteriorly around the uterosacral ligaments to the sacrum, releasing the entire anterior contents of the pelvis. For a total exenteration the dissection is even simpler: the mesentery of the sigmoid colon is opened and individual vessels clamped, divided and tied. The colon is divided, usually with a stapling device which allows the sealed ends of the colon to lie, without interfering with the operation in the upper abdomen (Figure 7). A dissection posterior to the rectum is then carried out from the sacral promontory, deep behind the pelvis; this dissection is rapid and simple and permits complete separation of the rectum from the sacrum. This allows complete and usually bloodless removal of the rectal mesentery including lymph nodes. Anteriorly, the bladder is dissected with blunt dissection from the cave of Retzius resulting in the entire bladder with its peritoneal covering falling posteriorly. This dissection is carried down to the pelvic floor, isolating the urethra as it passes through the pelvic floor (perineal diaphragm). As dissection is carried posteriorly into the paravesical spaces, the uterine artery and the terminal part of the internal iliac artery will become clearly visible. By steadily deepening this dissection the anterior division of the internal iliac will be isolated and the tissues of the lower obturator fossa identified; at this point, large exenteration clamps may be placed over the anterior division of the internal iliac artery and its veins (Figure 8). The ureter by this time will have been divided a short distance beyond the pelvic brim. The pelvic phase of the procedure is at this point completed and the perineal phase is now to be carried out.

The patient is placed in the extended lithotomy position and an incision made to remove the lower vagina (for an anterior exenteration) or the lower

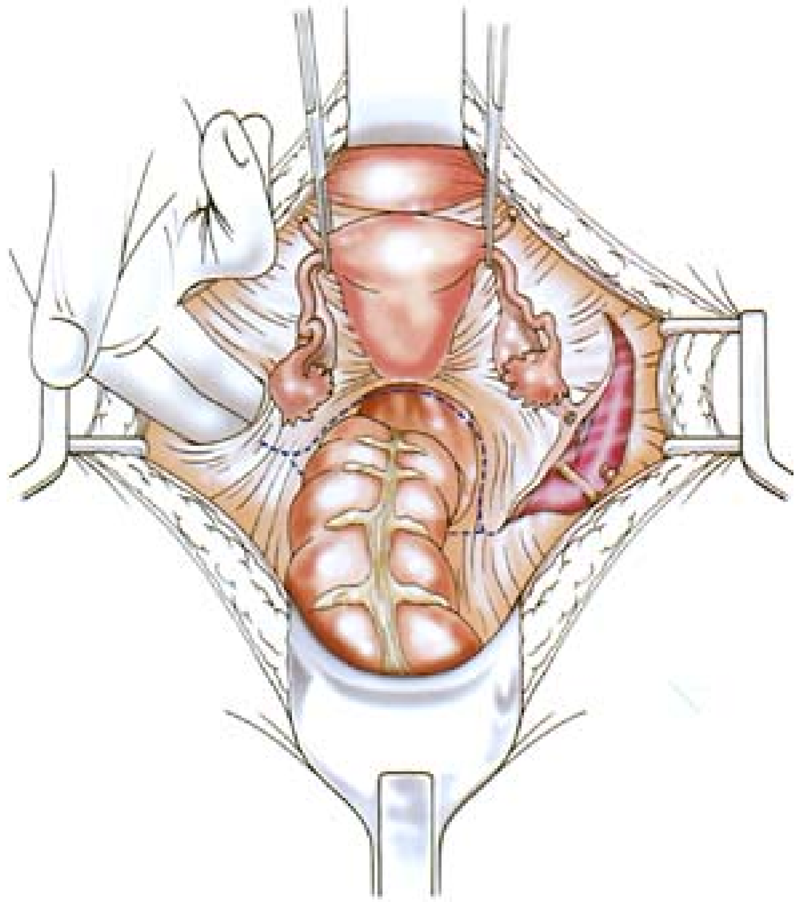

Figure 5

Deepening the lateral pelvic dissection to reveal the pelvic spaces

vagina and rectum (for a total exenteration) (Figure 9). Anteriorly the incision is carried through above the urethra just below the pubic arch to enter the space of the cave of Retzius which has been dissected in the pelvic procedure. The dissection is carried laterally and posteriorly, dividing the pelvic floor musculature, and the entire block of tissue is then removed through the inferior pelvic opening. Small amounts of bleeding will occur at this point, usually arising from the edge of the pelvic floor musculature. These can be picked up by either isolated or running sutures which will act as a hemostat. Once the perineal dissection has been completed and hemostasis achieved, the surgeon's choice will depend on the preoperative arrangements made with the patient. If in the preoperative assessment period it was decided by the clinician and the patient that a neovagina should be formed, than at this point either the primary surgeon or the plastic surgeon will initiate the development of a neovagina. This may be in the form of a myocutaneous graft using the gracilis muscle (see Chapter 24), or a Singapore graft may be used from alongside the vulva; other possible techniques involve the development of a skin graft placed within an omental pad, or transposition of a segment of sigmoid colon in order to form a sigmoid neovagina. For many patients, however, the desire to have a new vagina is a very low priority and it is surprising how frequently patients will put off these decisions until well after the time of exenteration. Surviving the cancer appears to be their uppermost desire. To this end the careful closure of the posterior parts of the pelvic musculature, a drawing together of the fat (Figure 10) anterior to that and a careful closure of the skin is all that is required. It is usually possible to preserve the clitoris, the clitoral fold and significant proportions of the anterior parts of the labia minora and labia majora so that when recovery is finally made the anterior part of the genitalia has a completely normal appearance. On some occasions patients will be able to have a neovagina formed some significant period of time following the exenteration. This is becoming the predominant pattern in the author's experience of some 89 cases.

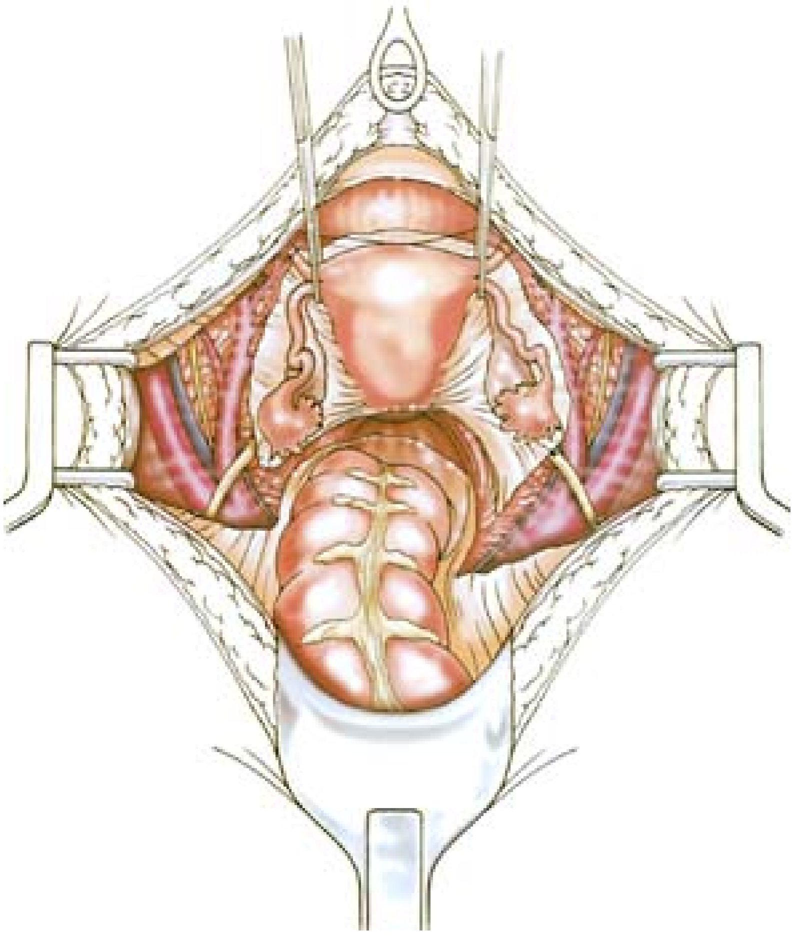

Figure 6

The pelvic incision for an anterior exenteration

Once the perineal phase is finished the legs can be lowered so that the patient is once more lying supine and attention can be addressed to dealing with the pedicles deep in the pelvis. All that remains following a total exenteration will be the two exenteration clamps on either side of the pelvis and a completely clean and clear pelvis. The pelvic side-wall dissection of lymph nodes can be completed before dealing with the clamps and any tiny blood vessels that require hemostasis are ligated. As the exenteration clamps are attached to the distal part of the internal iliac arteries it is important that comprehensive suture fixation is carried out (Figure 11). This is usually readily and easily done, although occasionally the large veins of the pelvic wall can provide difficulties and the use of mattress sutures may be necessary in order to deal with these complex vascular patterns. Having completed the dissection of the pelvis the clinician now moves to produce either a continent urinary conduit or a Wallace or Bricker ileal conduit, and if the procedure has been a total exenteration a left iliac fossa stoma will be formed (see Chapters 20 and 21).

Dealing with the empty pelvis

A problem which must be avoided is that of small bowel adhesion to the tissues of a denuded pelvis. This is particularly important when patients have previously had radiotherapy, as the risk of fistula formation in these circumstances is extremely high. A variety of techniques have been utilized to deal with this potentially life-threatening complication, including the placing in the pelvis of artificial materials such as Merselene (Ethicon, Edinburgh, UK), Dacron (DuPont) and Gortex sacs (WL Gore & Associates, Flagstaff, Arizona, USA), or even using bull pericardium.

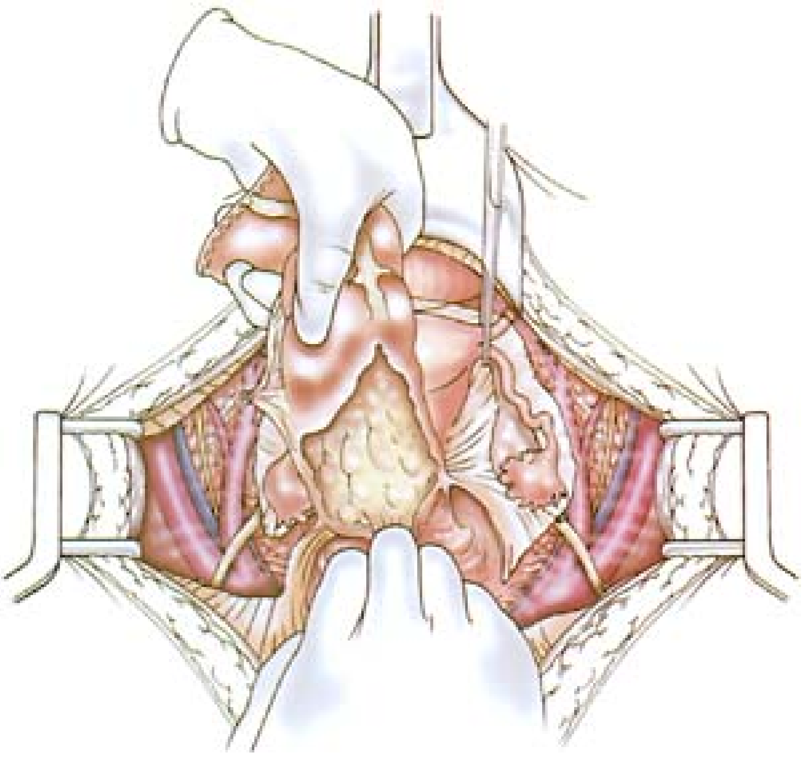

Figure 7

The pelvic incision for a total exenteration

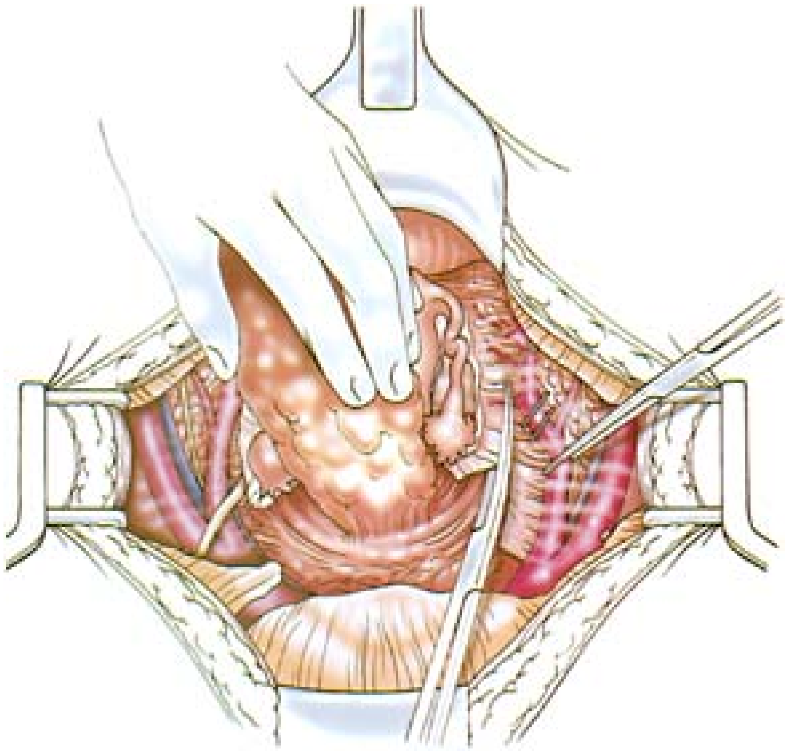

Figure 8

Exenteration clamps applied to the anterior division of the internal iliac arteries

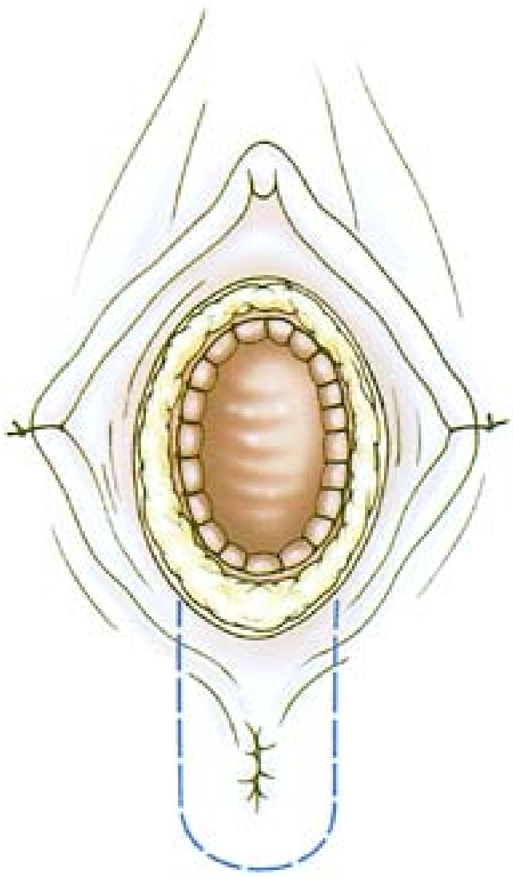

Figure 9

The perineal incisions for anterior and total exenterations

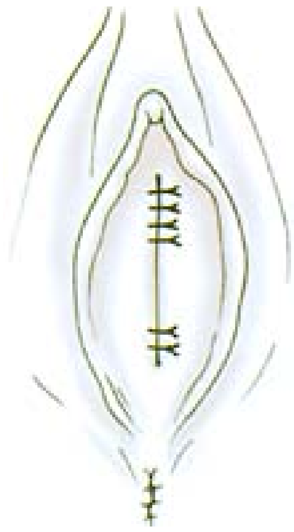

Figure 10

Closure of the pelvic floor musculature

Stanley Way in the 1970s described a sac technique in which he manufactured a bag of peritoneum which allowed the entire abdominal contents to be kept above the pelvis. This resulted in an empty pelvis, which from time to time became infected and generated a new problem, that of the empty pelvis syndrome. Intermittently over the years patching with the peritoneum has been used, but the most successful method appears to be the mobilization of the omentum from its attachment to the transverse colon leaving a significant blood supply from the left side of the transverse colon and allowing the formation of a complete covering of the pelvis by a soft ‘trampoline’ of omentum which will then stretch, completely covering and bringing a new blood supply into the pelvis. From time to time procedures such as bringing gracilis muscle flaps into the empty pelvis have been carried out to deal with the difficulty of a devitalized epithelium due to previous radiation.

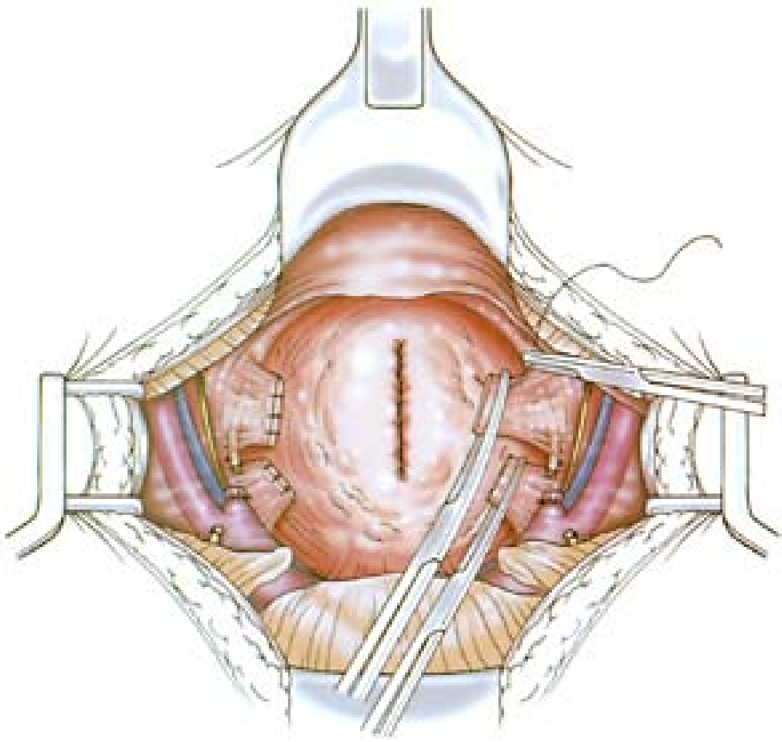

Figure 11

Suture of the internal iliac arteries and lateral pelvic pedicle

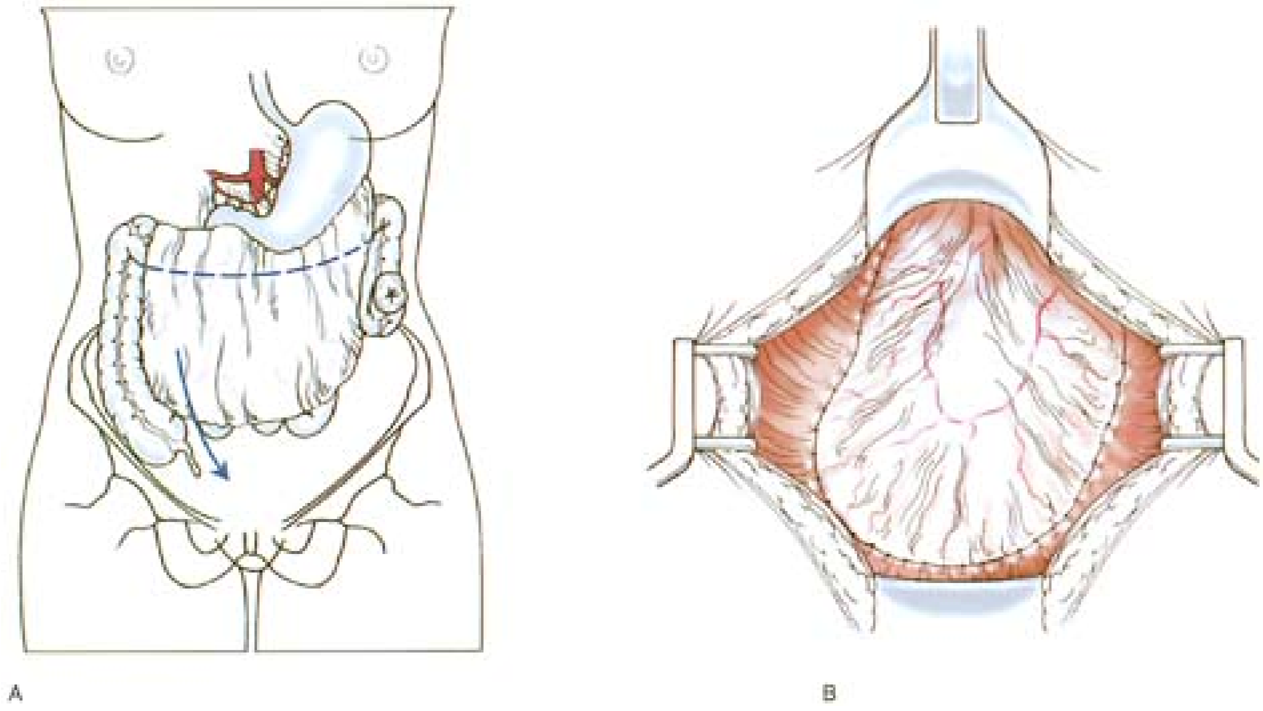

Figure 12

Development of the ‘omental pelvic floor’: (A) omental incision: (B) soft ‘trampoline’ area

It is the author's current preference to use an omental graft mobilizing the omentum from the transverse colon using a powered autosuture; this allows a broad pedicle to remain at the left-hand end of the transverse colon, maintaining an excellent blood supply to the omentum. This is brought down to the right side of the large bowel, dropping into the pelvis immediately to the left side of the ileal conduit which is anchored just above the sacral promontory. By careful individual suturing around the edge of the pelvis and sometimes by refolding the peritoneum upon itself, a complete covering of the true pelvis with a soft central 'trampoline' area can be generated (Figure 12). A suction drain is inserted below the omentum, which when activated will draw the omentum down into soft contact with the pelvic floor. The small bowel can thus come into contact with an area with a good blood supply, obviating the risk of adherence and subsequent fistula formation. At the end of the procedure the bowel is carefully oriented to make sure that no hernia can develop and the abdomen is closed with a mass closure. The stomas are dressed in theater and their appliances put in place. The patient leaves the operating theater and is then transferred back to the ward at the appropriate time.

Postoperative care

The postoperative care of exenterations is straightforward, essentially being a matter of maintaining good fluid balance, good hemoglobin levels and ideally a significant flow of urine of 2.5–3.5 liters per day. Bowel function often returns at the usual time of 2–4 days following the procedure, and a nasogastric tube (the author's preference) can be removed after 3–4 days; the return to oral intake, beginning with simple fluid, is initiated on the third day. During and following the procedure prophylactic antibiotic cover is maintained, as is subcutaneous heparin cover as prophylaxis against deep venous thrombosis. Mobilization should be rapid. Patients are usually discharged 10–15 days postoperatively, once they are used to dealing with the stomas and the ileal conduit tubes have been removed.

Results of exenteration

Most series show that the 5-year survival rate following exenteration is of the order of 40–60%; these figures depend very largely upon the selection of patients. A figure that is rather more difficult to obtain is the exact number who are assessed for exenteration but fail at one of the many hurdles that the patient must face before finally undergoing the procedure. It is therefore likely that the final, truly salvageable figure is an extremely low percentage. The value of exenteration procedures in patients who have lymph node involvement has been shown to be low but significant, and it is now many clinicians' practice to carry on with an exenterative procedure even in circumstances where one or two pelvic lymph nodes are involved by tumor.

References

Barber HRK (1969) Relative prognostic significance of preoperative and operative findings in pelvic exenteration, *Surg Clin North Am* **49**(2):431–7.

Brunschwig A (1948) Complete excision of the pelvic viscera for advanced carcinoma *Cancer* **1**:177.

Crawford RAF, Richards PJ, Reznek RH, et al. (1996) The role of CT in predicting the surgical feasibility of exenteration in carcinoma of the cervix. *Int J Gynecol Cancer* **6**:231–4.

Disaia PJ, Creasman WT (1981) *Clinical gynaecologic oncology; cancer of the cervix, pelvic exenteration,* Chapters 2–8. New York: Mosby; pp. 82–8.

Robertson G, Lopes A, Beynon G, Monaghan JM (1994) Pelvic exenteration: a review of the Gateshead experience 1974–1992. *Br J Obstet Gynaecol* **96**:1395–9.

Shingleton HM, Orr JW (1983) In: Singer A, Jordan J, eds. *Cancer of the cervix, diagnosis and treatment.* Edinburgh: Churchill Livingstone, p. 170.

Stanhope CR, Symmonds RE (1985) Palliative exenteration—what, when and why? *Am J Obstet Gynecol* **152**:12–16.

Symmonds RE, Webb MJ (1981) Pelvic exenteration. In: Coppleson M, ed. *Gynaecologic oncology.* Edinburgh: Churchill Livingstone, pp. 896–922.

Symmonds RE, Webb MJ (1992) Pelvic exenteration. In: Coppleson M, ed. *Gynaecologic oncology* (2nd edn). Edinburgh: Churchill Livingstone, pp. 1283–312.

Way S (1974) The use of the sac technique in pelvic exenteration. *Gynecol Oncol* **2**:476–81.

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14
Pelvic side-wall recurrence of cervical cancer: the LEER and CORT procedures

Michael Höckel

Introduction

Pelvic side-wall recurrences of cervical cancer are generally considered to be inoperable. If patients suffering from this type of relapse have not been irradiated in the pelvis before, radiotherapy or chemoradiotherapy can lead to remission. However, in about 95% of patients with side-wall recurrences the disease is diagnosed after primary or adjuvant pelvic irradiation, or has not been controlled by radiotherapy. Thus, for the majority of patients with side-wall recurrences of cervical cancer no chance of long-term survival existed.

The diagnosis of pelvic side-wall recurrence is suspected if a previously undetected mass fixed to the pelvic wall is palpated or if a tumor extending to the pelvic wall structures is identified with radiologic imaging after completion of the primary therapy. Frequently, one or more symptoms out of the triad of troubles are present: hydronephrosis, leg swelling, and pain in the lower back, pelvis or leg (Figure 1). The diagnosis is confirmed by histopathologic demonstration of neoplastic tissue compatible with the primary disease.

The location of the recurrent tumor at the anatomically complex pelvic side-wall is determined by oncologic and treatment-related factors. For a more accurate description of the multiple sites, a two-dimensional, topographic anatomic classification is proposed, based on the projection (not infiltration) of the tumor on the pelvic girdle and on its relation to the external/ common iliac vessels. Locations of pelvic side-wall recurrences can be periiliac or infrailiac in one dimension and ischiopubic, acetabular or iliosacrococcygeal in the other dimension (Figure 2). Periiliac recurrences can eventually be resected ‘en bloc’ as clusters with parts of the related vessels, nerves and pelvic wall muscles. However, the neurovascular structures vital for leg function (common and external iliac arteries, lumbosacral plexus) should be spared. Consequently, R0 resection of periiliac recurrences is rarely possible.

In cases of resections with close margins the combined operative and radiotherapeutic treatment (CORT) procedure may be applied by implanting guide tubes for postoperative brachytherapy and transposing non-irradiated autologous tissue from the abdominal wall or from the thigh at the pelvic wall.

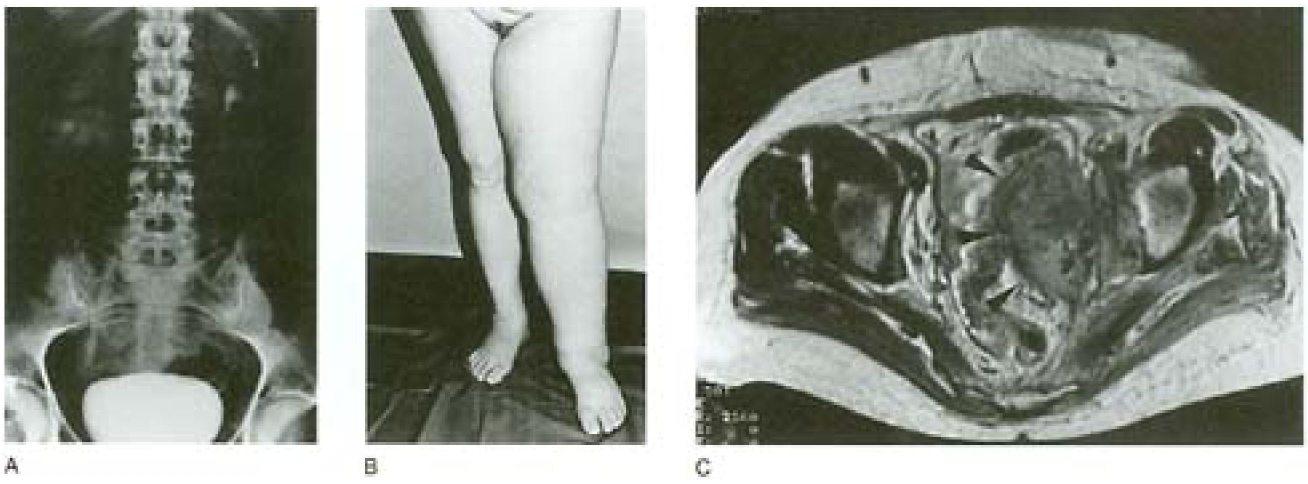

Figure 1

The most frequent symptoms of pelvic wall recurrences of gynecological malignancies are unilateral hydronephrosis (A), leg swelling and leg and pelvic pain (B). These symptoms have been regarded as evidence for inoperability. Since the LEER and CORT procedures lead to local control and open a possibility of long-term survival for patients with pelvic side-wall disease even in the irradiated pelvis *if the diagnosis is made early*, regular clinical follow-up examinations at short intervals are important. If a suspicious mass is palpated or symptoms are apparent, high-resolution pelvic magnetic resonance imaging (MRI) with and without contrast medium is now the optimal diagnostic imaging procedure. Pelvic wall recurrences can be detected much earlier than in the case shown above (C) in whom the LEER and CORT procedures are no longer applicable

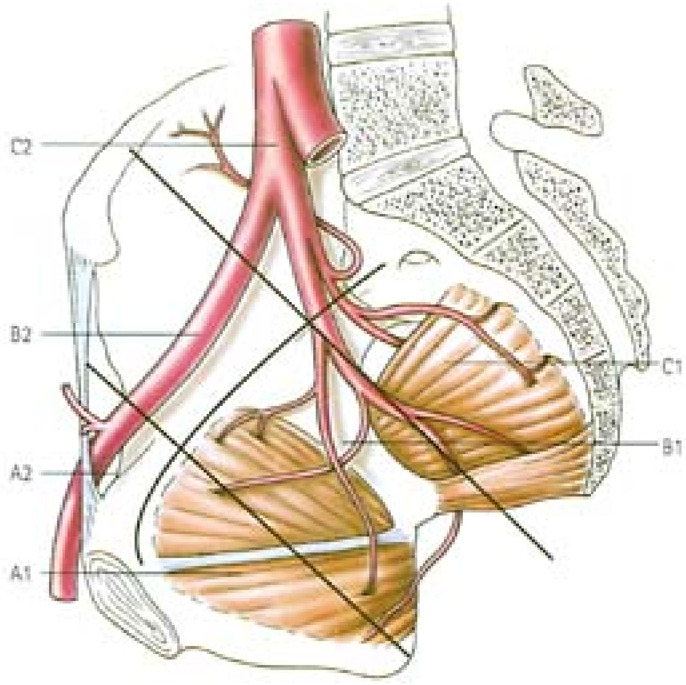

Figure 2

Topographical anatomical representation of different types of pelvic side-wall recurrences according to the suggested classification (Höckel et al. 1996). (After E.W.Hanns)
A1 Infrailiac ischiopubic
A2 Periiliac ischiopubic
B1 Infrailiac acetabular
B2 Periiliac acetabular
C1 Infrailiac sacrococcygeal
C2 Periiliac iliosacral

The pelvic wall plasty creates a compartmentalization of the tumor bed and a protective distance of several centimeters to the remaining hollow organs in the pelvis. Moreover, therapeutic angiogenesis is provided (Höckel et al. 1993). These three features allow the application of a high localized irradiation dose to the tumor bed despite prior irradiation (Höckel et al. 1989, 1991, 1996).
Infrailiac pelvic side-wall disease (except tumors infiltrating the sciatic foramen) can be treated with the laterally extended endopelvic resection (LEER). Since these tumors usually do not penetrate the endopelvic

fascia the inclusion of the adjacent striated pelvic wall muscles (obturator internus, pubococcygeus, iliococcygeus, coccygeus) provides clear resection margins (R0). Lateral extension of pelvic exenteration often necessitates the resection of the parietal branches of the internal iliac vessel system exposing the lumbosacral plexus.
The rate of severe complications of this extensive surgery is 25%. Lethal complications have occurred in less than 5%. Treatment sequelae are acceptable for tumor-free patients most of whom rated their quality of life as good (Höckel et al. 1996; Höckel 2003). Fiveyear survival probabilities between 40% and 50% are achieved in patients with pelvic side-wall recurrences of cervical cancer in an irradiated pelvis selected according to the criteria outlined below (Höckel et al. 1989, 1991, 1994, 1996, Höckel 1999a, b, 2003).

Indications

The LEER and CORT procedures are indicated for histologically confirmed, unifocal pelvic side-wall recurrences. Suitable candidates should be free from tumor dissemination (multifocal pelvic disease, intraperitoneal disease, distant metastases) with tumors limited to a maximal diameter of less than 5 cm. Medical conditions not compatible with major surgery or an unwillingness to accept urinary or fecal diversion would also disqualify a patient.

Anatomic considerations

Vascular supply

The blood supply to the pelvis is derived mainly from the internal iliac vessels. Collateral circulation is provided to the true pelvis by the inferior mesenteric artery through anastomotic channels with the superior rectal artery and the middle sacral artery, and to a limited extent by the external iliac vessels' minor anastomoses (e.g. external pudendal and deep circumflex iliac arteries).

Nerve supply

Nerve roots from as high as T10 all the way down to the sacral roots pass through or into the pelvis. The pelvic side-wall contains many nerves, including (from medial to lateral) the lumbosacral plexus, sciatic, obturator, femoral, genitofemoral, lateral femoral cutaneous, ilioinguinal and iliohypogastric nerves. There is a rich supply of autonomic nerves as well. Injury to these nerves is sometimes unavoidable in pursuit of complete surgical resection.

Muscles

The muscles of the endopelvis include the psoas, iliac, internal obturator, piriform, coccygeus, and the levator ani muscles. Depending on the requirements of the procedure, the rectus abdominis and transversus muscles may be used as a flap to resupply the area with healthy tissue. Transposition of these muscles does not lead to significant functional impairment.

Bony landmarks and general considerations

When evaluating a patient for any pelvic operation, the relationship of the anterior superior iliac spine should be noted. Regardless of the general body habitus, the operation will be limited laterally by the bony pelvis as indicated by the spine. Patients with generous amounts of soft tissue lateral to the spine can be difficult operative candidates.

Surgical procedure

Laterally extended endopelvic resection (LEER)

The patient is informed about the minimal and maximal version of the operation with respect to resection and reconstruction. Forty-eight hours before surgery mechanical bowel cleaning is begun. Using central venous access, total parenteral nutrition is established and a broad-spectrum antibiotic combination (e.g. ampicillin with clavulanic acid and metronidazole) is infused. Bilateral stoma sites in the epigastric and hypogastric regions are marked. If a gluteal thigh flap is considered for reconstruction the course of the inferior gluteal artery branch at the posterior thigh is drawn on the skin.
Standard surgical instruments for radical hysterectomy and Cobb periosteal dissectors are required. Surgical access is through a hypogastric and epigastric

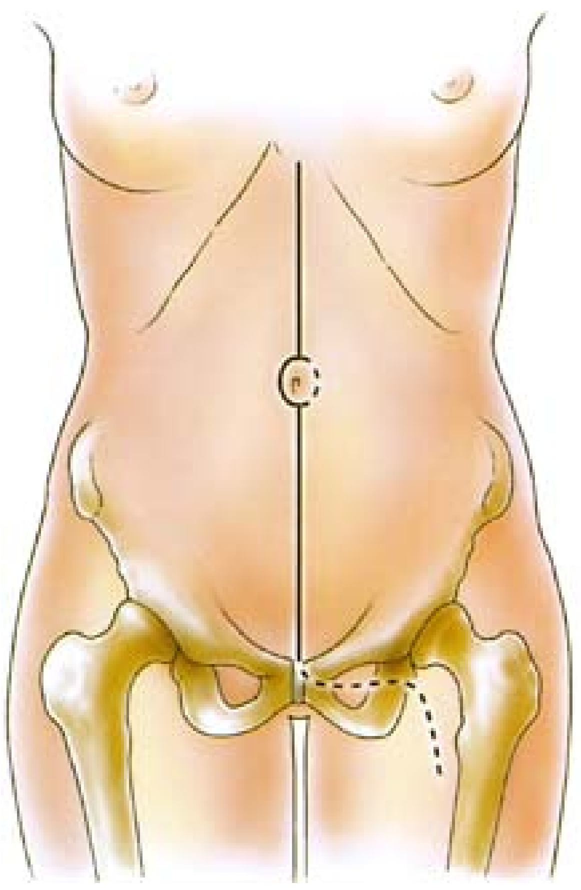

Figure 3

In most cases LEER is performed through a hypo- and epigastric midline laparotomy. In very obese patients a modified abdominoinguinal incision can be advantageous (after E.W.Hanns)

midline laparotomy circumventing the umbilicus. In very obese patients an abdominoinguinal incision can be helpful; this is made by advancing the laparotomy to the middle of the inguinal region at the side of the recurrence and separating the origin of the rectus abdominis muscle without severing the inferior epigastric vessels (Figure 3). For low recurrences, additional perineal incisions at the vaginal introitus (possibly including the anus), are necessary.
The surgical techniques of the most extensive version of LEER, the laterally extended total exenteration are illustrated in Figures 4–13. Pelvic wall resection is performed at the left side in this example.
All peritoneal adhesions are lysed and the abdominal and pelvic intraperitoneal compartments are systematically explored by inspection and palpation. Biopsies are taken from all suspicious intraperitoneal sites.

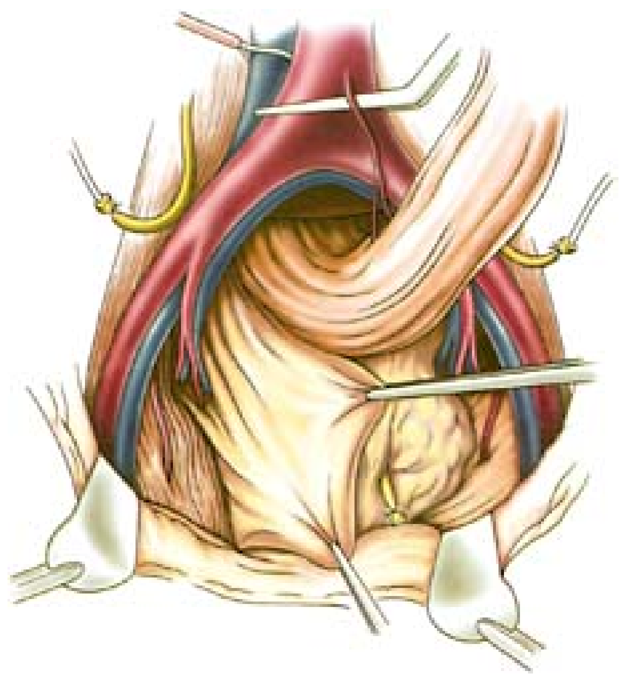

Figure 4

Placement of a tourniquét around the vena cava inferior and of a large vessel clamp on the aorta abdominalis at the level below the origin of the inferior mesenteric artery to prepare for temporary large vessel occlusion during later steps of the operation (after E.W.Hanns)

If intraperitoneal tumor dissemination can be excluded, the retroperitoneal pelvic and midabdominal compartments are opened. On both sides, the paracolic and pelvic parietal peritoneum is incised along the psoas muscles and the round ligaments are separated. The peritoneum at the base of the mesentery is dissected and the duodenum is mobilized against the vena cava and aorta. The small bowel and the right and transverse colon are packed into a bowel bag. The anterior visceral peritoneum of the bladder is incised and the space of Retzius is developed. Both paravesical and pararectal spaces and the presacral space are created. Depending on the location of the recurrent tumor these spaces may only be partially developed. Intralesional dissection should be strictly avoided. Both ureters are liberated. Selective periaortic and pelvic lymph node dissection is performed as dictated by the extent of earlier operations and the

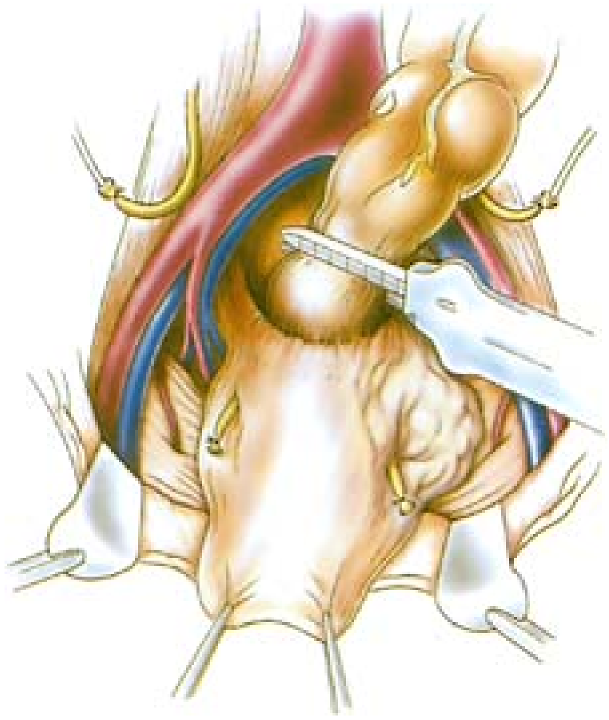

Figure 5

After the retroperitoneum is entered the pararectal and paravesical spaces are completely developed at the tumor-free pelvic side-wall (right). These spaces can only be developed in part on the side of the recurrent disease (left). Following selective periaortic and pelvic lymph node dissection both ureters are transected as deep in the pelvis as possible and stented. The bowel continuity is interrupted at the rectosigmoid transition (after E W.Hanns)

intraoperative findings. If lymphatic tumor dissemination cannot be demonstrated in frozen sections, LEER is started. A tourniquét is placed around the vena cava inferior at the level of the origin of the inferior mesenteric artery. The aorta abdominalis is mobilized at that site so that it can be easily undermined by a large vessel clamp. Temporary occlusion of the large vessels facilitates the control of severe bleeding at later steps of the operation (Figure 4).

The infundibulopelvic ligaments are divided and the ureters are cut as low as possible in the pelvis. Biopsies of the distal ureters are examined as frozen sections. Stents are inserted into the ureters. The mesosigmoid is skeletized and the blood vessels are ligated at the rectosigmoidal transition. The bowel continuity is interrupted at this site using a gastrointestinal stapler (Figure 5). The sigmoid colon is included in the bowel bag. At the right pelvic wall the urogenital mesentery containing the visceral branches of internal iliac vessels, the pelvic autonomic nerve plexus, and the sub-

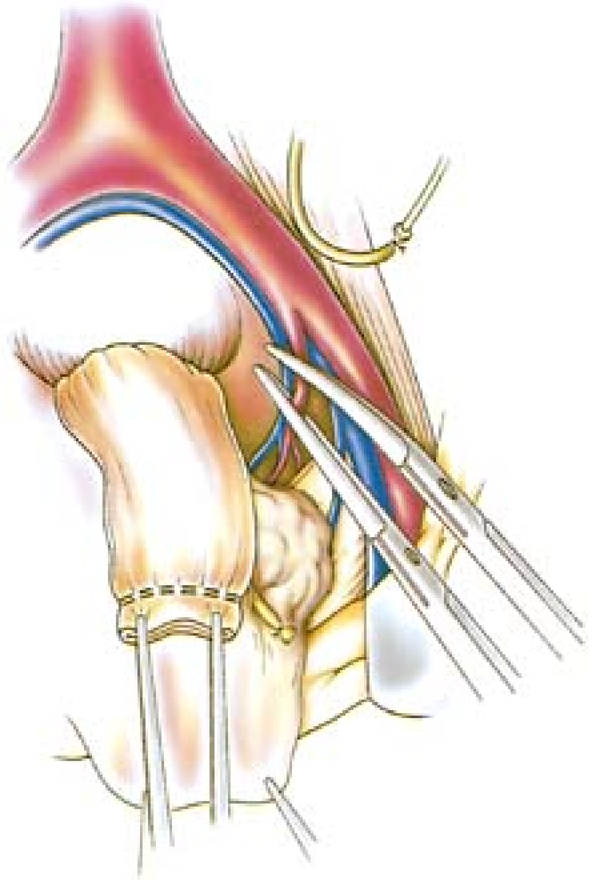

Figure 6

Ligation of the internal iliac artery (after E.W.Hanns)

peritoneal dense connective tissue is completely divided by use of Wertheim clamps as in conventional exenteration procedures.

The left internal iliac artery is ligated and divided where it branches off from the common iliac artery (Figure 6). Thereafter, all parietal branches of the iliac vessel system are transected between hemoclips or clamps: the ascending lumbar vein, superior gluteal artery and vein, inferior gluteal artery and vein, internal pudendal artery and vein (Figure 7). The internal iliac vein can now be divided at its bifurcation as well. The lumbosacral plexus and the piriform muscle are exposed by this maneuver. In case of severe hemorrhage the aorta should be clamped immediately below the origin of the inferior mesenteric artery and the prelaid tourniquét around the vena cava should be closed.

The internal obturator muscle is ventrally incised at the site of the obturator nerve, which is either elevated or divided if it is incorporated in the tumor

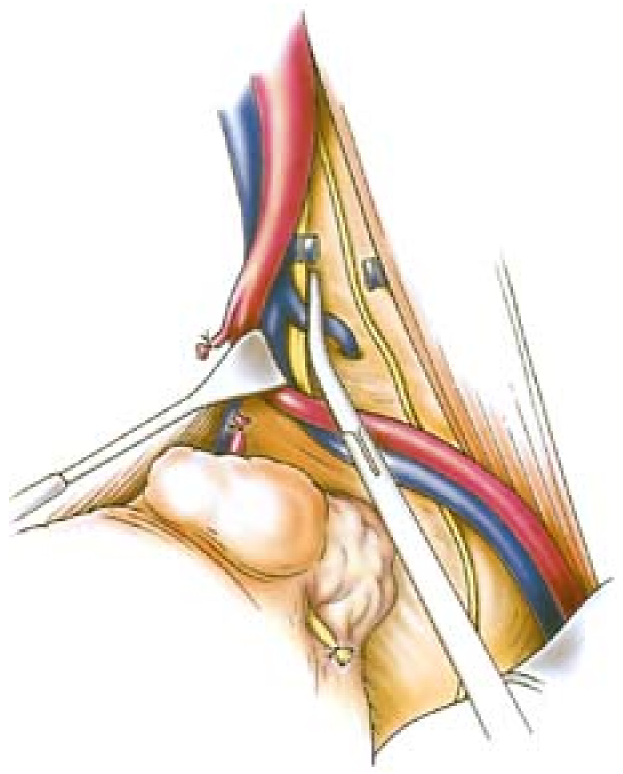

Figure 7

Transection of the parietal branches of the internal iliac artery and vein after retracting the common/external iliac vessels medially as a prerequisite for the ligation of the internal iliac vein (after E.W.Hanns)

(Figure 8). The muscle is separated from the acetabulum and the obturator membrane by use of a Cobb periosteal dissector (Figure 9). Below the ischial spine the obturator muscle which leaves the endopelvis at this point is divided again, with ligation of the muscle stump (Figure 10). The separated endopelvic part of the obturator muscle in continuity with the attached iliococcygeus and pubococcygeus muscles is retracted medially, exposing the ischiorectal fossa.

A superficial incision is made below the lumbosacral plexus between the ischial spine and the fourth sacral body and the coccygeus muscle is elevated from the sacrospinous ligament with a Cobb periosteal dissector (Figure 11).

At the level of the ischiorectal fossa the lateral vaginal wall is identified and incised. The anterior vaginal wall and urethra are transected. The anal canal is mobilized from the posterior vaginal wall which is divided after clamping as well. The anorectal transition is separated with an articulated stapling instrument. Now the complete specimen of the laterally extended total evisceration consisting of the urethra, bladder, vagina,

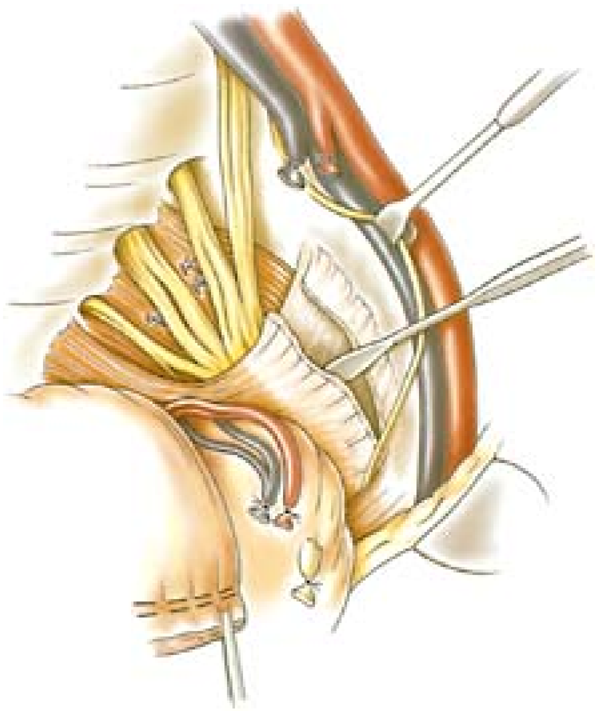

Figure 8

Ventral incision of the obturator internus muscle at the site of the obturator nerve which is retracted (after E.W.Hanns)

uterus and adnexa, rectum at the left side en bloc with the complete endopelvic urogenital mesentery, the coccygeus, iliococcygeus, pubococcygeus and the internal obturator muscle, can be removed and examined with multiple frozen sections for tumor margins. If necessary, the caudal dissection can be shifted further downward to include the vaginal introitus, urethral meatus and anus, necessitating secondary access from the perineum.

To improve wound healing in the irradiated pelvis, an omentum flap nourished by the ipsilateral gastroepiploic artery is elevated (Liebermann-Meffert and White 1983), transposed to the pelvis along the para-colic gutter and fixed to the pelvic surface (Figures 12 and 13). The inclusion of the anus and anal canal into the laterally extended pelvic evisceration necessitates the reconstruction of the perineum and pelvic floor. This can be accomplished by the use of a gluteal thigh flap (Hurwitz 1981) or a gracilis musculocutaneous flap (McGraw et al. 1976). For supravesical urinary diversion either a conduit or a continent pouch is constructed from non-irradiated colon segments (ascending, transverse or descending colon) with the Mainz techniques (Fisch and Hohenfellner 1991, Fisch et al.

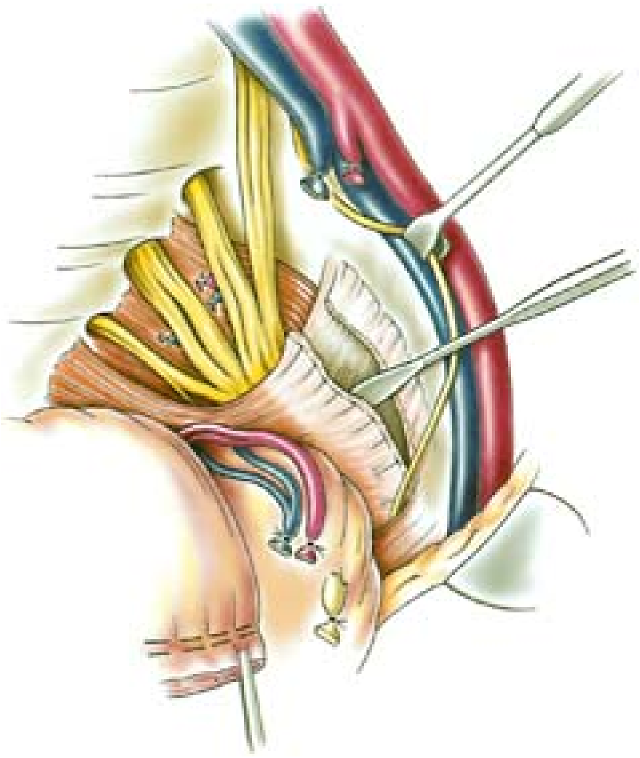

Figure 9

Separation of the obturator internus muscle from the acetabulum and obturator membrane with a Cobb periosteal dissector (after E.W.Hanns)

1996, see also Chapter 21). Fecal diversion is accomplished by an end sigmoidostomy (see Chapter 20). Following bowel anastomosis the patient receives total parenteral nutrition for at least 5 days. The postoperative care of the conduit or pouch for supravesical urinary diversion is carried out as described (Fisch and Hohenfellner 1991, Fisch et al. 1996).

Combined operative and radiation treatment (CORT)

The CORT procedure may be considered in case of clear but close resection margins to structures that are vital for leg function, especially the common or external iliac artery. In addition to the standard instruments for extended pelvic surgery a CORTset will be needed. The CORTset contains marker clips, fixation bridges, guide tubes and special surgical instruments for their handling.
The specific surgical steps are illustrated in Figures 14–20 in an example of close resection margins in the left periiliac acetabular region. The area of close resec-

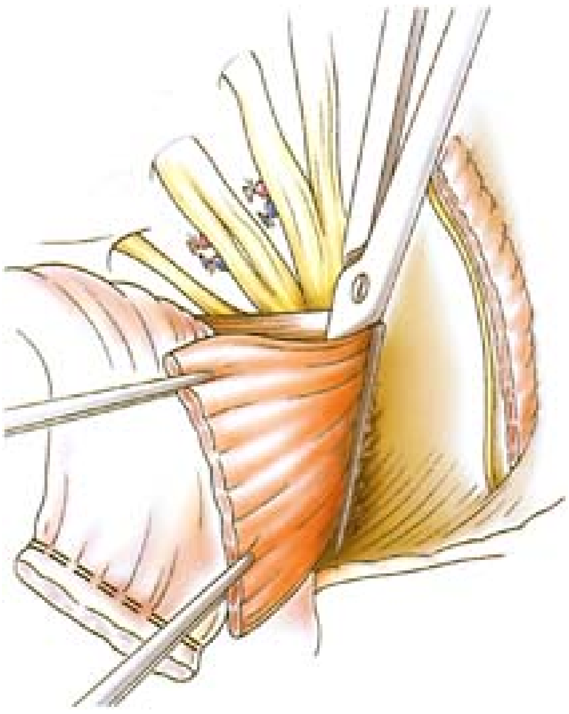

Figure 10

The obturator internus muscle is cut after its remaining part has been clamped at the lesser sciatic foramen (after E.W.Hanns)

tion margins is outlined with methylene blue and subsequently marked with specially designed titanium clips (Figure 14).
A titanium bridge implant for the fixation of the guide tubes is adjusted to fit to the midline of the marked area parallel to the linea terminalis and fixed with 3–0 poly glycolic sutures (Figure 15). The bridge implant must also be adapted to the irregular surface of the pelvic wall to maintain immediate contact of the guide tubes with the surface of the corresponding pelvic wall structures. This can easily be accomplished manually.
The retractors at the abdominal wall are temporarily removed. If cut previously the rectus abdominis muscle on that side is refixed to its origin by mattress sutures, and the fascia and skin layer of the inguinal extension of the laparotomy is closed. Bringing the abdominal wall flap to the midline, 8 mm skin incisions projecting just beyond the fixation rings of the titanium bridge are performed through which the flexible guide tubes are transabdominally implanted using a trocar (Figure 16).
The guide tubes are inserted into the fixation rings of the titanium bridge and fixed to the anatomical structures at the pelvic wall by an additional two or

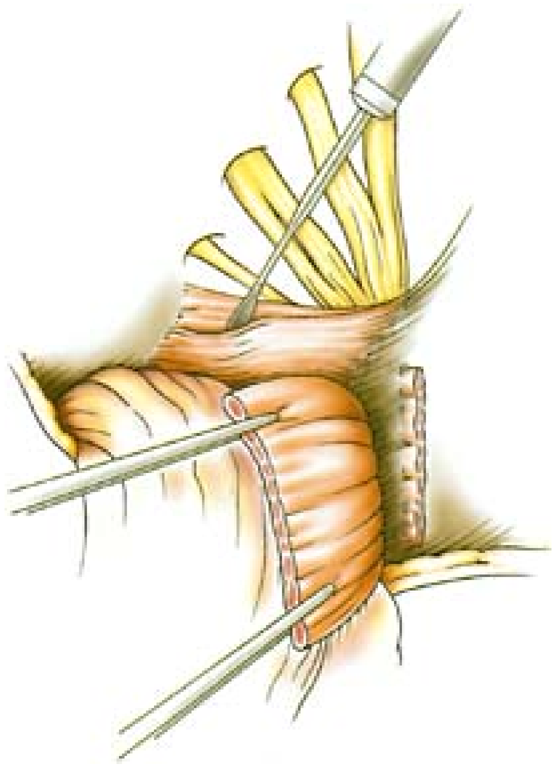

Figure 11

Elevation of the coccygeus muscle from the sacrospinous ligament with a Cobb periosteal dissector (after E.W.Hanns)

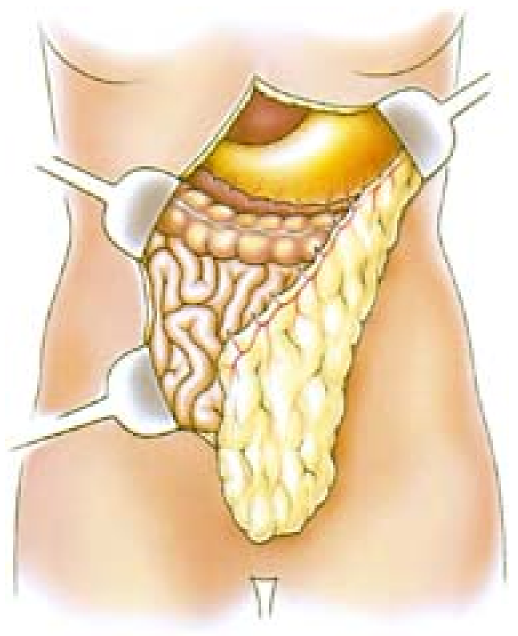

Figure 12

Omentum flap nourished by the left gastroepiploic vessels (after E.W.Hanns)

three 3–0 polyglycolic sutures. For optimal dosimetry of the brachytherapy the guide tubes must be strictly parallel and in direct contact with the pelvic wall surface (Figure 17). The endopelvic (closed) ends of the guide tubes should exceed the lower border of the close margin area by at least 2 cm. The external (open) tube ends are temporarily cut about 3 cm from the skin surface.
For the pelvic wall plasty either the TRAMP flap from the inner abdominal wall (Höckel et al. 1996), or the de-epithelialized extended vertical rectus abdominis musculocutaneous (VRAM) flap from the external abdominal wall (Taylor et al. 1984) (Figure 18), or the (partially) de-epithelialized gluteal thigh flap (Hurwitz et al. 1981) is used. These composite flaps are combined with an omentum flap to achieve the necessary area and thickness. The flap combination is always fixed with its muscular site to the pelvic wall. It should be at least 3 cm thick and completely overlie the array of guide tubes. A suction drain is placed between the tumor bed and the pelvic wall plasty to occlude any dead space (Figure 19).

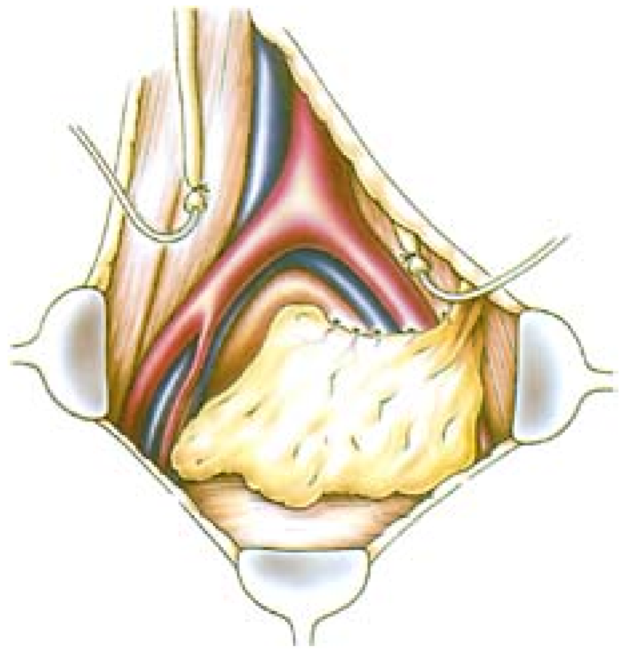

Figure 13

Omentum flap transposed to the pelvis for therapeutic angiogenesis (after E.W.Hanns)

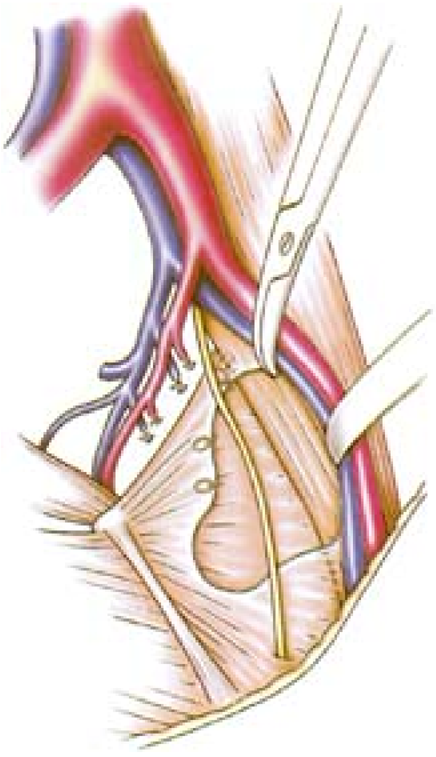

Figure 14

After the resection of a left periiliac acetabular side-wall recurrence, the close margin area is marked with methylene blue and specially designed titanium clips (after E.W.Hanns)

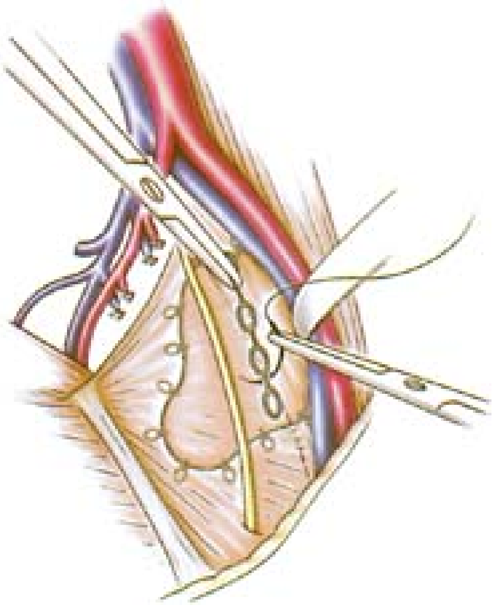

Figure 15

An adjusted titanium bridge implant is fixed to the pelvic wall in the middle of the close margin area parallel to the linea terminalis (after E.W.Hanns)

The selection of the flap combination for the pelvic wall plasty depends on the area to be irradiated, the extent of resection, the reconstructive surgical procedures to be performed, the amount of subcutaneous and amental fat, and tha locaiton of scars from previous operations. To ensure uncompromised blood supply the composite flaps should be raised from the side contralateral to the resected tumor. The omentum flap is elevated ipsilaterally. A flap containing the rectus muscle should not be harvested from the colostomy site.
After laparotomy closure, fixation plates are slipped over the external ends of the guide tubes and glued to them at the level of the skin surface with pharmaceutical dermal glue. Each fixation plate is anchored to the skin with four monofilament 3–0 polyamide sutures. The overriding open ends of the guide tubes are cut and closed with plugs (Figure 20).

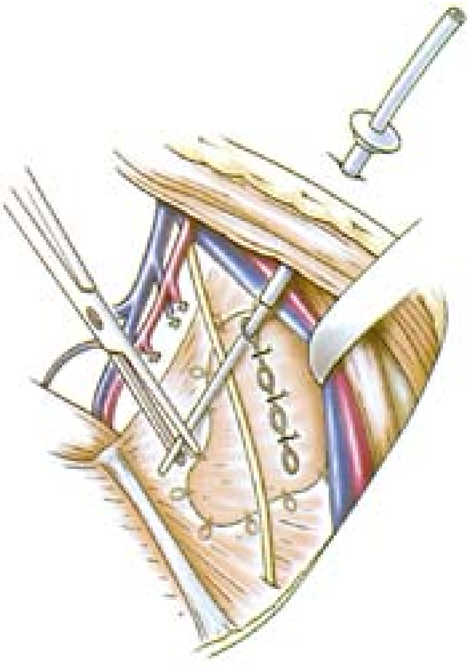

Figure 16

A flexible brachytherapy guide tube is placed transabdominally, implanted by use of a trocar (after E.W.Hanns)

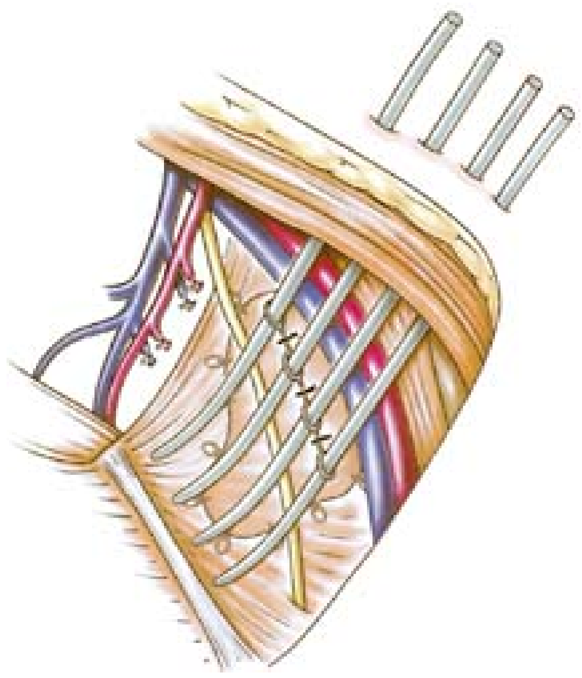

Figure 17

Complete array of transabdominal guide tubes for postoperative brachytherapy fixed to a close margin area by the bridge implant and additional sutures (after E.W.Hanns)

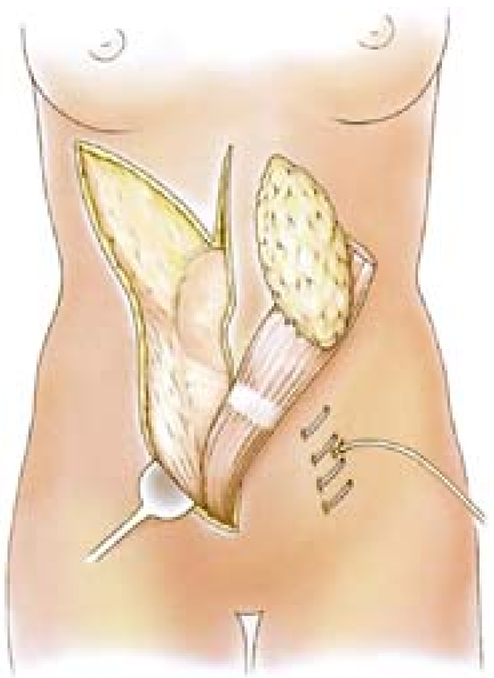

Figure 18

Elevation of a de-epithelialized extended VRAM flap based on the right deep inferior epigastric vessels (after E.W.Hanns)

One week after surgery, a series of magnetic resonance imaging (MRI) scans is performed to evaluate the viability and the location of the pelvic wall plasty. If no dead space between the pelvic wall plasty and the tumor bed can be detected, the suction drain is removed. The skin fixation of the guide tubes should be checked regularly for completeness; resuturing is sometimes necessary. The tube exits are protected with an adhesive film dressing.
The patient receives an oral sulfonamide as long as the guide tubes are in place. Prophylactic low-dose heparin is given during the entire hospital stay.

Radiotherapy

In principle, various modes of tube-guided brachy-therapy (low dose rate, high dose rate, pulsed dose rate) are possible with the CORT concept. Irrespective of the dose rate, treatment planning and dosimetry must be optimal and the total dose applied to the pelvic wall must be high enough to eradicate all residual occult tumor at the target site.

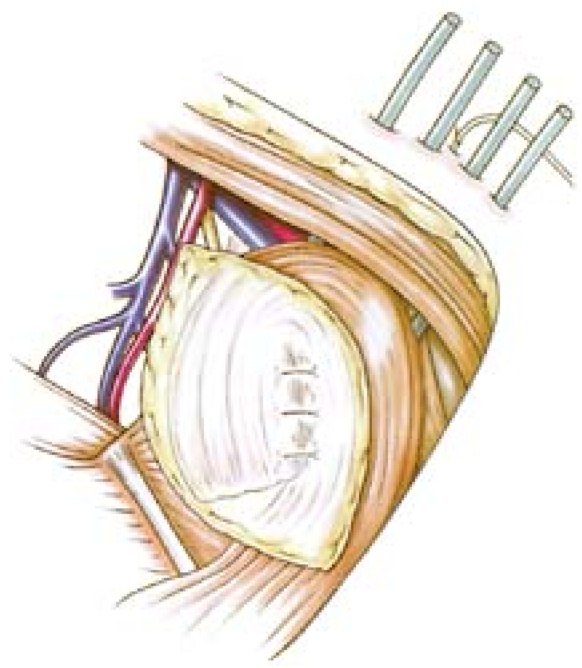

Figure 19

De-epithelialized extended VRAM flap used as pelvic wall plasty for CORT (after E.W. Hanns)

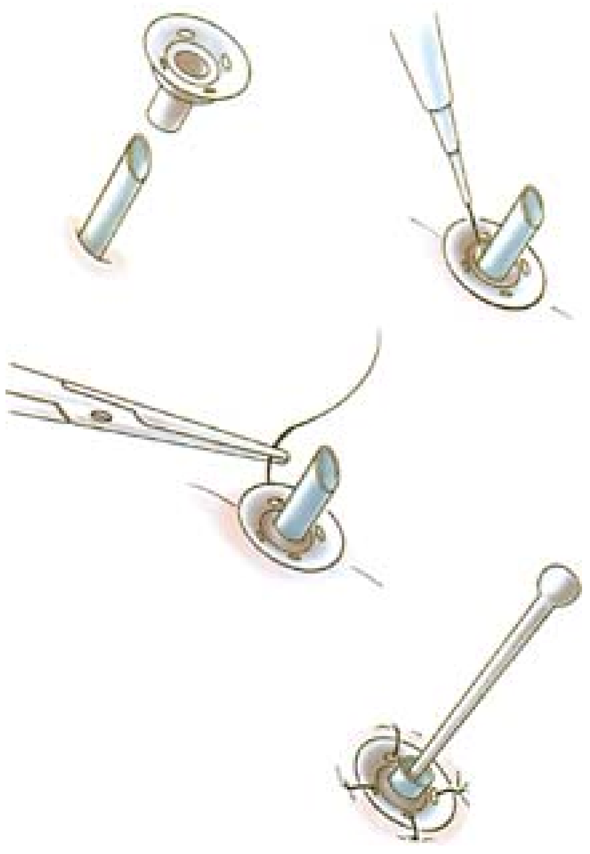

Figure 20

Adjustment and fixation of the guide tubes to the skin after laparotomy closure (after E.W. Hanns)

Radiotherapy is started as soon as possible postoperatively, but not before the anticipated neovascularization of the pelvic wall plasty and the adjacent pelvic wall is established. From animal studies it is known that sufficient vascular connections from the musculocutaneous flaps to the recipient beds are formed by 7 days, after which ligation of the nourishing vessels does not result in flap necrosis. Based on the assumption that the timing of angiogenesis is similar in pelvic wall plasty, and also taking into consideration that the primary recovery time of patients from the extended radical surgery is usually a week, treatment is planned at the beginning of the second postoperative week and brachytherapy is started on days 10–14 in an uneventful postoperative course.

With calibrating dummies inserted into the guide tubes, several X-ray films of the pelvis in defined planes are taken with a therapy simulator. The close margin area outlined intraoperatively with marker clips and the corresponding target area for irradiation are drawn on the simulator X-ray films. The locations of: (1) the guide tubes, (2) the target area, and (3) anatomic points of interest (e.g. adjacent hollow-organ segments) are digitized into the computer for optimal dosimetry. A 100% isodose image is generated, which includes the surface area of the close margin region with an approximately 2 cm circumferential overlap and a 1.0–1.5 cm depth of penetration of the pelvic wall tissues.

Immediately after the last brachytherapy fraction, the fixation sutures are cut and the guide tubes are removed. The titanium bridge implant stays in situ. The small stab wounds close spontaneously within 24 hours.

Acknowledgment

This work has been supported by a grant from Else-Kröner-Fresenius Stiftung, Bad Homburg, Germany.

References

Fisch M, Hohenfellner R (1991) Transversum conduit. *Akt Urol* **22**:1–14.

Fisch M, Wammack R, Hohenfellner R (1996) Kolon-trans-versum-ascendens/descendens-Pouch. *Akt Urol* **27**:1–8.

Höckel M (1996) The transversus and rectus abdominis musculoperitoneal (TRAMP) composite flap for vulvo vaginal reconstruction. *Plast Reconstr Surg* **97**:455–9.

Höckel M (1999a) Laterally extended endopelvic resection: surgical treatment of infrailiac pelvic wall recurrences of gynecologic malignancies. *Am J Obstet Gynecol* **180**:306–12.

Höckel M (1999b) Pelvic recurrences of cervical cancer: relapse pattern, prognostic factors and the role of extended radical treatment. *J Pelvic Surg* **5**:255–66.

Höckel M (2003) Laterally extended endopelvic resection: Novel surgical treatment of locally recurrent cervical carcinoma involving the pelvic side wall. *Gynecol Oncol* **91**:369–377.

Höckel M, Kutzner J, Bauer H, Friedberg V (1989) Eine neue experimentelle Methode zur Behandlung von Beckenwandrezidiven gynekologischer Malignome. *Geburtsh Frauenheilk* **49**:981–6.

Höckel M, Knapstein PG, Kutzner J (1991) A novel combined operative and radiotherapeutic treatment approach for recurrent gynecologic malignant lesions infiltrating the pelvic wall. *Surg Gynecol Obstet* **173**:297–302.

Höckel M, Schlenger K, Doctrow S, et al. (1993) Therapeutic angiogenesis. *Arch Surg* **128**:423–9.
Höckel M, Baussmann E, Mitze M, Knapstein PG (1994) Are pelvic side wall recurrences of cervical cancer biologically different from central relapses? *Cancer* **74**:648–55.
Höckel M, Schlenger K, Hamm H, et al. (1996) Five-year experience with combined operative and radiotherapeutic treatment of recurrent gynecologic tumors infiltrating the pelvic wall. *Cancer* **77**:1918–33.
Hurwitz DJ, Swartz WW, Mathes SJ (1981) The gluteal thigh flap: a reliable sensate flap for the closure of buttock and perineal wounds. *Plast Reconstr Surg* **68**:521–32.
Liebermann-Meffert D, White H (1983) Protective and reconstructive surgery with the omentum in man. In: Liebermann-Meffert D, White H, eds. *The greater omentum.* Berlin: Springer: 211–329.
McGraw JB, Massey FM, Shanklin KD, Horton CE (1976) Vaginal reconstruction with gracilis myocutaneous flaps. *Plast Reconstr Surg* **58**:176–83.
Taylor GI, Corlett RJ, Boyd JB (1984) The versatile deep inferior epigastric (inferior rectus abdominis) flap. *Br J Plast Surg* **37**:330–50.

15
Surgica management of trophoblastic disease

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Deborah CM Boyle
Michael Seckl
J Richard Smith

Overview

Management of trophoblastic disease in the first instance involves evacuation of the uterus. This should always be done using a suction curette and preferably with the help of ultrasound guidance. In the presence of persistently elevated human chorionic gonadotrophin (hCG) levels or continuing problems with hemorrhage, further evacuation may be necessary. This should normally be discussed with a gestational trophoblastic disease center because of the high risk of perforation, hemorrhage or infection. Thereafter, if the hCG levels remain elevated, chemotherapy should be instituted. The vast majority of patients will respond to these measures due to the inherent chemosensitivity of gestational trophoblastic disease (GTD). Chemotherapy produces high cure rates while maintaining fertility, allowing women to have further pregnancies.

For the small minority whose hCG levels remain elevated following chemotherapy, more definitive surgical management may be required in the form of a total abdominal hysterectomy. Elevated hCG levels predispose to ovarian cyst formation but this should not encourage bilateral oophorectomy at the time of the hysterectomy unless there is another pre-existing reason. Total abdominal hysterectomy in the presence of choriocarcinoma can prove very taxing. Uterine vascularity may be massively increased, presumably owing to the action of vasoactive peptides, etc., and the uterine arteries may be up to 1 cm in diameter. More troublesome still is the massive enlargement of the uterine venous plexus. This can lead to hemorrhage during ureteric dissection, particularly in cases where the tumor has spread beyond the uterus into the parametrium.

Preoperative assessment should include Doppler flow ultrasonography of the pelvis, computed tomography (CT) and/or magnetic resonance imaging (MRI) scans of the chest, abdomen and pelvis and an MRI of the head, together with hCG, full blood count and blood biochemistry measurements. GTD always produces hCG which allows screening and monitors treatment and follow-up. Four to six units of blood should be cross-matched. It is helpful, in the presence of extrauterine spread, to perform ureteric stenting. The laparotomy is performed, generally via a Pfannenstiel incision, but may require Cherney’s muscle cutting or a midline incision depending on the surgeon’s preference and the size of the uterus. In the presence of huge vessels, the authors have found it useful to commence the procedure by opening the broad ligament, identifying the ureter and dissecting it in a cephalad

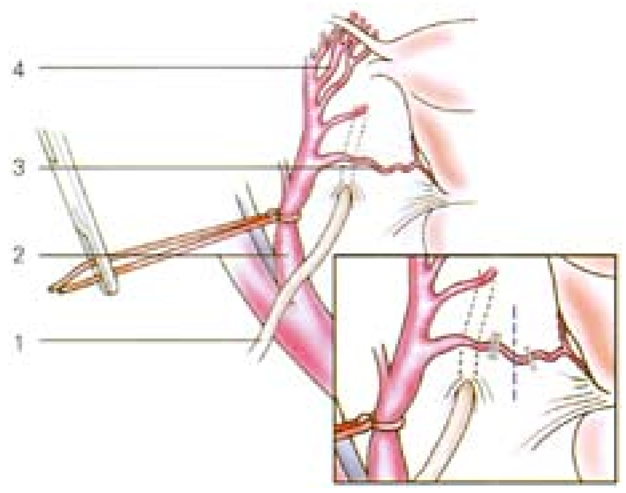


Figure 1

Vascular elastic slings are placed around the internal iliac vessels in case of hemorrhage.
(Inset) Ligation of the uterine artery (incision marked by dotted line)
1 Ureter
2 Internal iliac vessels
3 Uterine artery
4 Superior vesical arteries

direction as far as the bifurcation of the common iliac artery. Vascular elastic slings can be placed around the internal iliac vessels (Figure 1). These vessels can be temporarily ligated prophylactically using bulldog surgical clips or the slings left loose until the need arises.
These slings have proved useful to the authors in the face of the torrential hemorrhage that can arise. Dissection of the internal iliac arteries then takes place until the origins of the uterine arteries are identified, skeletonized and ligated using either polyglactin ties or surgical clips. The ureter is identified running under the uterine artery. The multiple uterine vessels are ligated by applying three surgical clips to each vessel and transecting the vessel between them, leaving two proximally (see inset in Figure 1). In general, the ureteric canal does not need to be opened; however, if the need arises, this should be done as described in Chapter 9. If a placental site trophoblastic tumor is suspected, removal of pelvic lymph nodes and para-aortic lymph nodes is advisable for gross lymph node disease involvement.
Excessive uterine manipulation should be avoided during the surgery when possible so as to reduce any possible risk of embolization of trophoblastic tissue. Because these patients may be hemodynamically

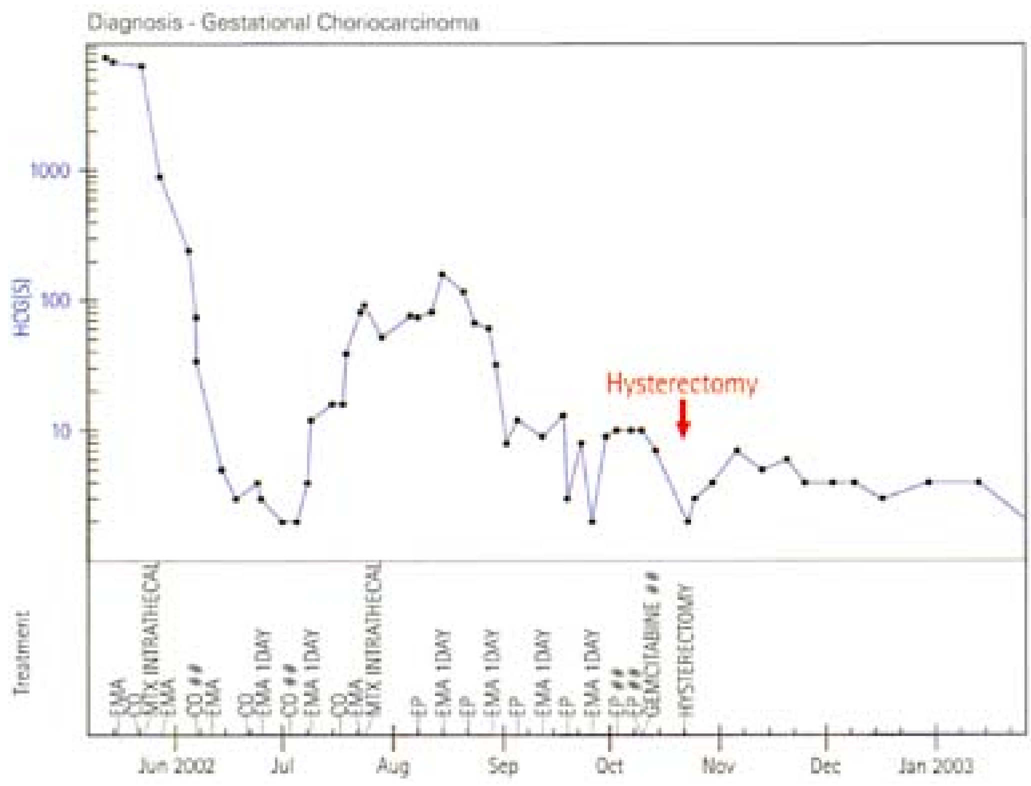


Figure 2

Therapeutic benefit of a hysterectomy in the management of chemoresistant gestational trophoblastic disease (GTD) localized to the uterus

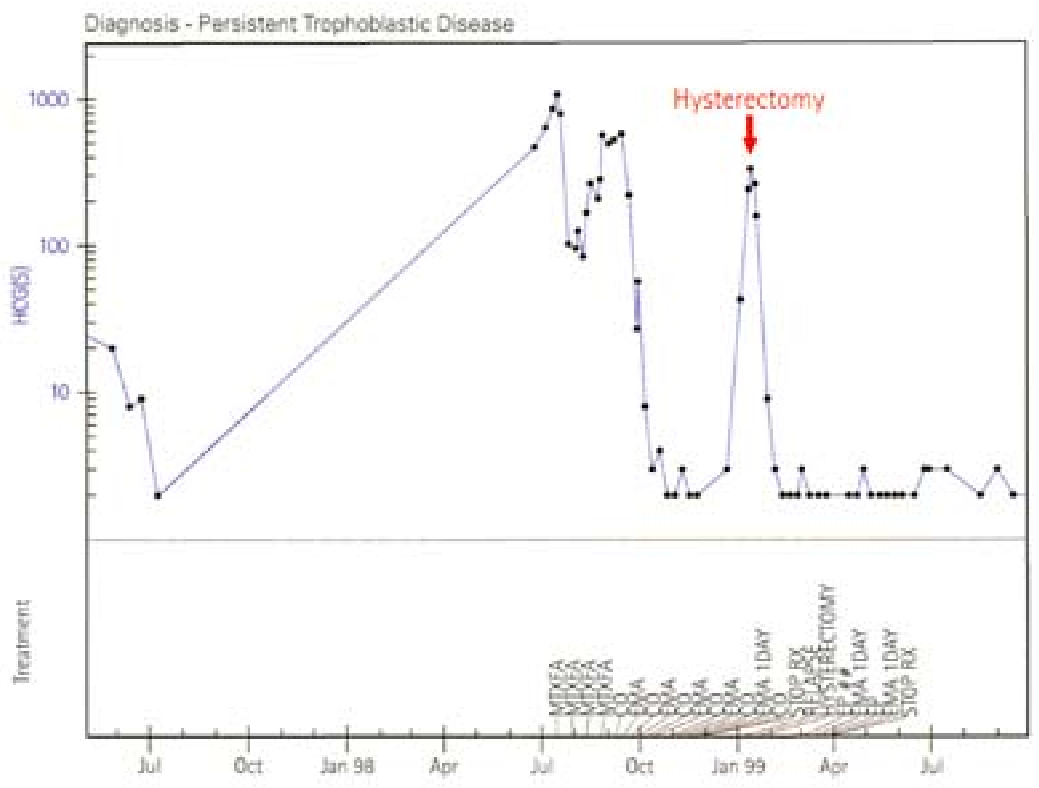


Figure 3

Therapeutic benefit of a hysterectomy during relapse of a gestational trophoblastic tumor (GTT)

unstable it is recommended that these procedures should be carried out by an experienced surgical team at a specialized center providing full medical support, including intensive care.

Studies

In a ten-year review from 1993 to 2003, 14/744(1.9%) cases were referred to the Chelsea and Westminster Hospital from Charing Cross Hospital (the London center for GTD) for some form of hysterectomy (Piver/Rutledge classification) for GTD depending on the extent of extrauterine spread. Despite having some type of hysterectomy followed by chemotherapy, 3/14 (21%) cases reviewed failed to survive. Their poor outcome was unrelated to the surgery but due to chemoresistant metastatic disease outside the pelvis. The review concluded that surgical management of primary drug-resistant and relapse cases of GTD in the form of different types of hysterectomies is a useful and safe adjunct to chemotherapy and has a satisfactory long-term outcome.

Figure 2 shows the therapeutic benefit of a hysterectomy using serum βhCG levels in the management of chemoresistant GTD which is localized to the uterus. The therapeutic benefit of a hysterectomy during relapse of a gestational trophoblastic tumor (GTT) is shown in Figure 3.

Summary

Total abdominal hysterectomy for trophoblastic disease is rarely required. It may be required for the management of excessive uterine bleeding either at presentation or after the onset of chemotherapy and in the management of chemoresistant disease localized to the pelvis. It is the treatment of choice in the management of placental site trophoblastic tumors confined to the uterus. When it is being performed, problems with hemorrhage should be anticipated and the suggested prophylactic measures should make uncontrollable hemorrhage less likely. Management of metastatic choriocarcinoma outside the area of gynecological competence, for example, in the thorax or brain, is beyond the scope of this book, but such tumors may well be amenable to management by the appropriate surgeon.

References

Hancock BW, Newlands ES, Berkowitz RS, et al. (eds) (2003) *Gestational trophoblastic disease,* 2nd edn.
ISSTD website: International Society for the Study of Trophoblastic Diseases, www.isstd.org/gtd/index.html (accessed March 2004)
Ngan HY (2002) The FIGO staging for gestational trophoblastic neoplasia 2000, FIGO Committee Report. *Int J Gynecol Obstet* **77**:285–7.
Ngan HYS, Odicino F, Maisonneuve P, et al. (2001) Gestational trophoblastic diseases. *J Epidemiol Biostat* **6** (1):175–84.
Piver MS, Rutledge FN, Smith JP (1974) Five classes of extended hysterectomy for women with cervical cancer. *Obstet Gynecol* **44**:265–72.
Sieunarine K, Rees H, Seckl M, et al. (2003) A review of the surgical management of gestational trophoblastic tumours from March 1993 to October 2003. In: *British Gynaecological Cancer Society.* Annual meeting:22.
Smith JR, Bridges JE, Boyle DCM, et al. (2000) Regarding ligation of the hypogastric artery and blood loss. *Int J Gyn Cancer* **10**:173.

16
Epithelial ovarian cancer

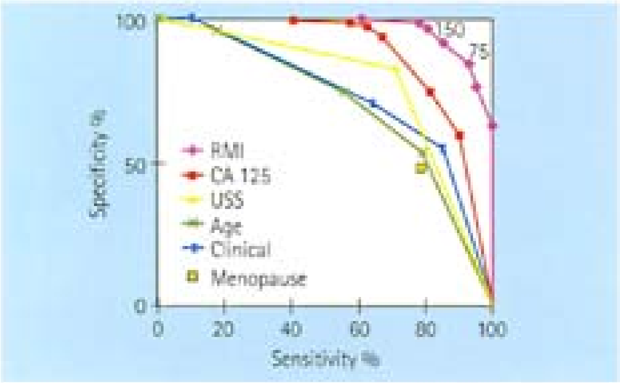
Jane Bridges
David Oram

Preoperative assessment

Ovarian cancer continues to frustrate. Clinicians are disadvantaged by the characteristics of unreliable, inconsistent symptomatology, which accounts for late presentation and poor associated survival figures. Even when the patient does present early, the preoperative diagnosis of ovarian cancer is frequently a difficult one to make. This is borne out by the fact that 50% of patients with this disease are initially referred to general physicians or general surgeons for investigation of symptomatology or ascites. The development by Jacobs et al. (1990) of a scoring system, the risk of malignancy index (RMI), which incorporates the use of the serum CA125 level, pelvic ultrasound features and the menopausal status of the patient, has greatly eased this preoperative difficulty. The details of the calculation are shown in Figure 1 and the RMI has now been validated in clinical practice. Using this calculation to assess the nature of an abdominopelvic mass helps to confirm the diagnosis of malignancy with greater than 95% accuracy. This is turn allows for an appropriate referral to a cancer center to be made, or at least prevents the initial surgery being inappropriately performed by an inexperienced surgeon. The importance of this has been demonstrated in data from the west of Scotland which confirm improved survival of patients with ovarian cancer if they are managed in a cancer center using a multidisciplinary team approach. Furthermore, accurate preoperative diagnosis enables appropriate counselling to be given to the patient and her family. Appropriate investigation and management planning can be embarked upon in a proactive manner, and by no means the least important consideration is that the patient's initial surgery and exploration can be performed through the correct surgical incision.

Preoperative investigations

Investigations should include an assessment of the patient herself, including her performance status and her nutritional status; if necessary, parenteral feeding through central lines can be instituted preoperatively. This should not, however, delay the initial surgery. A thorough hematological and biochemical assessment should be undertaken. A chest X-ray is required: if a pleural effusion is present, this should be aspirated and the fluid examined cytologically for malignant cells. Pelvic ultrasonography is usually performed as part of the initial assessment and is complemented by specialist imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) in assessing the extent of the disease spread, including intra-and extra-abdominal metastatic deposits (Figure 2). Preoperatively the patient requires a bowel preparatory agent, and in selected cases stoma counselling may be instituted.



RMI = U x M x serum CA125

where U and M are the ultrasound and menopausal scores.

Ultrasound was assessed for the following features suggestive of malignancy:

- multiloculated cysts
- evidence of solid areas
- evidence of metastases
- presence of ascites
- bilateral lesions.

A score of 0 was given where none of these was present; 1 if one was present; and a score of 3 for two or more.

A score of 1 or 3 was given to pre- or postmenopausal patients respectively.

An RMI of 200 had a sensitivity of 85% and a specificity of 97% for diagnosing ovarian cancer.

Figure 1

Risk of malignancy index (RMI)

Primary laparotomy

The correct staging of ovarian cancer is of paramount importance because it has implications for adjuvant therapy and also for appropriate counselling concerning prognosis. It is unfortunate that under-staging is commonplace in this disease, in spite of attention being drawn to this problem by various authors since the 1970s (Piver et al. 1976; Young et al. 1983; McGowan et al. 1985). The surgical procedure should be performed through a midline incision extending from the symphysis pubis to above the umbilicus if necessary. Any ascites present on opening the peritoneal cavity should be aspirated and sent

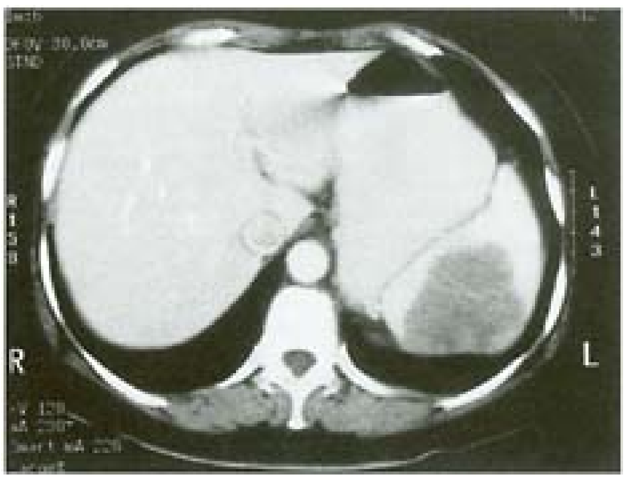


Figure 2

MRI demonstrating solitary splenic metastasis

for cytological assessment; otherwise the pelvis and paracolic gutters should be thoroughly irrigated with saline and the washings aspirated and sent for cytological assessment. Diaphragmatic swabs for cytology may also be taken. Thereafter thorough exploration and assessment of the extent of disease spread are crucial. Particular note should be taken of the tumor deposits in the upper abdomen: the hemidiaphragm should be palpated and inspected; the surface and parenchyma of the liver, the omentum, appendix and small and large bowel should be assessed, and thereafter all peritoneal surfaces including the paracolic gutters and the pelvic peritoneum. Attention is then turned to the extent of disease in the pelvis: the pelvic and para-aortic lymph nodes should, in the first instance, be palpated. In selected cases adherent tissue and adhesions should be sampled for biopsy and if it is felt to be helpful by the operating surgeon, frozen section of suspicious areas can be utilized. Where no obvious peritoneal disease is present, random biopsies should be taken from areas at high risk. Biopsy of the subdiaphragmatic peritoneum may be facilitated by the use of long-handled punch biopsy forceps. Depending on the stage of the disease the surgical problems differ. In advanced disease, the stage is usually obvious and the surgical challenge centers on cytoreductive surgery. In apparent early-stage disease, however, tumor resection is usually easy, but accurate surgical staging is a major consideration. In such cases pelvic and para-aortic lymph node assessment is indicated.

Surgical techniques for advanced disease

Following completion of the staging procedure, optimal cytoreduction becomes the goal. The surgical approach in ovarian cancer differs from that for other solid tumors where the aim is to remove the tumor with a wide area of normal tissue clearance. In epithelial ovarian cancer the priority is to remove as much of the bulk disease as possible, but if complete tumor clearance is not achievable then reduction of the tumor burden to minimal residual disease becomes the goal. Tumor debulking was advocated initially in the early part of the twentieth century by Meigs (1934) and Bonney (1912) and further developed by Brunschwig (1961). Munnell in the 1950s coined the phrase 'maximum surgical effort' and Griffiths quantified this in the 1970s in his seminal paper, which has dictated subsequent surgical practice (Munnell 1952, Griffiths 1975). Griffiths demonstrated an improved survival in patients who had their disease reduced to residual nodules of less than 1.5 cm. However, no prospective trials addressing the issue of benefit of aggressive cytoreduction have been undertaken, and so its exact value remains debatable. The surgery for advanced-stage disease is often difficult and, unlike

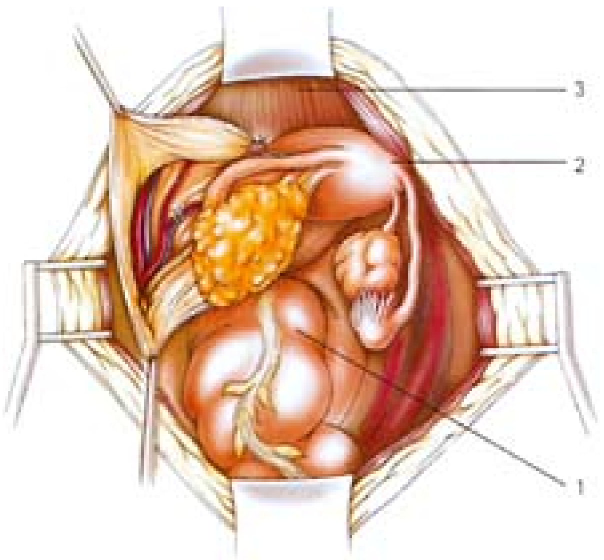


Figure 3

Extraperitoneal dissection
1 Rectum
2 Uterus
3 Bladder

other forms of cancer surgery, there are no set moves. It often requires persistence and a flexible approach by the operating surgeon, depending on available tissue planes. At the very least the procedure should incorporate total or subtotal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and removal of all bulk tumor deposits where possible. In most circumstances the retroperitoneal en bloc approach as described below should be used to clear all pelvic disease. Other surgical procedures that occasionally require to be undertaken include biopsy of parenchymal liver deposits. If the spleen is involved in the omental cake of tumor a splenectomy can be undertaken. Bowel resection (Chapter 20) is really only indicated in two clinical situations: the first is if there is bowel tumor causing impending obstruction, and the second is if resecting a segment of bowel will help to achieve complete tumor clearance. Prior to concluding the initial surgical procedure it is worth considering whether the patient might be suitable for intraperitoneal adjuvant chemotherapy: if so, an intraperitoneal catheter can then be inserted.

En bloc resection of advanced pelvic disease

The technique of en bloc resection was first described by Hudson (1968) in the management of patients with advanced pelvic disease where spread to the pelvic peritoneum, rectosigmoid and/or bladder had occurred. It facilitates resection of locally advanced tumors in one contiguous sample.
First the round and infundibulopelvic ligaments are divided and ligated. The pelvic peritoneum is then opened circumferentially from the symphysis pubis anteriorly to the rectosigmoid posteriorly. The peritoneum is dissected free in a lateral to medial direction, including that covering the dome of the bladder and the pelvis side walls. The uterine arteries are then divided and ligated in a lateral position close to their origin at the internal iliac artery, allowing the ureters to be mobilized laterally (Figure 3).
The anterior vaginal fornix is exposed by further dissection of the bladder anteriorly and opened transversely. The hysterectomy can then be performed in a retrograde fashion, dividing and ligating the uterosacral and cardinal ligaments. Development of the retrorectal space at this stage will allow elevation of the rectum, uterus and tumor from the sacral hollow, and an assessment of the need for rectosigmoid resection—depending on the

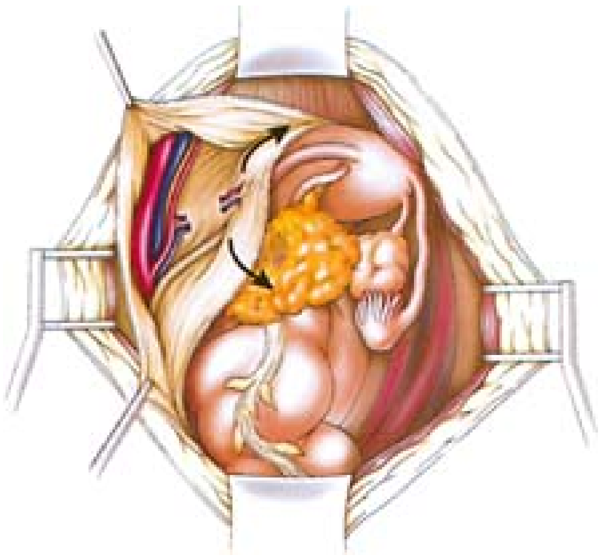


Figure 4

Development of the retrorectal space

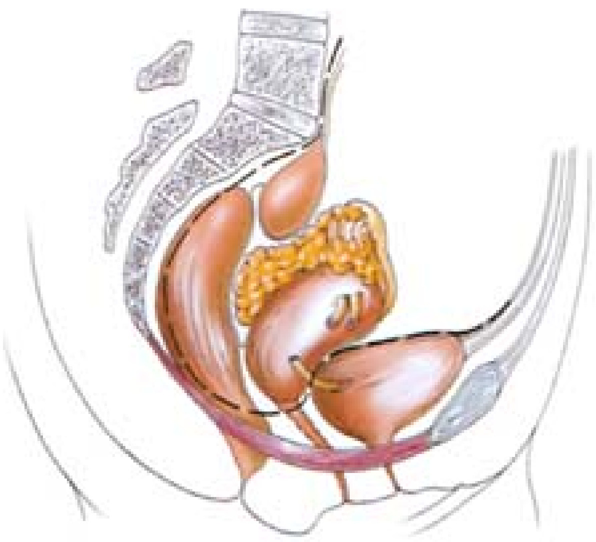


Figure 5

Resection outline

tumor mobility and invasion—can be made (Figure 4). Where superficial invasion of the sigmoid serosa only has occurred, the tumor may be dissected free by stripping the outer muscular layer from the underlying circular muscular layer and the mucosa. In patients with a small area of deep invasion, local resection of the anterior wall of the sigmoid may be performed and the bowel defect closed in the anterior plane. Resection will include the lateral pelvic and sigmoid peritoneum

Figure 6

Resection

within the specimen (Figures 5 and 6). Where there is more extensive rectosigmoid involvement, resection of this segment of the colon can be performed with a primary anastomosis. Initially the superior hemorrhoidal vessels are identified and ligated at the level of the sacral promontory. The sigmoid mesentery is then divided allowing margins for adequate tumor clearance, facilitated by division of the peritoneum and mobilization of the descending colon if necessary. The sigmoid is then divided, generally with a stapling device, and the proximal end of the sigmoid is placed in the left paracolic gutter while the final dissection of the tumor specimen is performed. Blunt dissection and traction on the distal rectosigmoid portion are used to mobilize the bowel, allowing the specimen to be drawn out of the pelvis and the resection margin of the rectum to be identified. At this stage the posterior anastomosis of the sigmoid to the rectal stump may be performed prior to the final division of the tumor en bloc specimen just above the anastomosis. The anastomosis can then be completed by hand or by a stapling device inserted through the anus. The anastomosis may be covered by a loop colostomy, but as the majority of women will not have received preoperative radiotherapy and will have had adequate bowel preparation, this may not always be necessary. Adequate drainage at the site of the anastomosis should be allowed at the end of the laparotomy, however, in the form of a large-bore tube drain.

The laparotomy should be completed with an omentectomy, with or without appendectomy and assessment of the para-aortic nodes.

Appendectomy

The appendix is a common site for metastatic disease but should only be removed when clearly involved by tumor (Fawzi et al. 1997). The appendix can be easily delivered through the midline incision. The meso-appendix is divided either following a single transfix suture if it is minimal, or by serial clipping section by section (Figure 7). A clip is then used to crush the base of the appendix, first close to the cecal wall and then immediately above it (Figure 8). A polyglactin tie is used to ligate the crushed area, and the suture ends are cut short. A purse-string suture is next inserted approximately 1 cm from the appendix, picking up only the seromuscular coat. The appendix is divided close to the clamp (Figure 9), the stump is invaginated and the purse-string suture tied (Figure 10).

Splenectomy

Splenectomy is extremely rarely necessary or indicated. However, at the time of surgical staging, disease spread to the spleen may be apparent as an extension of the omental plaque or as implants of more focal disease on the capsule and/or hilum. Occasionally it may appear as an isolated site of recurrence.
First the spleen should be mobilized to allow exposure and division of its ligamentous attachments. Traction in an inferior and medial direction will expose the filamentous attachments to the diaphragm (splenophrenic) and colon (splenocolic), and these may then

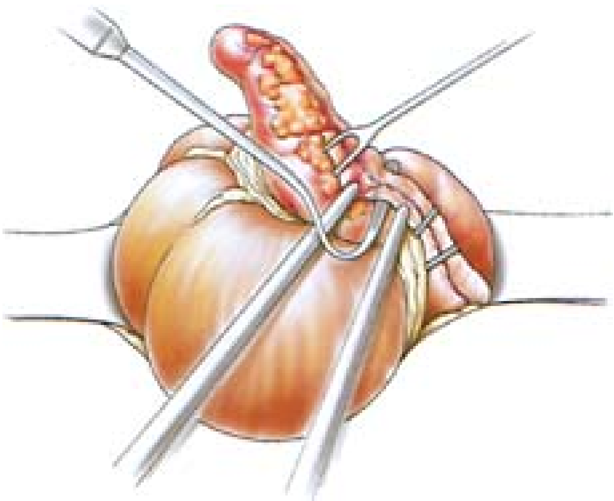


Figure 7

The mesoappendix is clipped

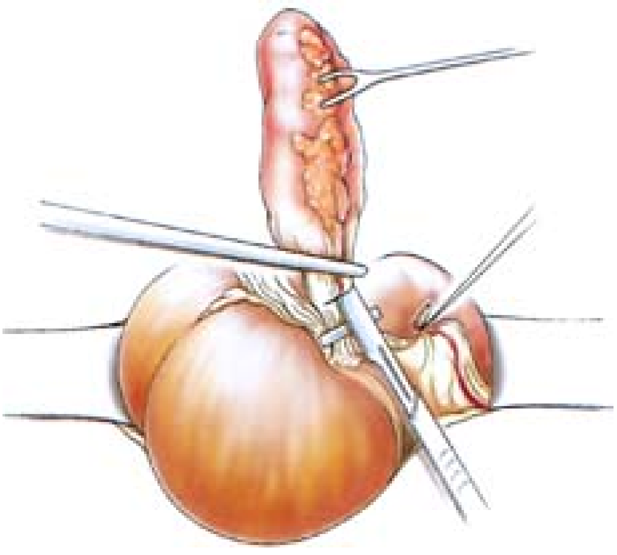


Figure 8

The base of the appendix is crushed

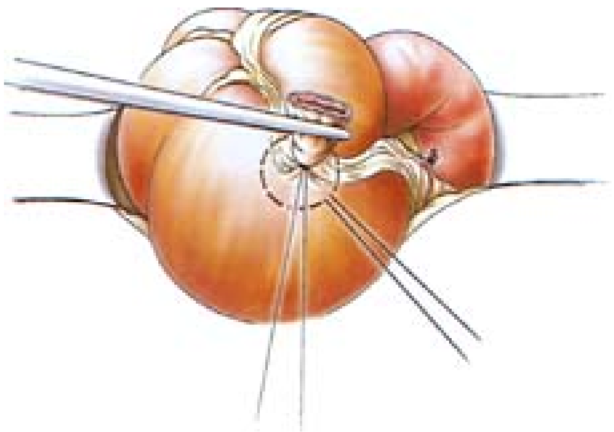


Figure 9

The appendix is divided

be divided and ligated. Entry into the lesser sac then allows exposure of the pancreas and the gastrosplenic ligament, which contains the short gastric arteries (Figure 11). Division of the short gastric vessels leaves only the splenorenal ligament intact, containing the splenic vessels and the tail of the pancreas. Holding the splenic hilum between the fingers, the operator identifies and protects the tail of the pancreas while the peritoneum over the ligament is taken and the splenic artery identified and divided (Figure 12). Finally the large splenic vein is identified, ligated and divided, and the spleen is delivered.

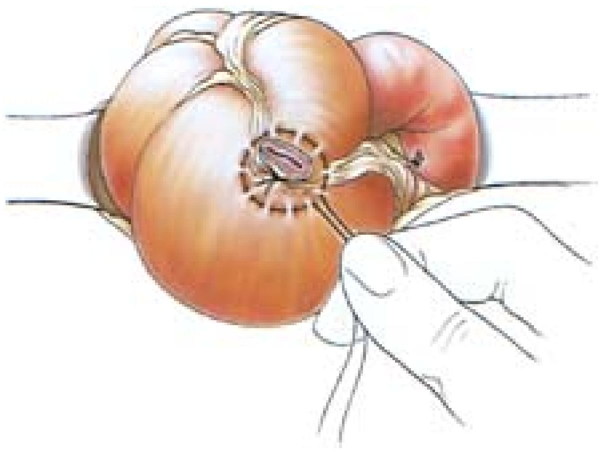


Figure 10

Purse-string suture

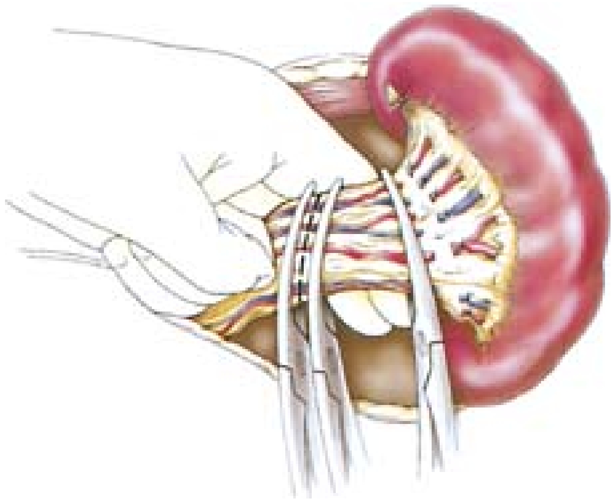


Figure 11

Exposure of the pancreas and gastrosplenic ligament

Omentectomy

The omentum is frequently the site of massive metastatic deposits of disease and may cause the presenting symptoms at the time of diagnosis. An omental 'cake', as it is commonly referred to, may be found at the junction of the greater omentum and the transverse colon. Although initial assessment may give the appearance of gross involvement of the transverse colon, this is usually not the case and the tumor mass can be carefully mobilized and resected without the

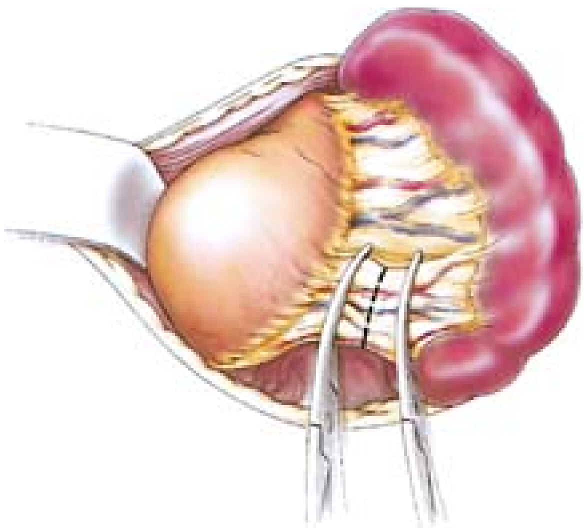


Figure 12

Division of the splenic artery

need for a transverse colectomy Care should be taken to assess whether the omentum is adherent to the anterior abdominal wall peritoneum, as this peritoneal layer can be stripped in continuity with the omentum if necessary.

Initially the omentum should be elevated to expose the transverse colon. The posterior leaf of the omentum is then divided, beginning to the left of the hepatic flexure. Gradual mobilization of this layer allows the transverse colon to be rolled in a caudal direction to expose the gastrocolic ligament. Care must be taken to avoid damage to the spleen when dissecting free the left lateral section of the omentum at the level of the splenic flexure. The vessels in the gastrocolic ligament can then be ligated with a series of clips (Figure 13).

Excision of liver nodules

Attempts at resection of large-volume disease are inappropriate as part of the tumor-reductive surgical process. However, in rare instances where the only remaining focus of macroscopic disease is the presence of small subcapsular liver deposits, resection may be performed. The deposits may be shelled out digitally after incising the liver capsule. Alternatively, they may be aspirated using a Cavitron ultrasonic aspirator (Cavitron Corporation, USA). Follo wing resection hemostasis may be achieved using diathermy with a roller-ball handpiece (Figure 14).

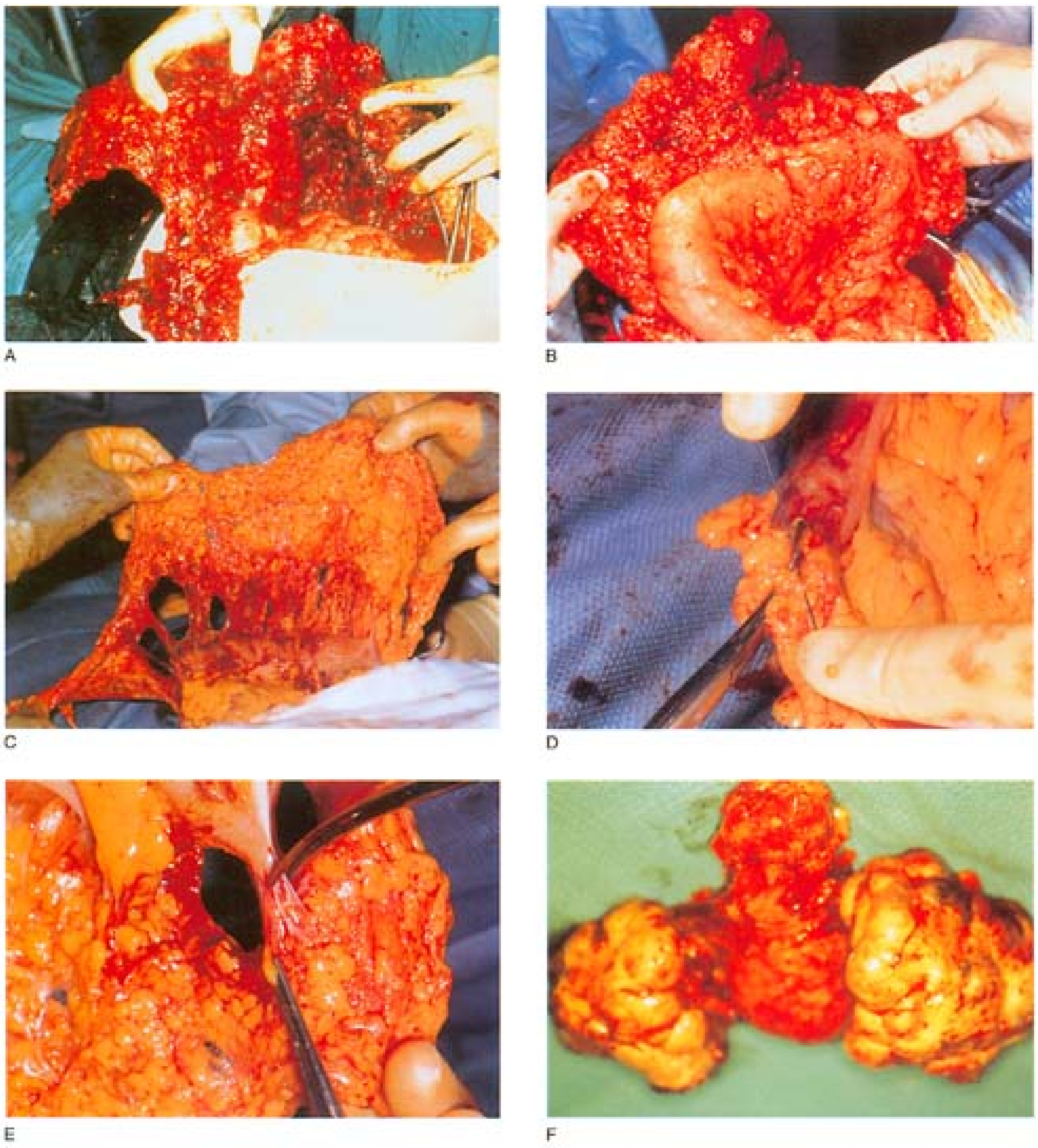


Figure 13

Omentectomy: (A) delivery of omentum with gross disease; (B) division of posterior leaf; (C) dissection of omentum; (D) ligature of vessels; (E) removal of omentum from bowel; (F) bilateral primary tumor

Figure 14

Excision of liver nodules

Surgery for apparent early-stage disease

At the time of initial laparotomy a proportion of women will have apparent early-stage disease. It is imperative that a meticulous surgical staging procedure is performed to allow counselling regarding prognosis, the place of adjuvant therapy and, where appropriate, fertility options. In women who have completed their family, a total or subtotal abdominal hysterectomy, bilateral salpingo-oophorectomy, together with omentectomy, para-aortic node sampling and peritoneal biopsies should be performed. More conservative surgery should only be considered in women desiring to maintain fertility options with stage IA disease and well-differentiated or borderline tumors; in these cases the uterus may be conserved and a simple oophorectomy with inspection and biopsy of the contralateral ovary performed (Figure 15). The remainder of the staging laparotomy should then be undertaken. Full counselling about risks, completion surgery after childbirth and the concept of cryopreservation of ova, embryos or ovarian tissue should be undertaken.

Interval debulking surgery

The concept of interval debulking has been assessed in two centers. Initially a Birmingham (UK) study failed to demonstrate a survival benefit (Lawton et al. 1990), but a later EORTC study, despite its critics, has suggested that interval debulking of tumor following three courses of initial chemotherapy did confer sur-

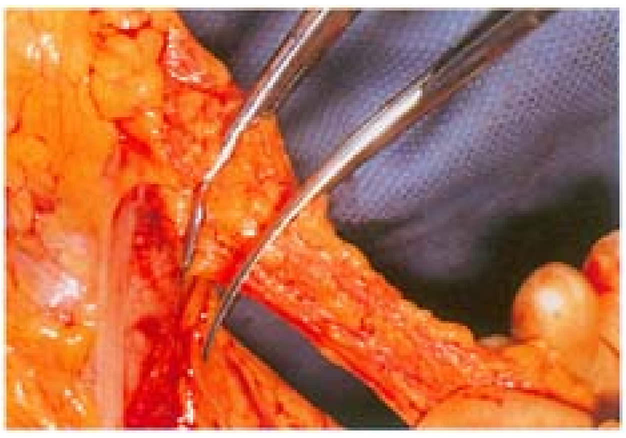


Figure 15

Oophorectomy

vival benefits of the order of 6 months if the patient underwent resection of visible disease (van der Burg et al. 1995). Further validation of this work is in progress, but it remains perhaps the first convincing evidence that interval surgery does have a significant role in management.

Second-look surgery

Second-look procedures, either laparoscopy or laparotomy following completion of chemotherapy, in order to test tumor response and establish the need for secondary debulking procedures, have not proved to be helpful in treatment decisions, nor in terms of patient benefit and improved survival. It is now broadly agreed that these should be only undertaken as part of defined research protocols.

Palliative and salvage surgery

Palliative procedures often have an important part to play in the management of the preterminal stages of this disease and are usually concerned with relieving the effects of intestinal obstruction. The most common of these procedures is the bypass of obstructive loops of small bowel, in which circumstance an ileocolic bypass anastomosis is to be favored over heroic attempts at mass resection (see Chapter 20). The use of such palliative and salvage surgery can provide a great degree of symptomatic relief for patients with bowel obstruction, but it is to be stressed that fine judgment needs to be exercised to ensure that the patient will benefit in her final weeks from such a surgical approach rather than merely have her discomfort increased by the pain of a laparotomy.

Germ cell and stromal tumors of the ovary

Germ cell and stromal tumors occur predominantly in younger women and adolescents. Preoperative diagnosis of these tumors may be facilitated by the use of tumor markers, and conservative surgery should be considered in all cases where fertility preservation is desired. Unilateral adnexectomy with biopsy of the contralateral ovary is sufficient as the pelvic surgical component in the majority of young women since the advent of successful adjuvant chemotherapy (Gershenson, 1988).

References

Bonney V (1912) The female genital tract. In: Choice CC, editor. *A system of surgery*, vol. 2. New York: Funk & Wagnalls.

Brunschwig A (1961) Attempted palliation by radical surgery for pelvic and abdominal carcinomatosis primary in the ovaries. *Cancer* **14**:384–8.

Fawzi HW, Robertshaw JK, Bolger BS, et al. (1997) Role of appendicectomy in the surgical management of ovarian cancer. *Eur J Gynaec Oncol* **18**:34–5.

Gershenson DM (1988) Menstrual and reproductive function after treatment with combination chemotherapy for malignant ovarian germ cell tumours. *J Clin Oncol* **6**:270–5.

Griffiths CT (1975) Surgical resection of tumour bulk in the primary treatment of ovarian carcinoma. Symposium on ovarian cancer. *Nat Cancer Inst Monog* **42**:101–4.

Hudson CN (1968) A radical operation for fixed ovarian tumours. *J Obst Gynaec Br Cwlth* **75**:1155–60.

Jacobs I, Oram D, Fairbanks J, et al. (1990) A risk of malignancy index incorporating CA125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer *Br J Obstet Gynecol* **97**:922–9.

Lawton F, Luesley D, Redman C, et al. (1990) Feasibility and outcome of complete tumor resection in patients with advanced ovarian cancer. *J Surg Oncol* **45**:14–19.

McGowan L, Lesher LP, Norris HJ, Barnett M (1985) Misstaging of ovarian cancer. *Obstet Gynec* **65**:568–72.

Meigs JV (1934) *Tumours of the female pelvic organs.* New York: Macmillan.

Munnell EW (1952) Ovarian carcinoma. Predisposing factors, diagnosis and management. *Cancer* **5**:1128–33.

Piver MS, Barlow JJ (1976) Preoperative and intraoperative evaluation in ovarian malignancy. *Obstet Gynec* **48**:312–15.

van der Burg ME, van Lent M, Buyse M, et al. (1995) The effect of debulking surgery after induction chemotherapy on the prognosis in advanced epithelial ovarian cancer. *N Engl J Med* **332**:629–34.

Young RC, Decker DG, Wharton JT, et al. (1983) Staging laparotomy in early ovarian cancer. *JAMA* **250**:3072–6.

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17
Radical vulvar surgery

John M Monagh:

Introduction

When Basset published his monograph on the surgical treatment of cancer of the clitoris in 1912 he outlined the major criteria for the operative management of cancer of the vulva which was utilized worldwide for most of the 20th century. Basset outlined the importance of the metastases to the groin and the equal importance of removing the lymphatic ray connecting the primary tumor on the vulva with the primary lymph node drainage site in the groin. It is important to remember that although Basset outlined these surgical maneuvers, all his work was performed on cadavers and the procedure was rarely used in live subjects.

In the 1920s, Victor Bonney, continued the tradition of radical vulvectomy and groin node dissection in British patients. However, it was Stoekel, working initially in Munich, and later in Berlin, who demonstrated the need for individualization of surgical treatment. Stoekel, in his seminal monograph of 1930, outlined every known variant of surgical treatment, many of which have later been ‘rediscovered’ by other experts around the world. Closer to home, Stanley Way, working in Gateshead in the 1940s, re-confirmed the importance of the lymphatic ray and the drainage of the vulva, and suggested that a wide local excision of the lesion on the vulva should be combined with an extensive dissection of the skin of the suprapubic area and the groin. Unfortunately, although the cure rates for cancer of the vulva improved markedly when radical treatment was adopted, the adverse effects of such massive surgery were that patients spent a considerable time in hospital and were left with large wounds requiring intensive nursing care. Interestingly, the long-term result of these large wounds was frequently a remarkably satisfactory cosmetic effect.

As a consequence of the realization that not all patients required such radical surgery; in the latter part of the 20th century, moves towards individualization of care, first outlined by Stoekel in 1930, were resurrected. It is now common practice to accurately stage the cancer of the vulva with careful measurement, both clinical and pathological, and based on these measurements, to determine exactly the most appropriate surgical procedure to achieve high cure rates with minimal adverse cosmetic effect.

Anatomic considerations

Blood supply

The blood supply to the vulva is derived from the internal pudendal artery, a terminal branch of the anterior division of the hypogastric artery (internal iliac artery). A contribution from the superficial and deep external pudendal artery originating from the femoral artery is of variable amount. The internal pudendal artery continues as the posterior labial vessels that supply the posterior part of the labia majora, labia minora and the vestibule. The anterior labial branches of the external pudendal vessels and the small arteries of the ligamentum teres, a branch of the inferior epigastric, may also contribute to the blood supply.

Nerve supply

The nerve supply of the vulva is derived from a variety of sources. The mons pubis and upper labia majora are innervated by the ilioinguinal nerve and the genital branch of the genitofemoral nerve. The superficial perineal branches of the pudendal nerve supply the labia majora and the structures of the external genitalia. The deep branches supply the clitoris, vestibular bulb and muscles of the region.

Lymphatic drainage

Most carcinomas of the vulva affect the labia majora and minora. The second commonest site is the clitoris. All these skin areas have a lymphatic drainage which passes in a narrow ray through the groin into the superficial inguinal lymph nodes and then through the cribriform fascia into the femoral nodes, which are in close proximity to the femoral artery and vein immediately below the fossa ovale. Whilst the superficial groin nodes are disparate and variable in their position, the femoral nodes are more constant, lying in close proximity to the vessels. The drainage from the femoral nodes then passes cranially through the inguinal ligament to enter the lymphatics of the external iliac system.

Alternative routes of lymph drainage

In the past, there was concern that lymphatic drainage may occur directly through the perineal membrane into the external iliac lymphatic system, but this has been disproved in a variety of studies. However, it will be noted that retrograde spread may sometimes occur down into the nodes alongside the saphenous vein when the nodes of the femoral group are heavily involved with tumor.

Indications

Over many years it has been demonstrated that for virtually all patients with truly invasive cancer of the vulva it is mandatory not only to perform a wide local excision of the tumor on the vulva, but also to remove the groin nodes. This broad instruction initially generated by Basset in 1912 has been modified and made more sophisticated due to an understanding of the metastatic spread patterns depending on the depth of invasion of the tumor. Careful measurement of tumor invasive depths has demonstrated that where the tumor invades for less than 1 mm, that is, stage IA, then the risk of nodal metastases is zero. In these circumstances a wide local excision of the lesion on the vulva is all that is required. For any depth of invasion beyond 1 mm the risk of nodal metastases rises markedly and it is vital that all patients should be subjected to groin node dissection.

Initially, this instruction was interpreted as requiring a radical excision of the lesion on the vulva in continuity with the lymphatic ray and the groin node dissection itself. Stoekel, in 1930, and other authors since, have demonstrated that because of the initial pattern of metastatic spread, that is, embolization rather than permeation of lymphatic vessels, it is possible to leave behind the skin bridge between the groin and the vulva, and by carrying out separate groin dissections the patient can safely and confidently be cured of her condition (Grimshaw et al. 1980). For all small tumors, where there is no clinical involvement of the groin nodes, the use of separate groin incisions is now the preferred method of management.

It has also been shown where a tumor is placed laterally on the vulva, that is, that the tumor does not impinge on a line drawn below the clitoris, or behind a line drawn through the fourchette, then the patient need only be subjected to a unilateral (ipsilateral) groin node dissection. The risk of contralateral groin node spread is vanishingly small.

Roleofthe ‘enbloc’ dissection

It is the author’s belief that when groin nodes are obviously grossly involved that a full radical vulvectomy with an en bloc dissection of the groin nodes is the optimal management. The reason for this is that once nodes are filled with metastatic tumor there will be stasis in the lymphatic ray and a high risk of leaving active tumor behind if separate incisions are used.

Pelvic node dissection

In the past, the pelvic nodes were also routinely dissected, but these should only be dissected and/or included in a treatment field, when there is gross involvement of the groin nodes and where there is clear evidence of tumor continuity through the femoral canal into the external iliac system.

Identification of lymphatic spread and nodal involvement

The techniques available for identification of involved groin nodes have been many and various. It has been known for many years that palpation is of very limited value and modern imaging techniques, including computed tomography (CT), nuclear magnetic resonance (NMR) imaging, ultrasound and lymphangiography, have all demonstrated variable results. In 1979, Philip Disaia et al. described the use of a 'sentinel node' technique for determining metastatic spread to the groin nodes. The concept was perfect but the difficulties in identifying the true sentinel node made its use uncertain. More recently, Levenback and colleagues (Levenback et al. 2001), have demonstrated that by injecting a vital blue dye into the leading edge of the tumor it is possible to pick up blue nodes in the groin, which can be regarded as the sentinel nodes for the remainder of the groin lymphatics. Although this blue dye technique confirmed the presence of a sentinel node or nodes, it was not of the quality required for its general use as guidance as to whether the groin nodes should be dissected or not. In a number of centers following its use in breast cancer, sentinel node identification using a radiolabeled material (technetium) has been elevated to the point at which one can confidently utilize the sentinel node technetium technique in order to determine the involvement or otherwise of the groin nodes (De Cicco et al. 2000). If the sentinel node is negative when removed, then the clinicians may be able to dispense with a formal groin node dissection, thus markedly reducing the morbidity for the patient. If the groin node shows involvement then a formal dissection of the groin is mandatory.

Surgical procedure

Patient preparation

All patients should be admitted one to two days prior to surgery. Blood is typed and cross-matched and consent obtained. It is important that the patient understands fully all real and potential complications of the surgery as wound breakdown continues to occur in spite of many modifications, and that some femoral nerve bundles may be resected during the groin dissection leaving anesthesia and paresthesia over areas of the anterior thigh.

Thromboembolic prophylaxis

The average age of patients developing vulval cancer is in the late seventh decade and the risk of developing thromboembolic disease is high. It is important to initiate thromboembolic prophylaxis shortly before surgery and to maintain it using a variety of methods until the patient is fully ambulant. The use of subcutaneous heparin, anti-thromboembolic stockings, and intraoperative muscle pumps are all of great value (see Chapter 1). Early mobilization following surgery, however, remains the cornerstone of efforts to reduce thromboembolic risks.

The patient is placed in the supine position on the operating table with the ankles separated by approximately 20 cm. This allows the groin folds to be opened and gives easy access for the groin dissection.

Skin incision

For the vast majority of patients separate groin node dissections will be performed. The incision should run from approximately 4 cm medial to the anterior superior iliac spine down to a point some 4 cm below the pubic tubercle. Although it is common for surgeons to use a single incision the author has found that by performing a double incision, leaving a skin strip approximately 1 cm wide along the length of this incision, will allow easier manipulation of the block of lymph nodes which will be dissected below this incision. The incision is carried down in a manner which allows a triangular block of tissue to be removed down to the superficial fascia. When outlining the incision it is important to utilize bony landmarks and to ignore natural skin folds, which may be very variable, particularly in obese patients. Figure 1 shows the incisions to the groin and vulva.

Defining the fascial planes in the groin incisions

The thin strip of skin in the groin is picked up using tissue forceps so that the whole block of tissue in the groin can be maneuvered during the dissection. Gentle tension is put on the upper edge of the skin incision with the left hand and the surgeon incises in a slightly angular fashion upwards, down to the level of the aponeurosis of the external oblique muscle above the groin. In a similar fashion, the fascia over the sartorious muscle that forms the lateral boundary of the femoral triangle can now be identified in a similar manner. The

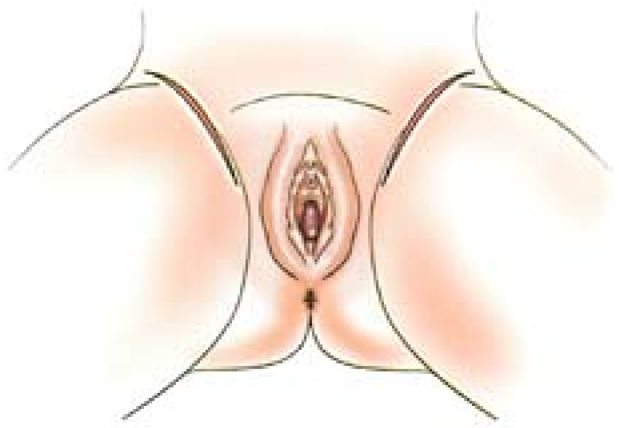

Figure 1

The incision used in the ‘triple incision’ technique

fascia over the sartorious muscle is incised longitudinally from just below the anterior superior iliac spine to the lower apex of the femoral triangle (Figure 2). Small vessels in the fat and on the muscle surface may be cut and should be meticulously identified and tied or diathermied.

Division of the saphenous vein

In the lower part of the femoral triangle the saphenous vein may be identified as it curves inferiorly It can be easily isolated where it lies above the fascia lata and is then divided and ligated at the apex of the lower part of the dissection.
Some surgeons preserve the saphenous vein, dissecting it out and cleaning it in its superficial passage, and then identifying it as it drops through the fossa ovale. The author does not believe that cutting the saphenous vein significantly increases the risk of lymphedema.

Developing the deep dissection

The medial edge of the incised fascia over the sartorious muscle is now picked up using two small Spencer Wells clips (Figure 3). Strands of the femoral nerve can now be seen in the soft tissue at the medial side of the sartorious muscle and should be preserved wherever possible. On the medial side of the sartorious muscle the femoral artery will be identified and should be cleaned from the lower part of the femoral triangle cranially to the inguinal ligament. This meticulous cleaning will then reveal the femoral vein lying on the

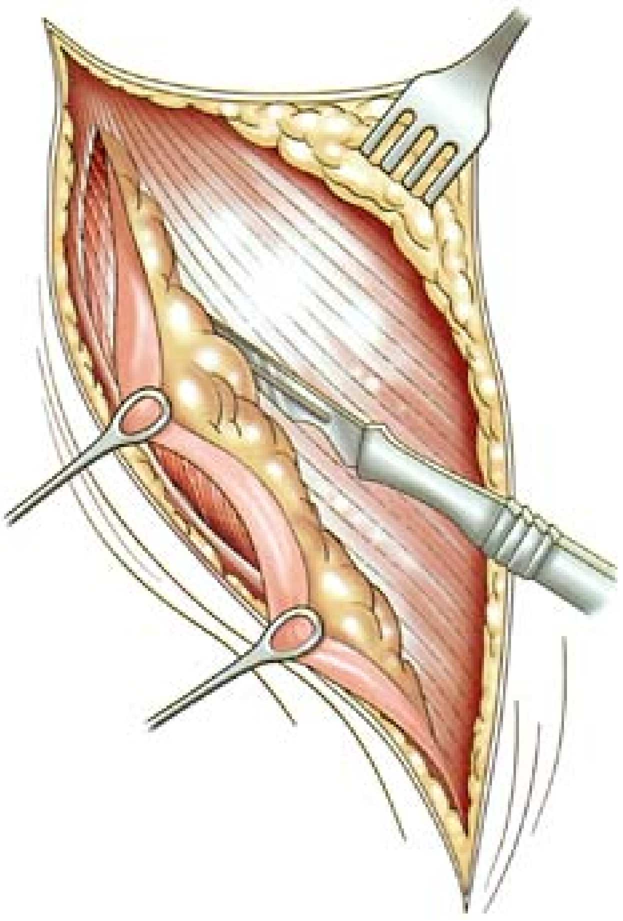

Figure 2

Incising the fat and fascia down to the external oblique apneurosis and the sartorious muscle

medial side of the femoral artery. The saphenous vein will now be noted to be passing from the superficial lymph node area through the fossa ovale into the femoral vein, roughly at its midpoint in the exposed femoral triangle. The saphenous vein should be clamped close to its entry into the femoral vein as shown in Figure 4. With the surgeon’s left hand raising the block of tissue containing the superficial lymph nodes, the femoral vein can be seen lying on the medial side of the femoral artery with the divided saphenous vein passing through the fossa ovale, which is now turned over to reveal its underside. Meticulous cleaning of all tissue around the femoral artery and vein will remove all the femoral lymph nodes. This cleansing should be carried out up to the inguinal ligament and occasionally the node of Cloquet or Rosenmuller will be identified as it fills the femoral canal. In normal circumstances this will be the upper limit of the nodal dissection.

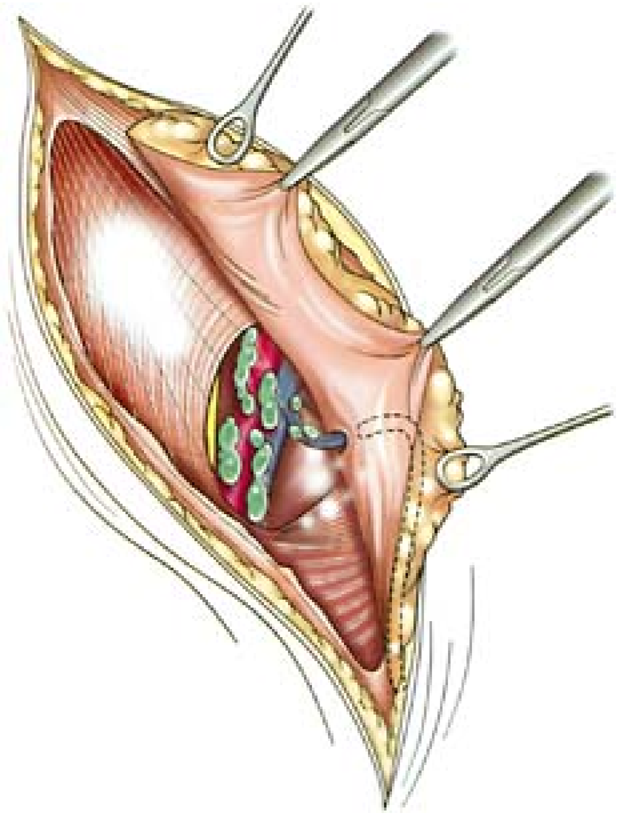

Figure 3

The medial edge of the sartorius fascia is elevated by forceps

Cleaning the adductor muscles

The block of tissue elevated by the surgeon containing all superficial and femoral nodes can now be put on tension by drawing it medially, and the surgeon continues a dissection under the fascia covering the adductor muscles on the medial side of the femoral vein. This dissection will continue through to the outer part of the adductor muscles over a distance of approximately 5–6 cm. Small veins that enter the muscles may require ligating at this point but most of the tissue plane is avascular. The dissection is completed by cutting through small amounts of fat on the medial side of the elevated block of tissue, and the comprehensive dissection of the groin nodes has been achieved (Figure 5).

The completely cleansed femoral triangle will now be lying open. The two skin edges will lie together very closely without any tension. It is important first of all to put in place a small suction drain. The author finds it valuable to utilize a continuous fat stitch, drawing together the subcutaneous fat, and thereafter the skin incisions can be easily stapled in a linear fashion.

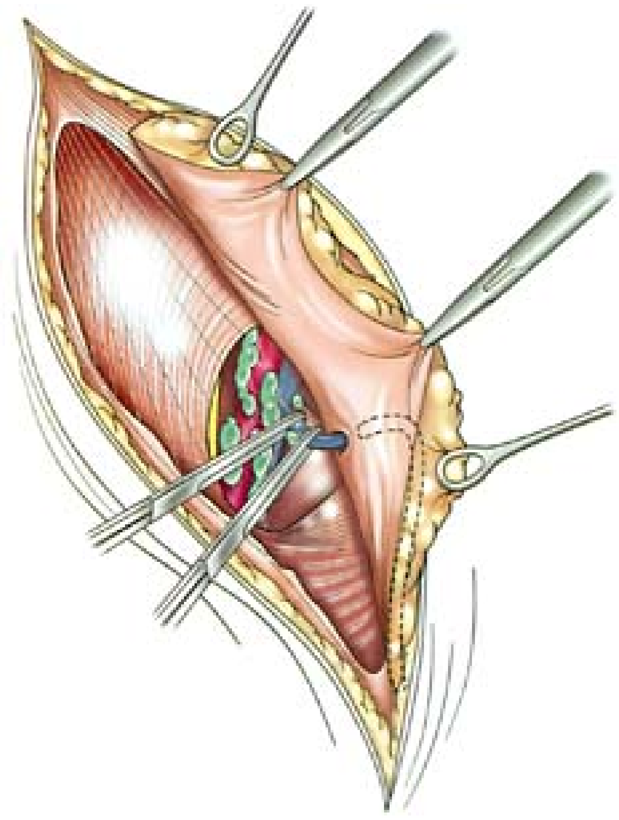

Figure 4

The saphenous vein is identifiable as it passes through the fossa ovale from the superficial compartment

The fat stitch assists in making the sutured incision airtight. Once the suction drain is activated, the skin will depress into the defect generated by removal of the groin nodal mass. This suction should be maintained for some days until drainage reduces markedly or ceases altogether.

The vulval incision

The most important element in performing radical vulvectomy is to be certain of performing a wide excision of the tumor. The margin generally recommended is 2 cm, and it is important to remember that this 2 cm margin must not only occur laterally and medially, but also deeply, so that the dissection should be carried down to the superficial fascia below the fat layers.

Where the tumor lies close to the urethra or anus it may not always be possible to gain the full 2 cm margin, but it is important to remember that the terminal urethra can be sacrificed and extension of the incision closer to the anus will be achievable without

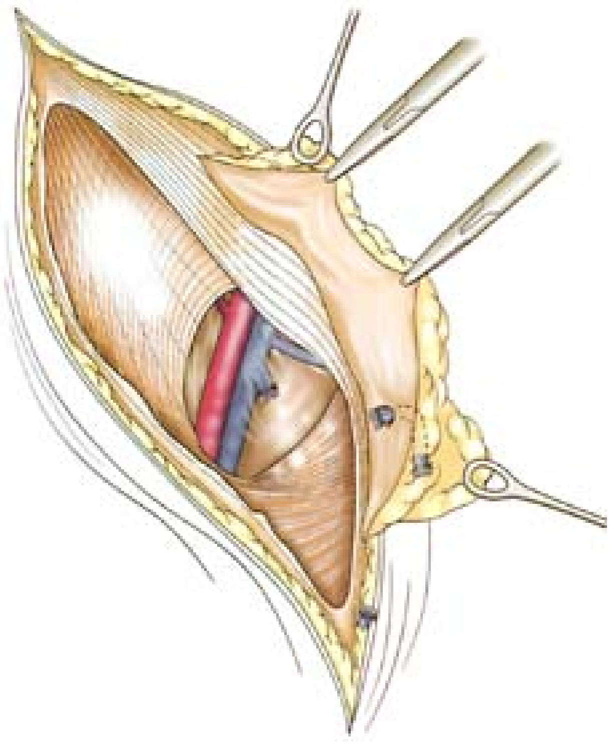

Figure 5

The superfical groin nodes are removed en bloc and the final cleansing of the femoral vessels can be achieved

compromising continence. Figure 6 shows the incisions which can be utilized in a small tumor with extensive skin change affecting most of the vulva. The use of posterior releasing incisions may only be necessary where the tumor is very large and apposition of the skin is not so easily achieved at the end of the dissection.
The author would recommend that the incision begins anteriorly some 2 cm above the clitoris, passing in an elliptical fashion, providing the 2 cm margin around the tumor, and also performed in a similar fashion on the opposite side in order to produce a symmetrical result. In those circumstances where the tumor is small and laterally placed it may be possible to perform a hemivulvectomy and ipsilateral groin node dissection achieving a high chance of cure with an excellent cosmetic result.
However, the preservation of vulval skin on the opposite side may increase the risk of new tumor occurring in the future.
During radical vulvectomy surgery, significant vessels will be identified around the clitoral base, and posteriorly the deep labial branches of the internal pudendal artery. These three sites are the major sources of bleeding. It may be necessary to utilize square mattress sutures in dealing with the bleeding

Figure 6

The vulva incision to be used when there is a small tumor and the removal of associated skin changes is required, such as VIN

around the clitoral base, but the pudendal vessels can normally be dealt with by simple clipping and tying. Diathermy and tying of small vessels below the skin in other parts of the vulva should be meticulous achieving a high level of hemostasis.
Primary closure of the vulval wound is easily achieved utilizing a series of interrupted sutures. The vertical mattress suture is particularly helpful where the tissues are deep due to excessive fat.
It may be necessary in a small number of patients to perform an en bloc dissection and this will result in removal of the skin in the skin bridge between the groin and the vulva. This is best achieved using a variation of the skin incision shown above, sometimes described as the ‘butterfly incision’ (Figure 7).
This incision will give a comprehensive dissection of the lymphatic ray and resulting in an en bloc dissection of the groin and vulval lesion.

Pelvic node dissection

As noted above, the indications for removing the pelvic nodes are rare. In order to achieve a margin when the groin nodes are involved it may be necessary to dissect the pelvic nodes, although in many practices radiotherapy is utilized as an adjuvant treatment to extend the field of management.
If the pelvic nodes are to be dissected they are best approached following the completion of the groin phase. The incision to access the pelvic nodes is made some 2 cm above the inguinal ligament (Figure 8) in a line along the external oblique aponeurosis. A second incision is now made deep to this along the line of the

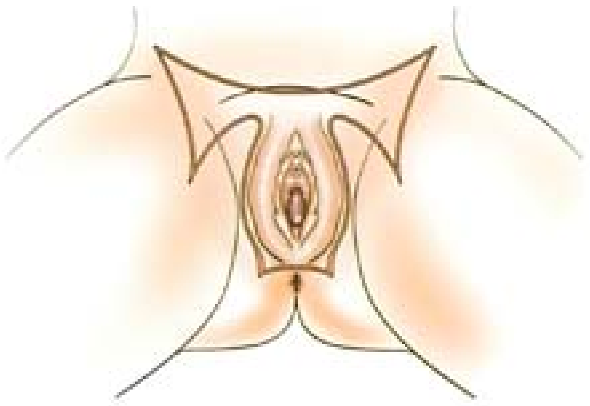

Figure 7

Skin incisions for the ‘butterfly incision’

internal oblique muscle fibers, roughly at right angles to the first incision.The second incision is taken down through transversalis muscle to the peritoneum. The peritoneum is kept intact, and using the fingers, it is gently swept medially revealing the brim of the pelvis and the external iliac vessels.
Using appropriate retraction the entire external iliac, obturator and internal iliac nodes to the common iliac can be dissected.
It is sometimes prudent to split the inguinal ligament to improve access but care to identify and sometimes ligate the inferior epigastric artery is necessary at this time.
The wounds in the muscles are repaired in reverse order to achieve a strong closure with minimal risk of hernia development.

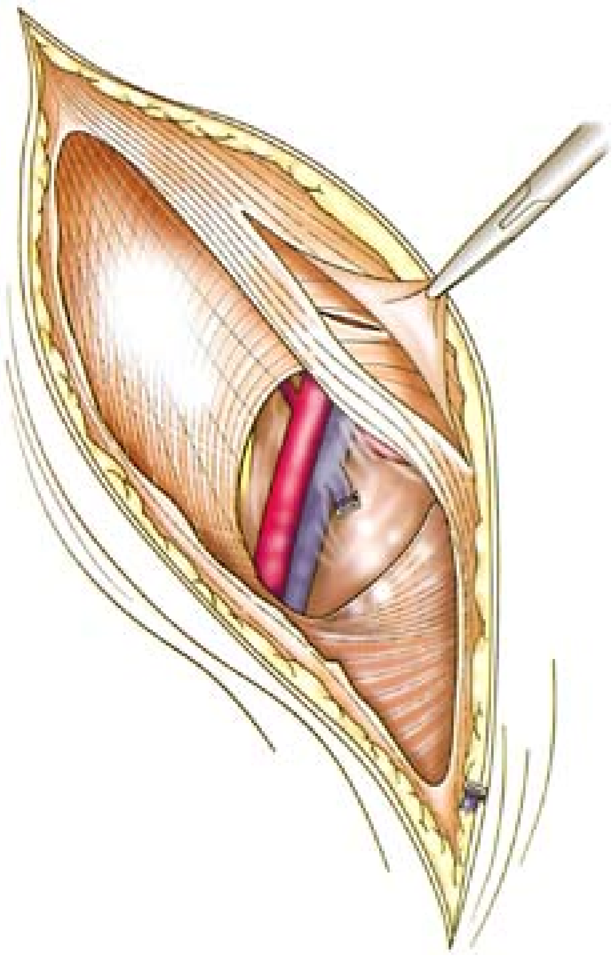

Figure 8

The external oblique aponeurosis is incised superolaterally

References

Basset A (1912) Traitement chirurgical operatoire de l’epithelioma primitif du clitoris. *Rev Chir (Paris)* **46**:546.
Bonney V (1920) Operations on the vulva. In: Berkeley C Bonney V, eds. *A textbook of gynaecological surgery*. London: Cassell: 122.
De Cicco C, Sideri M, Bartolomei M, et al. (2000) Sentinel node biopsy in early vulvar cancer. *Br J Cancer* **82** (2):295–9.
Disaia PJ, Creasman WT, Rich WM (1979) An alternate approach to early cancer of the vulva. *Am J Obstet Gynecol* **133**:825–30.
Grimshaw RN, Murdoch JB, Monaghan JM (1993) Radical vulvectomy and bilateral inguinal-femoral lymphadenectomy through separate incisions—experience with 100 cases. *Int J Gynec Cancer* **3**:18–23.
Levenbach C, Coleman RL, Burke TW, et al. (2001) Intraoperative lymphatic mapping and sentinel node identification with blue dye in patients with vulvar cancer. *Gynecol Oncol* **83**(2):276–81.
Monaghan JM, Hammond IG (1984) Pelvic node dissection in the treatment of vulval carcinoma—is it necessary? *Br J Obstet Gynaecol* **91**:270–4.
Stoeckel W (1930) Zur Therapie des Vulvakarzinoms. *Zentralblatt für Gynakologie* **1**:47–71.
Way S (1948) The anatomy of the lymphatic drainage of the vulva, and its influence on the radical operation for carcinoma. *Ann R Coll Surg Engl* **3**:187.

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18
Laparoscopy

Farr Nezhat
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Introduction

This chapter describes the procedures of appendectomy, hysterectomy (both standard and radical), omentectomy, palliative end colostomy and lymphadenectomy (encompassing both para-aortic and pelvic lymph nodes). Whole textbooks have been devoted to laparoscopic surgery but in line with the 'cookbook' approach of this volume, we believe these procedures are more than adequately described in the following text.

Appendectomy

Since the first use of laparoscopy for appendectomy by Kurt Semms in Germany and Nezhat and others in the USA in the 1980s and early 1990s, this procedure has become widely accepted.
Two different techniques have been utilized for laparoscopic appendectomy: one uses sutures or bipolar electrodesiccation for severing the appendiceal blood vessels; the other uses a linear stapling device across the mesoappendix and appendix simultaneously.

Indications

Appendectomy is frequently performed incidentally in association with other pelvic surgical procedures, or whenever pathological changes are identified as in patients with infection, endometriosis or benign or malignant tumor. In certain ovarian cancers, such as mucinous cystadenocarcinoma, the appendix may be removed as part of the staging procedure.

Anatomic considerations

The appendix is an elongated vestigial diverticulum of the cecum which is richly endowed with lymphoid tissue. It is normally 7–10 cm in length but lengths up to 30 cm have been recorded. It receives blood supply from the appendicular artery, which is a branch of the lower division of the ileocecal artery. An accessory appendicular artery may be present in almost 50% of patients. The major vessels enter the mesoappendix a short distance from the base of the appendix. The location of the appendix is variable; up to 70% will be retrocecal and the remainder present primarily in front of the large bowel. Although it is usually found in the right iliac fossa, in maldescent of the cecum or advanced pregnancy the appendix may be seated in the right hypochondrium. In rare conditions, such as situs inversus, the appendix is in the left iliac fossa.

Surgical procedure

1. *Trocar and cannula placement:* the primary trocar is placed intraumbilically for introduction of the video laparoscope. Two 5 mm secondary

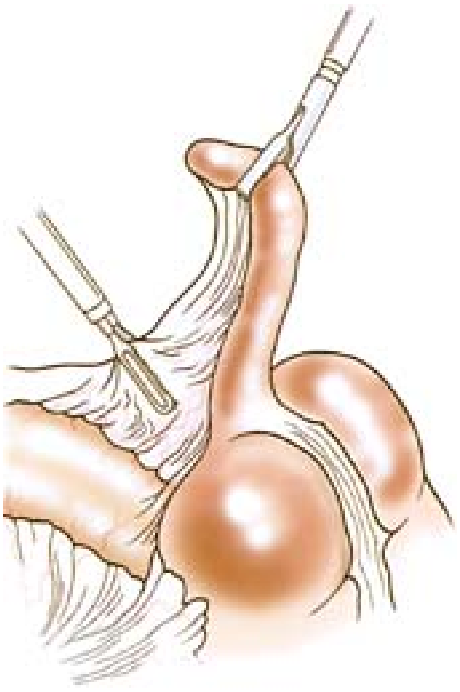

Figure 1

Bipolar electrodesiccation is applied to the base of the mesoappendix

punctures are made lateral to the inferior epigastric vessels, one on the right and one on the left at the level of the iliac crest, and a 10 mm (or 12 mm if a linear stapling device is being used) puncture is made suprapubically 5 cm above the symphysis pubis.

2. After thorough evaluation of the abdominopelvic cavity any periappendiceal adhesions or attachments are lysed and the appendix is mobilized.
3. While the appendix is being elevated and put on traction, bipolar electrodesiccation is applied to the base of the mesoappendix for hemostasis of the appendiceal vessels (Figure 1). After adequate desiccation, the mesoappendix is cut using sharp or electrosurgical scissors until the base of the appendix is reached. Caution should be exercised to avoid thermal injury to the cecum or the ileum.
4. Next, the base of the appendix is ligated by applying two polydioxal or chromic Endoloop sutures (Ethicon Endosurgery, Somerville, NJ, USA). The third Endoloop suture is applied 5 mm distal to the first two sutures. The appendix is cut between the two sets of sutures (Figure 2).

Alternatively, suturing is used for ligation of the appendiceal artery. An opening is made in the mesentery near the base of the appendix and a lig

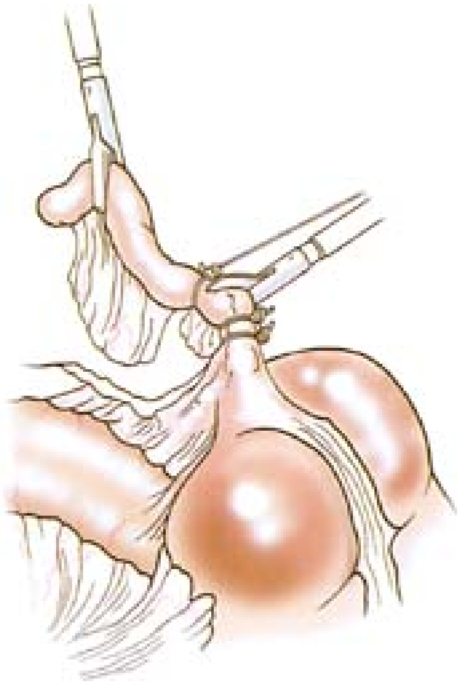

Figure 2

The appendix is cut between the sutures

ature of polyglactin is introduced into the opening. One ligature is tied around the base of the mesosalpinx and another is tied on the base of the appendix. Similar sutures are placed on the specimen side, and the appendix and mesoappendix are subsequently cut using sharp scissors (Figures 3 and 4).

A linear stapling device can be directly applied across the mesoappendix and the appendix, speeding up the procedure (Figure 5).

5. After removal of the appendix, the abdominoperitoneal cavity is thoroughly irrigated. The appendix is removed through the 10 mm or 12 mm suprapubic trocar sleeve using Babcock forceps or by putting the appendix in a laparoscopic bag.

Hysterectomy

Hysterectomy is one of the most frequently performed major surgical procedures in women. Approximately two thirds of hysterectomies are performed abdominally and one third vaginally. The purpose of laparoscopic surgery for hysterectomy is to avoid the adverse effects of laparotomy, maintain the principles

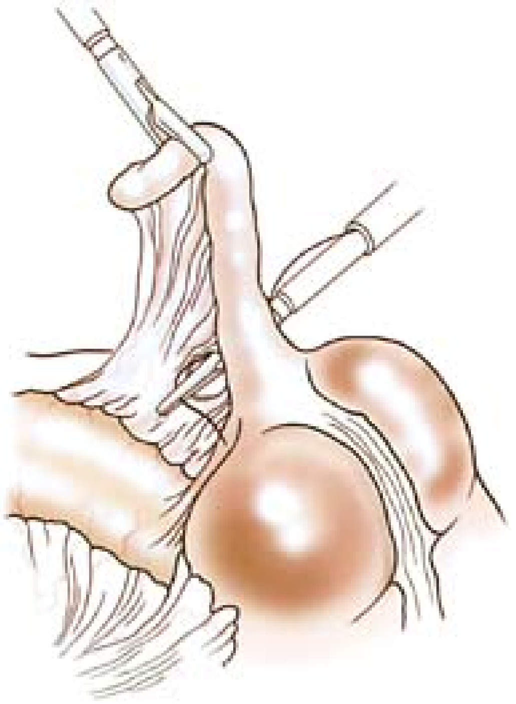

Figure 3

Ligatures are tied around the base of the appendix

Figure 4

The appendix and mesoappendix are cut

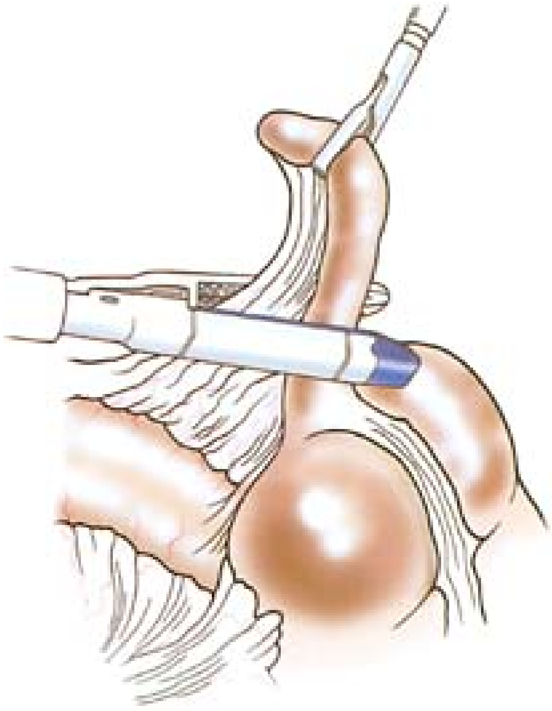

Figure 5

Linear stapling device

of oncologic surgery, and offer the advantages of a vaginal approach. Since its introduction in the late 1980s, numerous variants have been developed, described by terms such as 'laparoscopically assisted vaginal hysterectomy', 'laparoscopic hysterectomy' or 'total laparoscopic hysterectomy'. While there may be technical differences and different skill requirements between the various laparoscopic procedures, there is no significant difference in postoperative pain, recovery, complications or cost. In this chapter total simple laparoscopic hysterectomy and radical hysterectomy are described.

Indications

In gynecologic oncology, hysterectomy has been performed either as part of the treatment and staging of endometrial, ovarian or fallopian tube carcinoma, in the form of intra- or extrafascial hysterectomy, or as radical hysterectomy for treatment of cervical and occasionally vaginal cancer.

Anatomic considerations

The blood supply of the uterus is from the uterine artery, which anastomoses with the ovarian and vaginal arteries. The nerve supply is from the urogenital plexus.

Surgical procedure

1. *Trocar placement:* as well as the primary intraumbilical trocar sleeve which is used for introduction of the video laparoscope, three other low abdominal trocar sleeves are introduced for the passage of the ancillary instruments. For hemostasis, bipolar electrodesiccation or linear stapling devices are currently favored; suturing or the ultrasonic harmonic scalpel may also be used. For cutting, sharp or electrosurgical scissors or lasers are commonly used.
2. After the anatomy of the pelvis is evaluated and any associated procedures (such as treatment of pelvic adhesions or endometriosis, or peritoneal biopsy) are performed, hysterectomy and salpingooophorectomy proceed as follows. If oophorectomy is planned, first the infundibulopelvic ligament blood supply is severed using bipolar electrodesiccation or a stapling device. The direc-

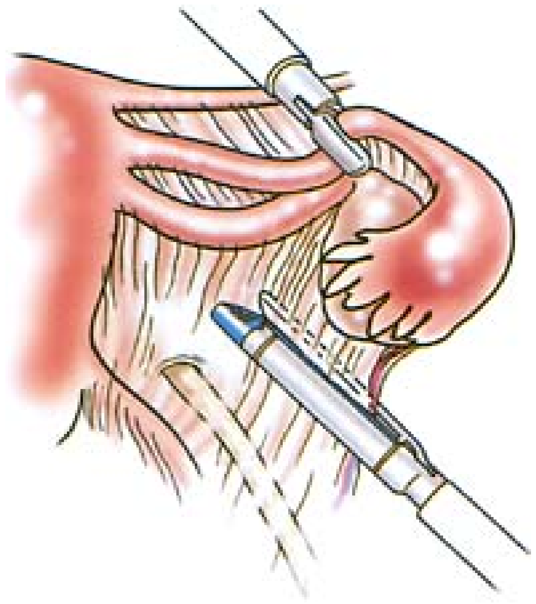

Figure 6

Bipolar forceps are applied to the infundibulopelvic ligaments

tion of the ureter crossing the pelvic brim over the bifurcation of the common iliac artery should be identified. In these patients the ureter can often be visualized, observed for peristalsis and avoided without mobilization. In obese patients, specific dissection may be required to identify and thus avoid injury to the ureter. Retroperitoneal or intraperitoneal ureteral dissection should be performed when there are severe adhesions or tumor involvement between the ovary and the pelvic side-wall. The adnexa should be grasped with the forceps and retracted medially and caudally to stretch and outline the infundibulopelvic ligaments before application of the bipolar forceps or linear stapling device (Figure 6).
3. The round ligament is transected (Figure 7) or electrodesiccated approximately 4–5 cm lateral to the uterus, and the anterior leaf of the broad ligament is dissected using blunt, sharp or hydrodissection. The bladder is separated from the lower uterine segment and cervix (Figures 8 and 9). These steps are accomplished bilaterally.
4. While the assistant retracts the uterus to one side using an intrauterine manipulator, the uterine blood supply is skeletonized and severed, using

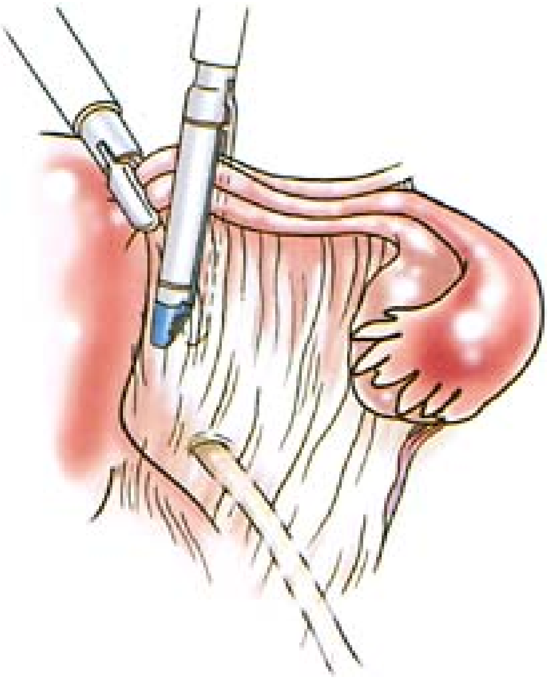

Figure 7

A stapler is used to transect the round ligament, ovarian ligament and fallopian tube

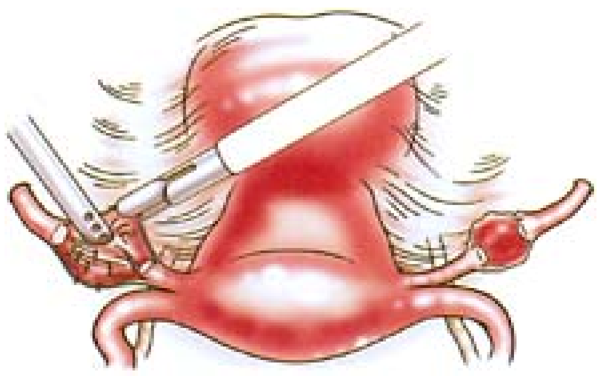

Figure 8

The anterior leaf of the broad ligament is dissected

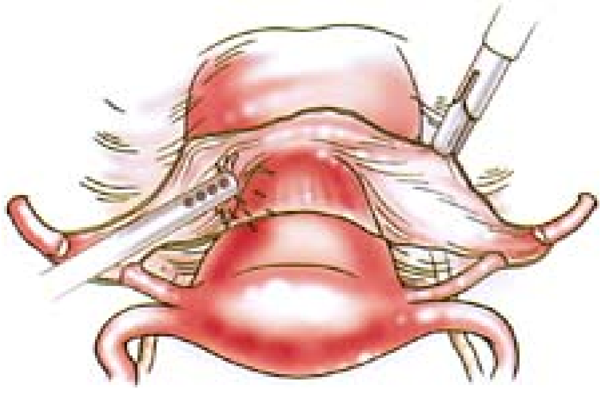

Figure 9

Hydrodessication of the bladder

bipolar electrodesiccation or a linear stapling device (Figure 10).

5. The direction of the ureters should be further identified and dissected laterally, especially for an extrafascial hysterectomy. The bladder is dissected away completely from the cervix and slightly from the upper vagina. The cardinal and uterosacral ligaments are electrodesiccated and cut or stapled (Figure 11). For anterior and posterior culdotomy, a folded 10 cm×10 cm gauze in a sponge forceps, or the tip of a right-angled retractor placed in the vagina, can be used to mark the anterior or posterior vagina cuff (Figure 12). The vaginal wall is thus clearly demonstrated, allowing horizontal transection with the cutting instrument. The uterus should be positioned anteriorly for a posterior cul-

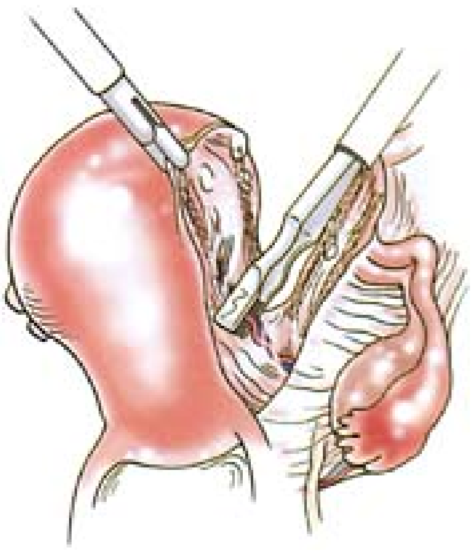

Figure 10

Uterine vessel dessication

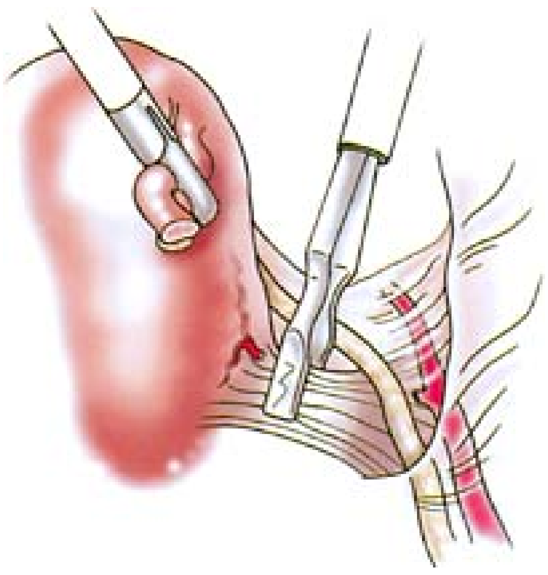

Figure 11

The cardinal and uterosacral ligaments are electrodessicated

dotomy and posteriorly for anterior culdotomy (Figures 13 and 14). The remaining attachment of the uterus laterally is circumferentially dissected and after the uterus is completely freed it is removed vaginally by introducing a tenaculum through the vaginal vault to grasp the cervix, or to pull the uterus out with the previously attached elevator (Figure 15).

Figure 12

Marking the posterior vaginal cuff and performing posterior culdotomy

Figure 13

Anterior culdotomy. Anterior vagina is distended by placing sponge forceps attached to a10×10 cm gauze transvaginally

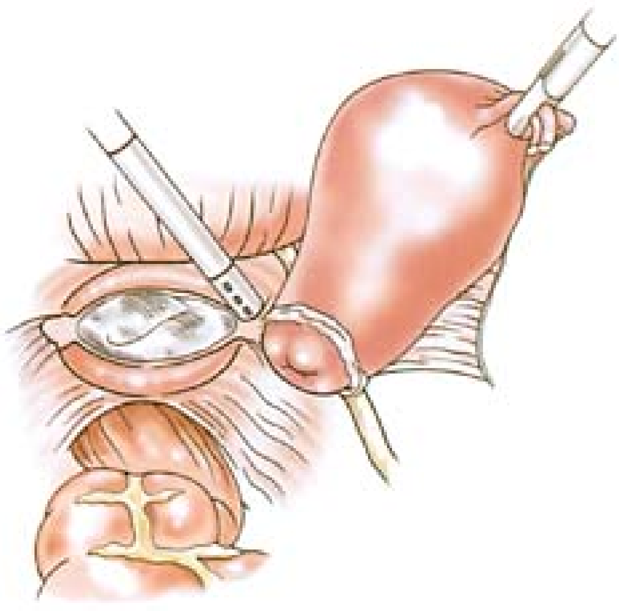

Figure 14

Detachment of uterus from vaginal cuff

6. Vaginal vault closure and support: the vaginal vault can be closed either laparoscopically or transvaginally. In a larparoscopic approach to prevent loss of pneumoperitoneum, either the uterus or a partially inflated surgical glove containing a folded gauze is left in the vagina. The uterosacral ligament is elevated with a grasping forceps and sutured to the vaginal angle on each side; the knot tying may be extra- or intracorporeal. The vaginal cuff is closed in the middle using several interrupted sutures, or a single or continuous suture (Figures 16 and 17).

Radical hysterectomy

The most common indications for the radical procedure are stage IA2, IB and IIA carcinoma of the cervix.
Less common indications include small centrally recurrent postradiation cervical cancers, adenocarcinoma of the endometrium with clinical involvement of the cervix, and stage I–II carcinoma of the vagina.

Figure 15

The uterus is removed transvaginally

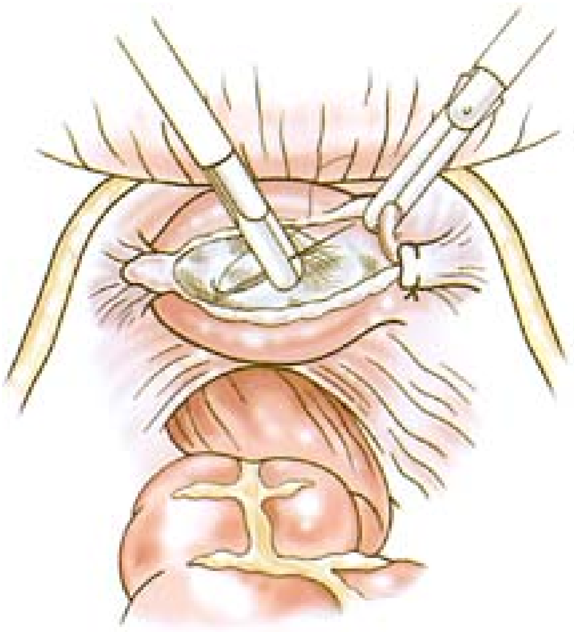

Figure 16

The vaginal cuff is closed in the middle

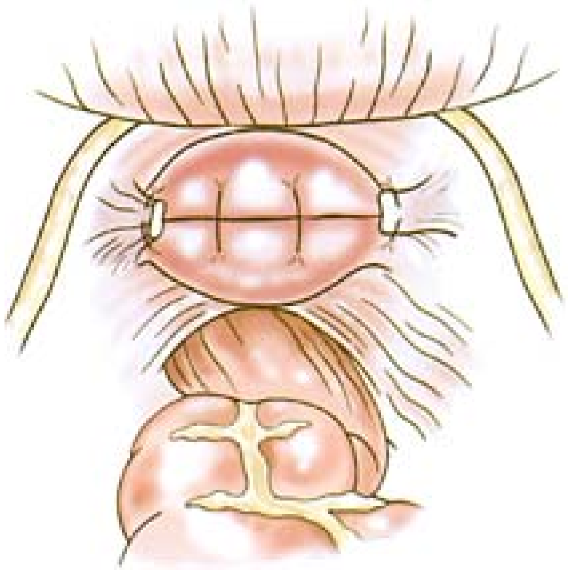

Figure 17

Final appearance

Surgical procedure

1. *Development of the rectovaginal space:* an assistant elevates the uterus with a uterine manipulator, and with the other hand performs a rectovaginal examination, delineating the rectum and the vagina. The cul-de-sac peritoneum between the attachment to the rectum and to the vagina is incised laparoscopically and the rectum is separated from the posterior vaginal wall using sharp and blunt dissection to a level of 3–4 cm below the cervix (Figure 18). The pneumoperitoneum will help identify the correct plane.
2. Development of the vesicovaginal space: round ligaments are electrodesiccated and cut close to the pelvic side-wall. The peritoneum is incised lateral and parallel to the ovarian vessels. Anterior leaves of broad ligament are incised towards the vesicouterine peritoneal reflexion. Using hydrodissection, or sharp and blunt dissection, the vesicouterine ligament is divided and the bladder is pushed off the cervix and the upper third of the vagina (Figure 19).

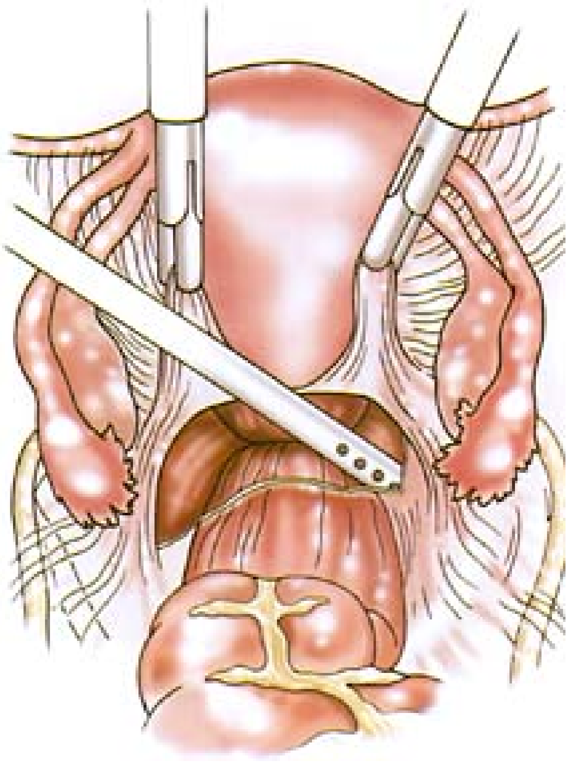

Figure 18

The cul-de-sac peritoneum is incised laparoscopically and the rectovaginal septum is developed

3. Development of the paravesical spaces: the obliterated hypogastric artery is identified and is retracted medially with a suction irrigator probe or a grasping forceps. The paravesical space is

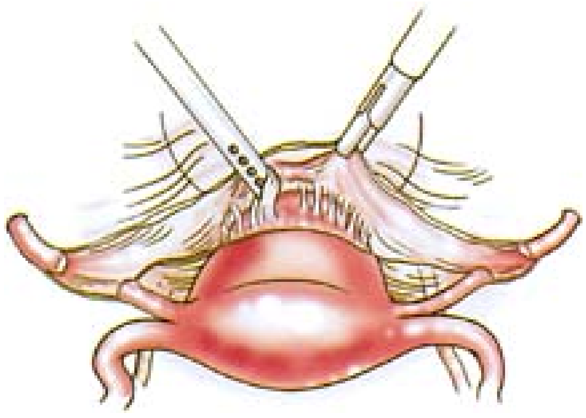

Figure 19

The vesicovaginal space is developed and the vesicocervical uterine ligament is dissected

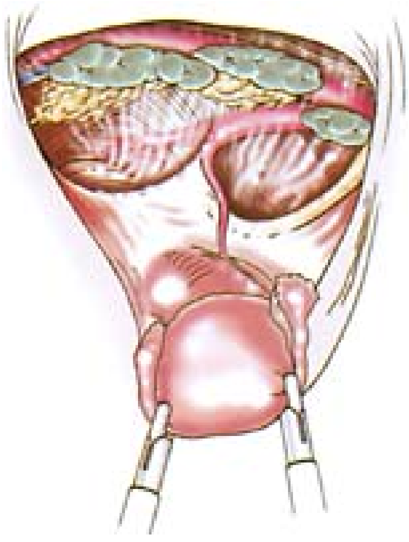

Figure 20

The paravesical and pararectal space is developed

developed between the obliterated hypogastric artery and the external iliac vein (Figure 20).

4. Development of the pararectal space: while the infundibulopelvic ligament and adnexa are retracted medially the obliterated hypogastric artery is traced down until the ureter is identified retroperitoneally and traced from the pelvic brim towards the bladder. While the ureter is retracted medially the pararectal space is entered using blunt dissection between the hypogastric artery laterally and the ureter medially and posterior to the uterine artery. Ureteral dissection is performed and the uterine artery is identified at its origin from the hypogastric artery (Figure 21).

5. Ligation of the uterine artery and unroofing the ureter: the uterine artery is electrodesiccated or clipped just medial to its origin, transected and rotated anterior to the ureter (Figure 22). An angled tip clamp or the tip of the suction irrigator probe is used to widen the ureteral canal; an incision is made anteriorly it is opened completely and the ureter mobilized. The ureter is unroofed from the ureteral canal and the parametrium is freed. Bipolar electrodesiccation, staples or surgical clips can be used for achieving hemostasis of the hypogastric venous plexus (Figure 23). The uterosacral ligaments and the parametrium are stapled or electrodesiccated with bipolar forceps ligature or hormonic shears and sequentially transected approximately 1.5–3 cm lateral to the

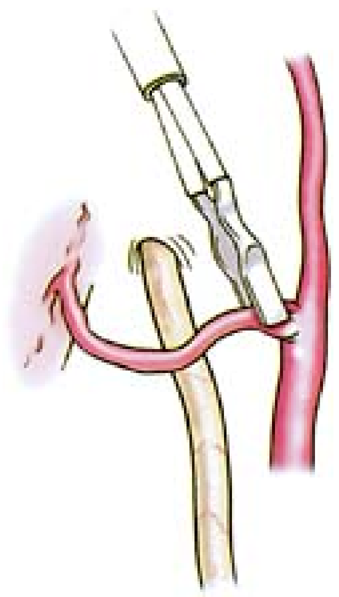

Figure 21

The uterine artery is electrodessicated or clipped at its origin from the hypogastric artery

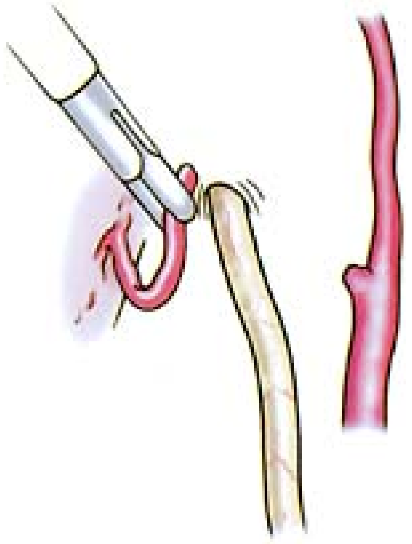

Figure 22

The uterine artery rotated over the ureter

cervix, based on the type of radical hysterectomy being performed. The dissection is taken to 2–3 cm below the cervix (Figure 24). Anterior and posterior culdotomy are performed as described above. After removal of the uterus the vaginal cuff is closed either laparoscopically or vaginally.

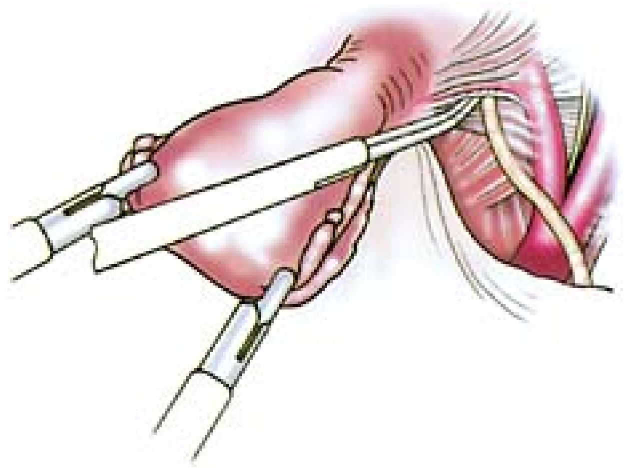

Figure 23

The parametrium is freed

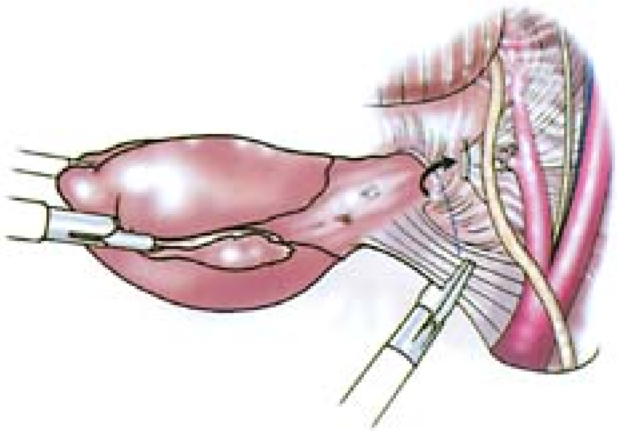

Figure 24

The dissection is taken to 2–3 cm below the cervix

Omentectomy

Omentum frequently is involved with metastatic lesions whenever there is intra-abdominal spread of cancer. Omentectomy is part of the staging of ovarian cancer and is often performed in treating or staging other gynecologic cancers, such as uterine papillary serous adenocarcinoma.

Anatomic considerations

The greater omentum is a fatty apron attached to the transverse colon and draped over coils of the small intestine. It is attached along the first part of the duodenum; its left border is continuous with the gas-trolienal ligament. If it is lifted and turned back over the stomach and liver, it can be seen to adhere to the transverse colon along the latter's whole length across the abdomen.
The omentum receives its blood supply from the gastro-omental arcade which is formed by the anastomosis of the left (a branch of the splenic artery) and right (a branch of the gastroduodenal artery) gastroomental arteries.

Surgical procedure

1. *Patient position and trocar placement:* the patient should be lying flat or in a slightly reversed Trendelenburg position for better access to the omentum. Primary and secondary trocar placement is similar to that described for appendectomy. Although stapling or bipolar electrodesiccation can be used for hemostasis of the omental vasculature, the harmonic scalpel is preferable because of its unique advantages of reducing both tissue damage and smoke plume production.
2. The omentum is elevated using two atraumatic grasping forceps introduced through the 5 mm tro-

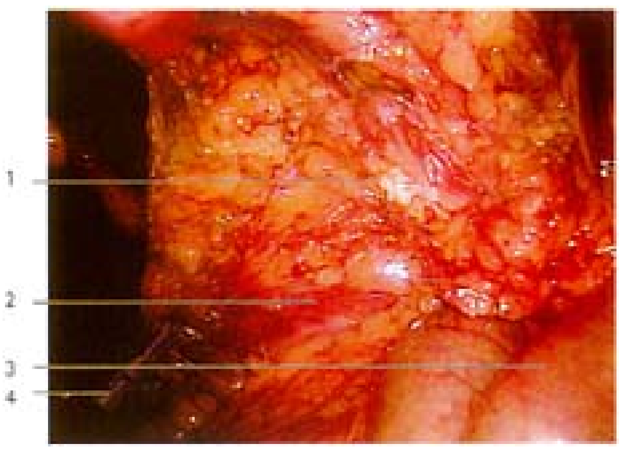

Figure 25

1 Omentum is under the stretch
2 Transverse colon
3 Small bowel
4 Omentectomy is started from the hepatic flexure

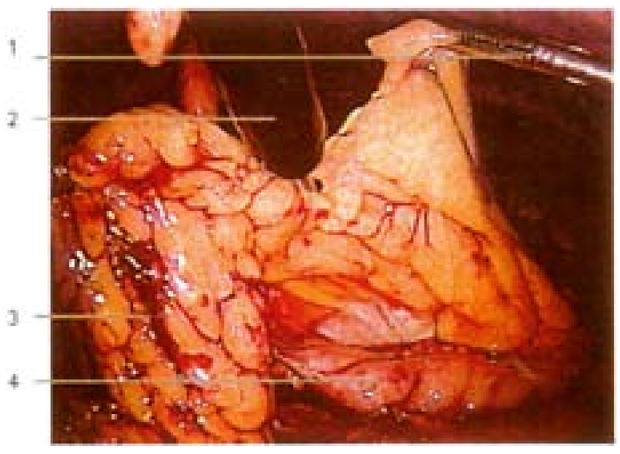

Figure 26

1 Grasping forceps elevate the omentum
2 Harmonic scalpel
4 Transverse colon 3 Segment of detached omentum

car sleeves. After exposure of the omentum and assessment of its relation to the transverse colon, a harmonic scalpel is introduced through the lateral or midline trocar and the omentectomy is started from the middle or the hepatic flexure, proceeding towards the splenic flexure at the line of reflection onto the transverse colon. Attention should be paid to avoiding injury to the colon and its mesentery and the short gastric vascular cascades (Figures 25, 26 and 27), especially if the anatomy has been distorted by the tumor deposit or adhesions.

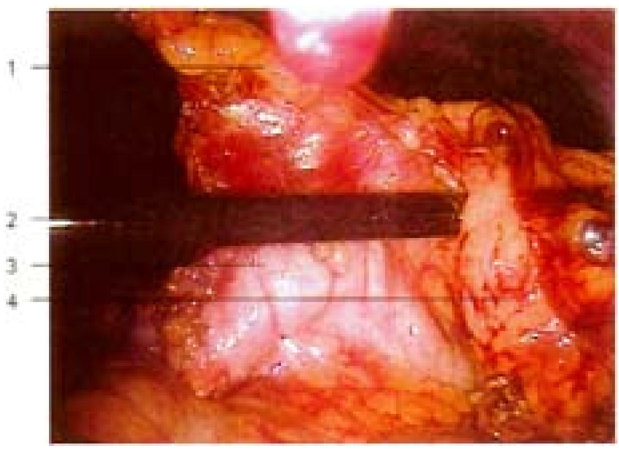

Figure 27

1 Omentum being elevated for exposure of transverse colon
2 Harmonic scalpel
3 Transverse colon
4 Splenic flexure and part of omentum

3. After the omentum has been detached it can be extracted from the abdominal cavity in different ways. Following laparoscopic or laparoscopically assisted vaginal hysterectomy, it can be extracted through the vagina either directly or after placing it in a bag. Alternatively the omentum can be removed through a 12 mm trocar sleeve or an enlarged anterior abdominal trocar site after enclosure in an endoscopic bag. Before termination of the procedure, hemostasis should be assured by decreasing the pneumoperitoneum pressure and evaluating the site of the resection. Individual bleeding sites can be treated with bipolar electrocoagulation, application of clips or suture techniques.

Palliative end colostomy

In palliative end colostomy the fecal stream is diverted above the rectum. End sigmoid colostomy with a Hartmann pouch or distal exteriorization of the distal portion of the sigmoid colon as a fistula in lieu of the Hartmann pouch may be utilized. Palliative end sigmoid colostomy with the Hartmann pouch is most frequently employed in gynecologic oncology when permanent diversion is required.

Indications

Palliative end colostomy in gynecologic oncology is required when the distal bowel has been removed or is permanently unusable, as in the case of non- resectable pelvic tumor causing sigmoid colon obstruction or irreparable fistula caused by tumor or radiation necrosis.

Anatomic considerations

The blood supply of the entire large intestine comes from the superior and inferior mesenteric arteries, with the former mainly supplying the midgut-derived right and transverse colon whereas the latter supplies the hindgut-derived left colon. The marginal artery of Drummond serves to connect the vascular territories of the two arteries.
The inferior mesenteric artery (IMA) arises from the dorsal side of the aorta often to the left at the level of L3, about 3–4 cm proximal to the bifurcation of the aorta. After veering to the left it gives off the left colic artery which divides into ascending and descending branches. The sigmoid colon is supplied by two to four arteries. The first one, which is the largest, comes from the left colic artery (30% of cases) or the IMA. From this first sigmoid vessel, second or third vessels may originate, or may arise directly from the IMA. As the IMA enters the pelvis, it becomes the superior rectal (hemorrhoidal) artery.
Venous and lymphatic drainage of the large intestine follows the general pattern of the arterial supply

Surgical procedure

1. *Patient position and trocar placement,* the patient is placed in a supine position or slightly turned toward the right side. A principal intraumbilical trocar for video laparoscopy is inserted, with three or four other trocars for introduction of the ancillary instruments (Figure 28). Two trocars are placed on the left side: one 12 mm trocar between the umbilicus and iliac crest for introduction of a Babcock clamp or linear stapling device, and one 5 mm trocar at the level of the iliac crest for introduction of a grasping forceps. One 12 mm midline trocar is placed 5 cm above the symphysis pubis for introduction of the stapler, clip applier, scissors or harmonic scalpel, and one 5 mm trocar on the right side at the level of the iliac crest for introduction of a grasping forceps (Figure 28).
2. After thorough evaluation of the abdominal and pelvic cavity, the sigmoid colon is identified and mobilized from its attachment to the pelvic side-wall. By means of a Babcock grasping forceps introduced through the left trocar incision, the sigmoid colon is elevated. Electrosurgery, a harmonic scalpel or a stapling device is used to divide the mesentery of the sigmoid colon and a ‘window’ is made. Vascularity of the proximal end of the bowel should not be compromised. While the bowel is elevated with the Babcock clamp, a laparoscopic linear stapling cutter introduced through the left upper quadrant or supra-publc trocar is passed across the bowel, which is then divided (Figures 29 and 30).

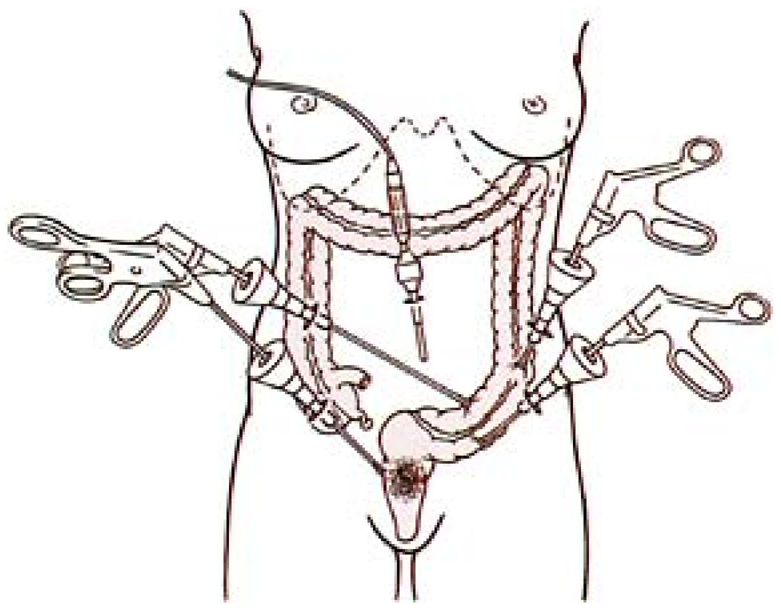

Figure 28

Port sites placement for end colostomy

3. After removal of the left lower quadrant trocar cannula, a disk of the subcutaneous fat at this site is incised and removed in preparation for location of the stoma. The fascia is incised and is enlarged using two fingers. Under direct laparoscopic visualization, a Babcock clamp is introduced through the left quadrant incision and

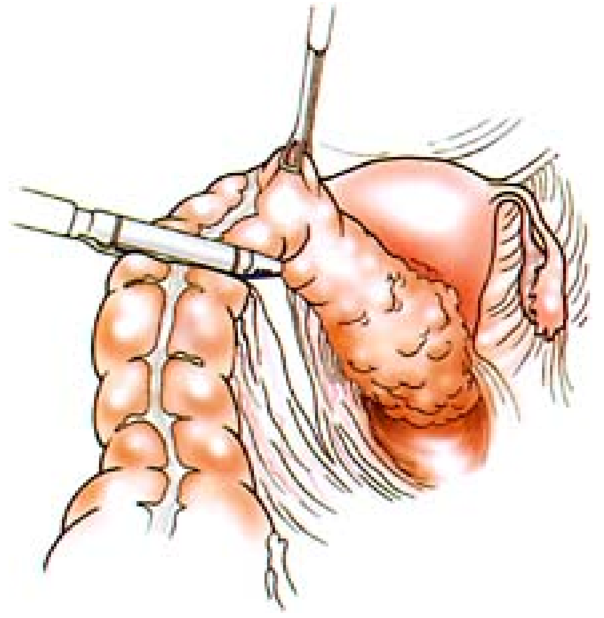

Figure 29

A linear stapling cutter is used to divide the bowel

the proximal portion of the sigmoid colon is grabbed and brought out through the incision (Figure 31).

4. The stapled end of the proximal colon is removed and a 'rosebud' stitch is used to evert the colon onto the skin, creating the stoma (Figure 32). Laparoscopically the serosa of the sigmoid colon is sutured to the peritoneum for prevention of internal hernia, using 2–0 polyglactin.

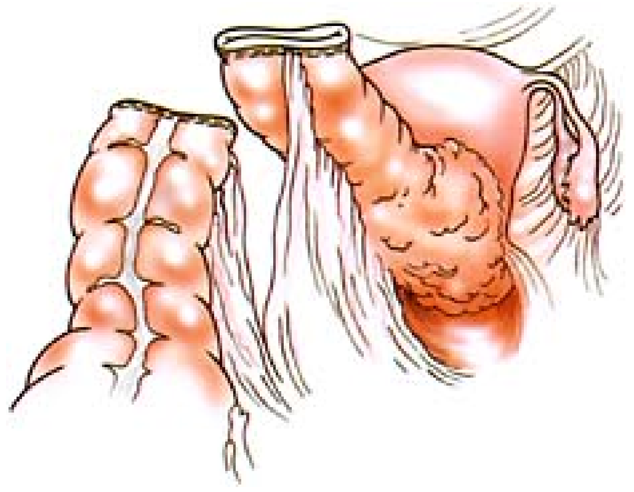

Figure 30

Division of the bowel

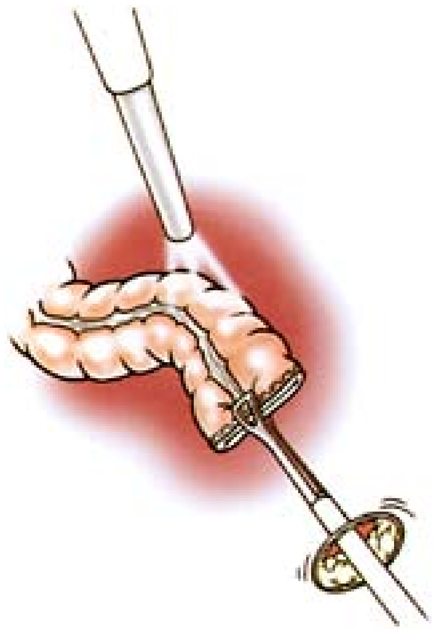

Figure 31

The proximal portion of the sigmoid colon is brought out through the incision

Lymphadenectomy

Since the initial descriptions of laparoscopic pelvic and para-aortic lymphadenectomy in the late 1980s and early 1990s, numerous reports have verified

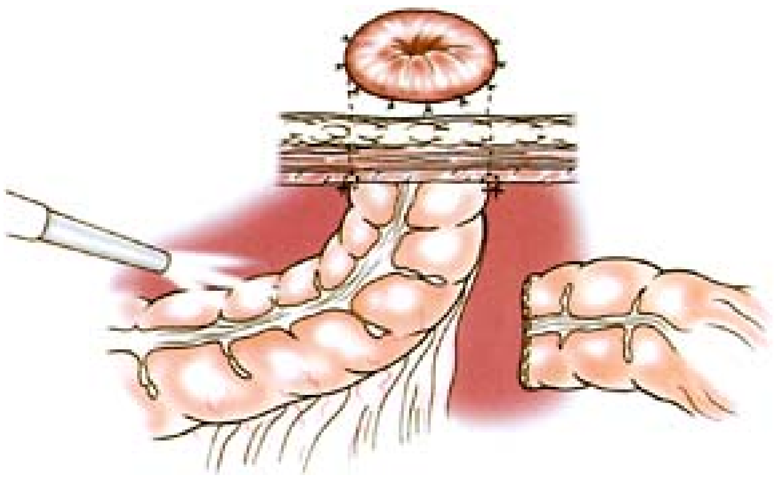

Figure 32

The serosa of the sigmoid colon is sutured to the peritoneum

the feasibility and safety of this technique. Its advocates point to the better magnification, fewer complications and superior visualization of the anatomy of blood vessels and lymph nodes provided by the video laparoscope in comparison with conventional techniques. In the hands of the experienced laparoscopist the efficacy of laparoscopic lymphadenectomy is equal to—if not better than—that achieved during laparotomy, with fewer complications.

Indications

Laparoscopic lymph node resection is performed as part of the treatment of cervical cancer, and node sampling is performed as part of the staging for endometrial or ovarian cancer.

Anatomic considerations

Para-aortic nodes

The landmarks which should be kept in mind for para-aortic lymphadenectomies (Figure 33) are as follows, from right to left:

- psoas muscle
- right ureter, which is medial to the psoas muscle, lateral to the inferior vena cava and crosses the bifurcation of the common iliac artery

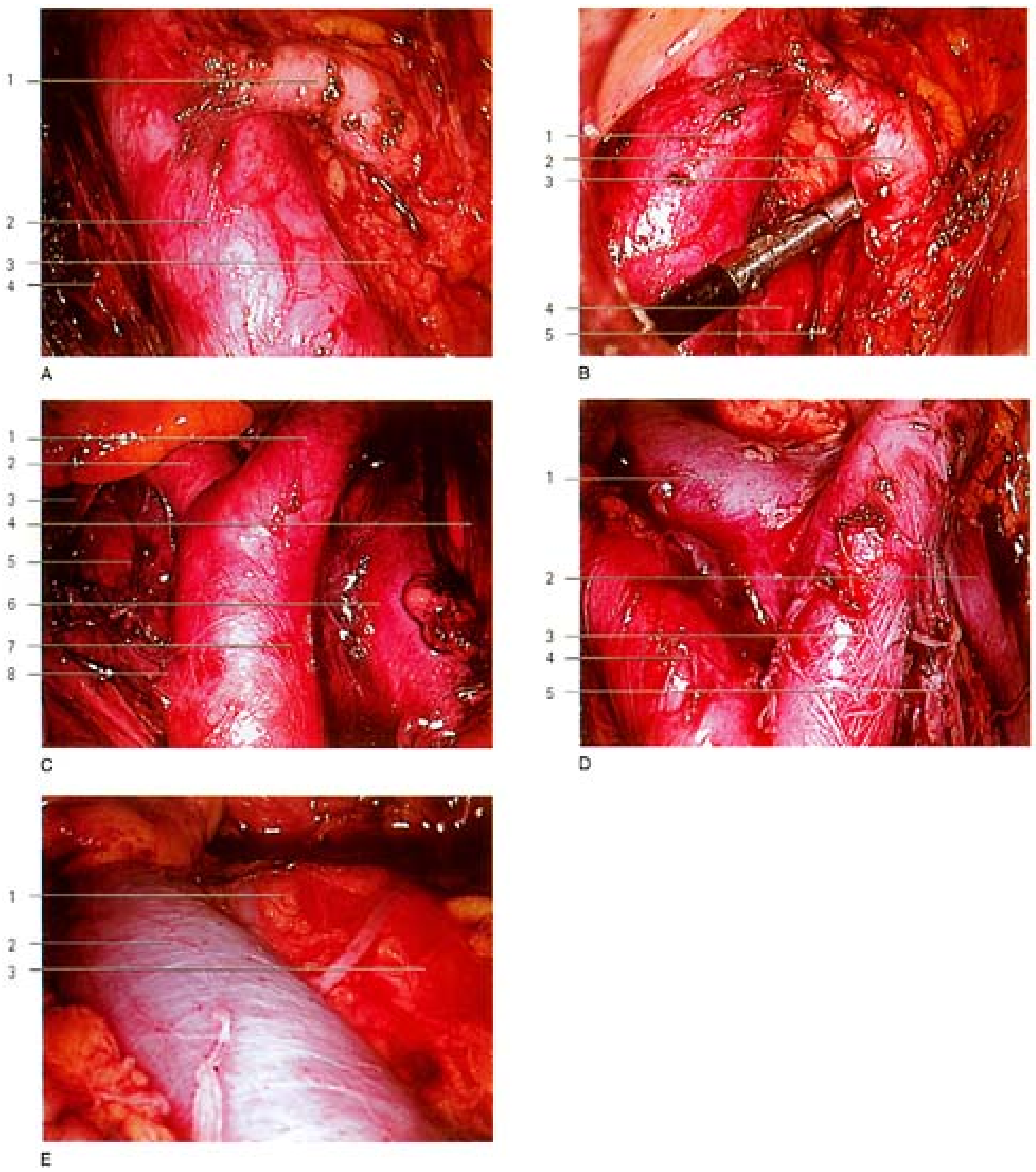

Figure 33 Retroperitoneal anatomy during para-aortic lymphadenectomy

A
1 Inferior mesenteric artery
2 Aorta
3 Left para-aortic nodes
4 Paracaval nodes
B Grasping forceps is used to retract inferior mesenteric artery for identification of left ureter
1 Aorta
2 Inferior mesenteric artery
3 Remaining left para-aortic nodes under the inferior mesenteric artery
4 Left para-aortic area after lymphadenectomy
5 Left ureter
C
1 Right common iliac artery
2 Left common iliac artery
3 Left ureter
4 Left ureter
5 Left para-aortic area after lymphadenectomy
6 Vena cava
7 Aorta
8 Inferior mesenteric artery
D
1 Left common iliac vein
2 Vena cava
3 Right common iliac artery
4 Left common iliac artery
5 Remaining vena caval nodes
E
1 Midsacral vessels
2 Left common iliac vein after lymphadenectomy
3 Sacral promontory

- vena cava (which is lateral to the aorta)
- aorta and both common iliac arteries
- below the bifurcation of the aorta superficially is the superior hypogastric nerve plexus and beneath it is the left common iliac vein crossing from the left to the right
- on the left side of the aorta are the inferior mesenteric artery, the ureter, sigmoid colon and its mesentery; the lumbar veins and artery are deep and can be seen after left lymphadenectomy
- on the far left is the left psoas muscle.

Pelvic nodes

The important landmarks for pelvic lymphadenectomy (Figure 34) are:

- laterally, the psoas muscle, the genitofemoral nerve, and the external iliac artery and vein
- distally, the deep circumflex vein, superior pubic ramus, and obturator internus fascia
- proximally, the common iliac bifurcation and bowel
- anteriorly, paravesical space, obturator nerve and superior vesical artery
- medially, the anterior division of the hypogastric artery and the ureter and paravesical space
- inferiorly, the sacral plexus, hypogastric vein, and pararectal space.

Surgical procedure

Para-aortic lymphadenectomy

The operating room set-up, the patient’s position, and the equipment may require minor variations. These include additional 5 mm or 10 mm trocars and positioning the video monitor at the head of the operating table, or using two monitors, one on each side of the patient: one for the surgeon’s view and the other for the assistant’s. The surgeon can stand on the right or left side of the patient, although some prefer to stand between the patient’s legs. As well as the umbilical port, three to four additional ports are necessary for introduction of the grasping forceps, scissors and clip applier or bipolar electrocoagulator. The location of the ancillary trocars is adjusted according to the surgeon’s preference. The patient is rotated to the left side for better exposure of the para-aortic area.

After insertion of the ancillary instruments and evaluation of the para-aortic area, the aorta is identified under the peritoneum up to the level of the mesenteric root. An incision is made over the posterior peritoneum at the level of the aortic bifurcation and extended towards the right iliac artery. The peritoneal incision is extended to the root of the mesenteric artery and, in the case of ovarian cancer, to the root of the left renal vein. Using two atraumatic grasping forceps, the peritoneum on each side is lifted and retracted laterally. Using blunt and occasionally sharp dissection with the tip of the suction irrigator or scissors, the retroperitoneal fatty tissue is dissected and the retroperitoneal vessels are identified (Figure 35).

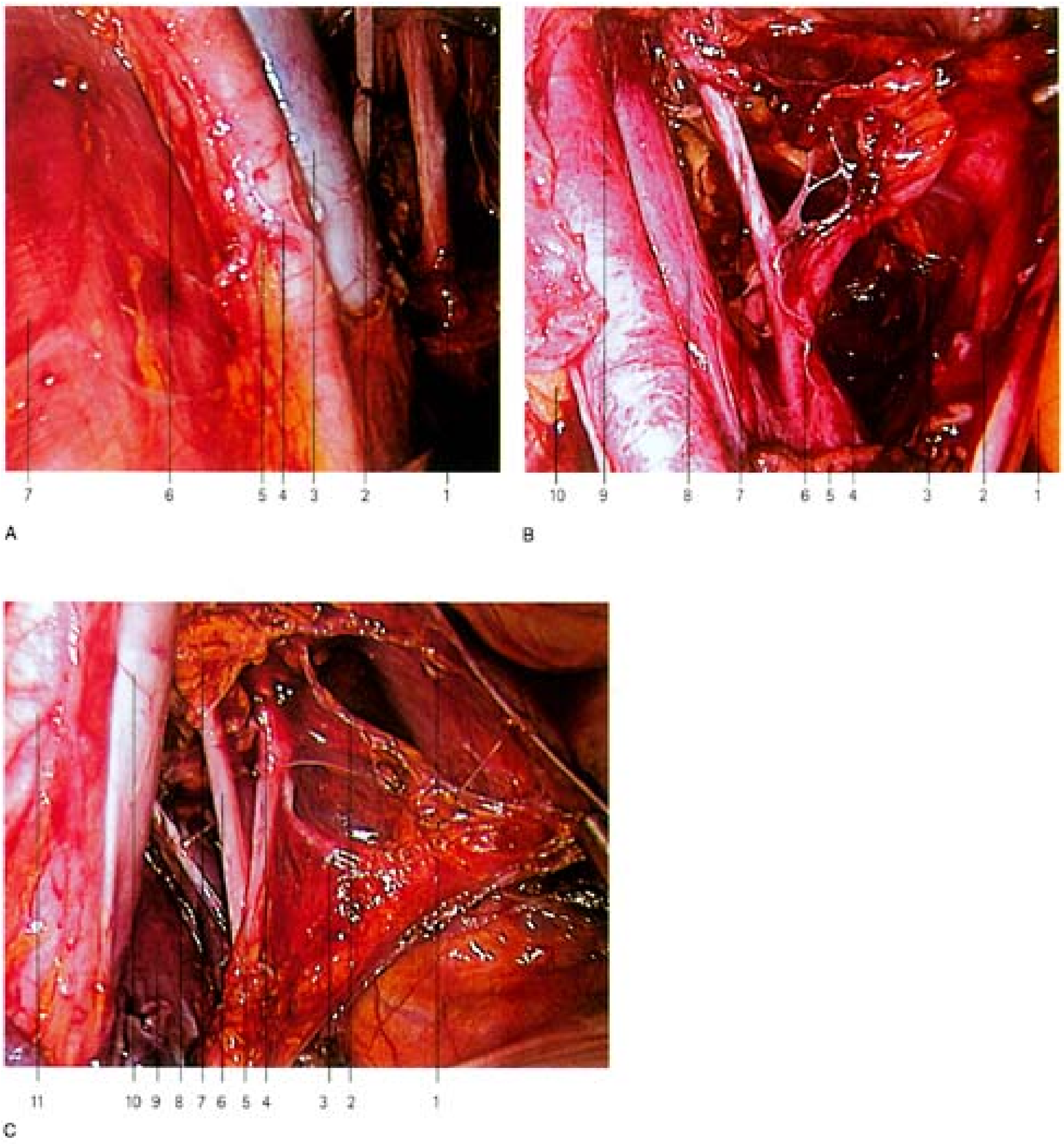

Figure 34

Retroperitoneal pelvic side-wall anatomy dissection during pelvic lymphadenectomy
A
1 Obliterated hypogastric artery (superior vesical)
2 Obturator nerve
3 External iliac vein
4 Left external iliac artery
5 Genitofemoral nerve
6 Left external iliac nodes
7 Left psoas muscle
B Grasping forceps retracts peritoneum medialky
1 Peritoneum
2 Left ureter
3 Pararectal space
4 Uterine artery branching from hypogastric artery
5 Remaining hypogastric nodes
6 Hypogastric artery
7 Superior vesical artery
8 External iliac vein
9 External iliac artery
10 External iliac nodes
C Grasping forceps retracts peritoneum medially
1 Right ureter
2 Superior vesicle artery
3 Uterine artery
4 Obliterated hypogastric artery
5 Hypogastric artery
6 Remaining obturator nodes
7 Obturator nerve
8 Obturator artery and vein
9 Right obturator internus muscle
10 Right external iliac vein
11 Right external iliac artery

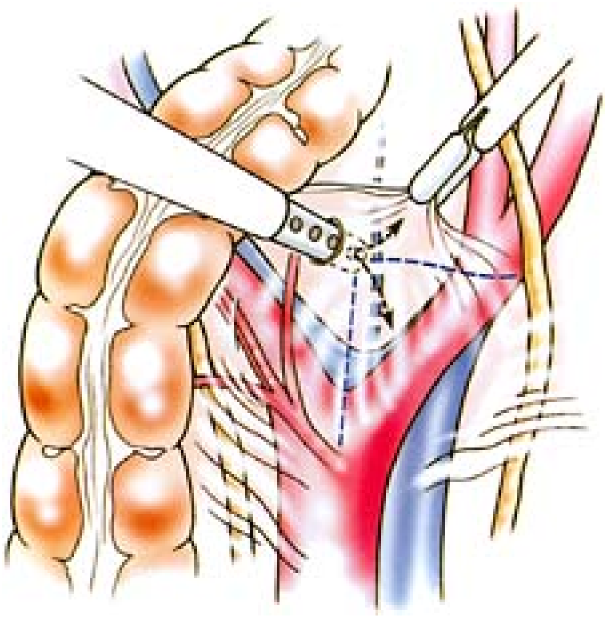

Figure 35

Exposure of aortic caval bifurcation

For left para-aortic lymphadenectomy, the rectosigmoid colon is retracted laterally and, after identification of the inferior mesenteric artery and ureter, the nodal packet lateral to the aorta and above the left common iliac artery is resected using blunt and sharp dissection. Careful attention should be paid to avoid injury to lumbar vessels, the left common iliac vein, left ureter and inferior mesenteric artery For ovarian cancer staging, the lymphadenectomy can be extended to the level of the left renal vein (Figures 36 and 37).

For resection of the paracaval nodes, the right ureter is identified and, while gentle traction is applied using atraumatic grasping forceps, the peritoneum and the ureter are retracted laterally over the psoas muscle. The nodal packet attached to the right common iliac artery is dissected off the vessels using blunt and occasionally sharp dissection. Using a laparoscopic Babcock clamp, the nodal packet is elevated and, using blunt and sharp dissection, the nodal packet is removed from the inferior vena cava. Care must be taken to avoid injury to the perforator veins. Clips or bipolar electrodesiccation can be used for achieving hemostasis. The level of the paracaval lymphadenectomy can be extended to the level of the right ovarian vein and, at times, the ovarian vein can be clipped and dissected for a better approach to the nodal packet in this area (see Figure 37).

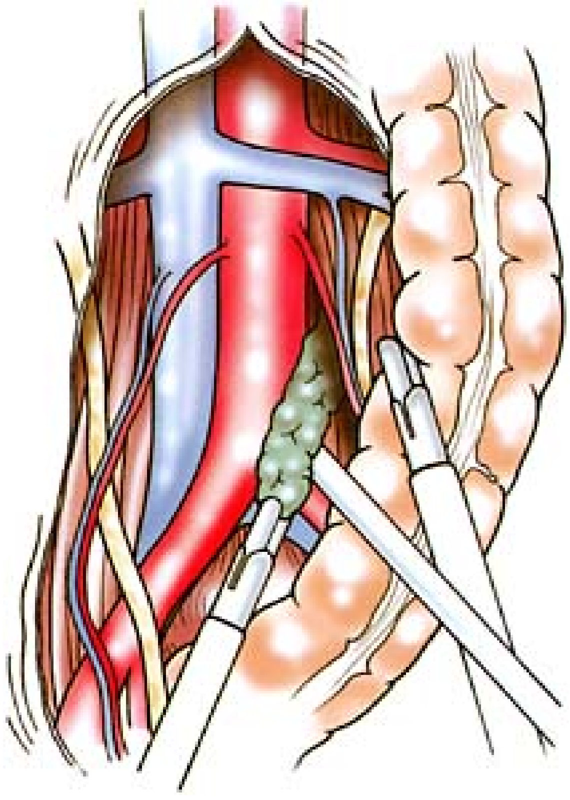

Figure 36

Renal vessel exposure

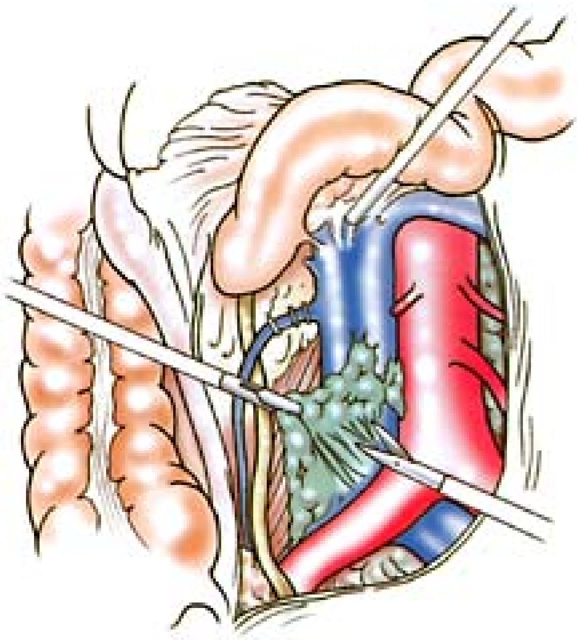

Figure 37

Caval exposure

Pelvic lymphadenectomy

In addition to the primary intraumbilical trocar which is used for introduction of the video laparoscope, two ancillary 5 mm ports in the right and the left lower quadrants lateral to the inferior epigastric vessels at the level of the iliac crest and an additional 10 mm port in the midline 5 cm above the symphysis pubis are required. The lymphadenectomy may be performed either before or after hysterectomy. The procedure begins with an incision of the peritoneum between the round and infundibulopelvic ligaments, parallel to the axis of the external iliac vessels (Figure 38). The round ligament is electrodesiccated and cut, the broad ligament between the round and the infundibulopelvic ligament is opened, and the psoas muscle, genitofemoral nerve, iliac vessels, and ureter are identified. Next the paravesical space is entered and widened by blunt dissection between the umbilical artery medially and external iliac vessels laterally. Caution should be exercised to avoid injuries to the external iliac vein and aberrant obturator veins (Figures 39 and 40).

The fat and the lymphatic pad between the psoas muscle and external iliac artery are elevated, dissected, and removed distally and proximally towards the circumflex vein and common iliac artery respectively. The nodal packet below the external iliac vein is grasped medially and, using blunt dissection, separated from the vein. While gentle traction is applied on the

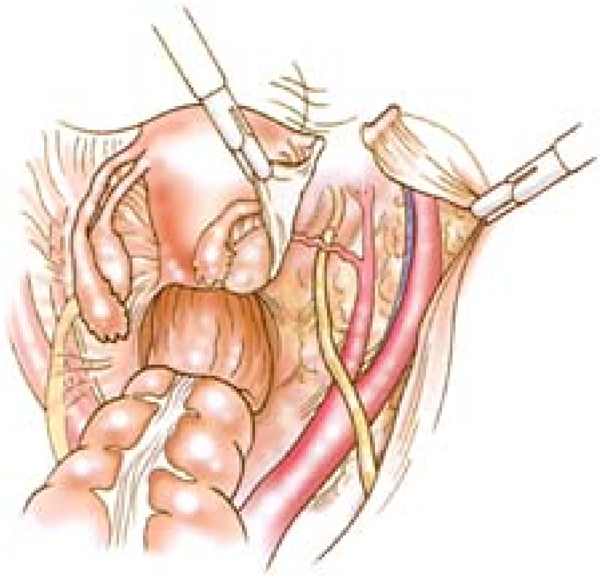

Figure 38

Pelvic side-wall exposure

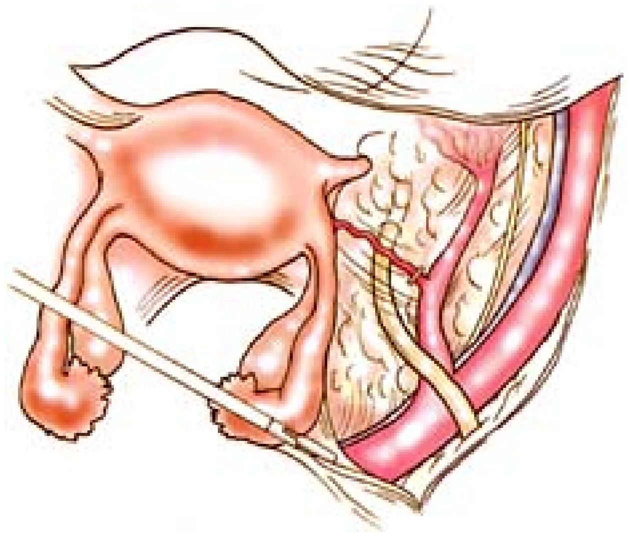

Figure 39

Obturator fossa exposure

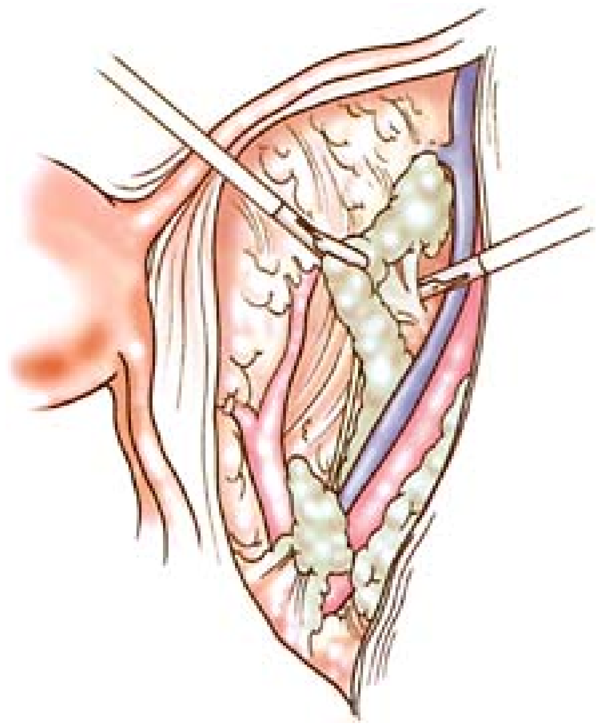

Figure 40

Obturator node removal

nodal packet medially, the obturator nerve is identified inferiorly and the obturator nodal packet is dissected and removed from the obturator nerve up to the level of the bifurcation of the external iliac artery; care is taken to avoid the hypogastric vein which often comes directly up from the pelvic floor. Inferiorly, the nodal packet is removed at the level where the obturator nerve exits from the pelvis. The fatty and nodal tissue between the obturator nerve and the external iliac vein is grasped and thoroughly separated from the pelvic wall by blunt dissection using the suction irrigator or the closed tip of the grasping forceps. Clips can be applied before the removal of the nodal tissue. After removal, the pelvic bone and internal obturator muscle can be seen.
The lymphatic nodal package of the hypogastric artery is grasped and gently separated using blunt dissection from the external and internal iliac artery to the level of the division of the common iliac artery. Interiliac nodes between the external iliac artery and vein are removed (Figure 41).

At the end of the procedure, the nodal package is removed through the trocar using a Babcock clamp or after placement inside the laparoscopic bag, and the

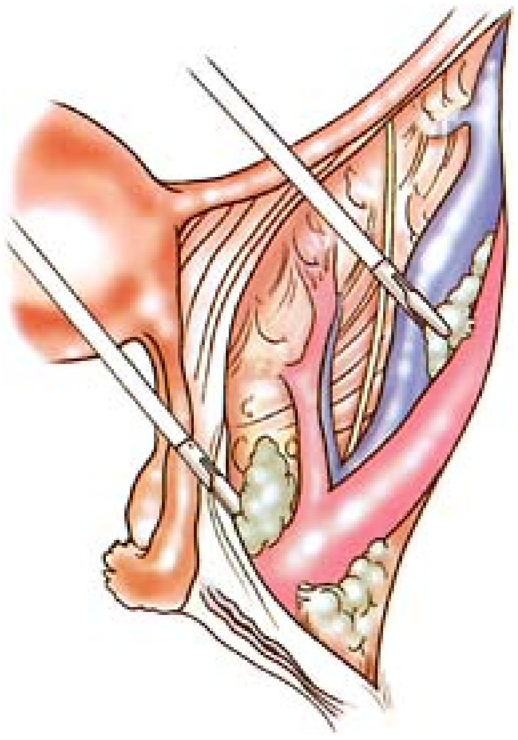

Figure 41

Interiliac-external iliac node removal

area is thoroughly irrigated. Pneumoperitoneal pressure is decreased for evaluation of hemostasis; the peritoneum is not closed, and no retroperitoneal drain is applied.

References

Childers J, Surwit E, Tran A, Hatch K (1993) Laparoscopic para-aortic lymphadenectomy in gynecologic malignancies. *Obstet Gynecol* **82**:741–7.

Dargent D, Mathevet P (1992) Hystérectomie élargie laparoscopico-vaginale. *J Gynecol Obstet Biol Reprod* **21**:709–10.

Leahy PF (1989) Technique of laparoscopic appendectomy. *Br J Surg* **76**:616.

Morrow CP, Curtin JP (1996) Surgical anatomy. In: Morrow CP, Curtin JP, Osa EL, eds. *Gynecologic cancer surgery*. Edinburgh: Churchill Livingstone: 67–139; 181–268.

Nezhat CR, Nezhat FR, Ramirez CE, et al. (1993) Laparoscopic radial hysterectomy and laparoscopic assisted vaginal radial hysterectomy with pelvic and para-aortic node dissection. *J Gynecol Surg* **9**:105–20..

Nezhat C, Nezhat F (1991) Incidental appendectomy during videolaseroscopy. *Am J Obstet Gynecol* **165**:559–64.

Nezhat C, Nezhat F, Silfen SL (1990) Laparoscopic hysterectomy and bilateral salpingo-oophorectomy using multifire GIA surgical stapler. *J Gynecol Surg* **6**:287.

Nezhat C, Nezhat F, Gordon S, et al. (1992) Laparoscopic versus abdominal hysterectomy. *J Reprod Med* **37**:247–50.

Nezhat C, Siegler A, Nezhat F, et al. (2000) The role of laparoscopy in the management of gynecologic malignancy. In: Nezhat C, Nezhat F, Luciano A, eds. *Operative gynecologic laparoscopy principles and techniques*, 2nd edn. New York: McGraw-Hill: 301–27.

Piver MA, Rutledge FN, Smith JP (1974) Five classes of extended hysterectomy for women with cervical cancer. *Obstet Gynecol* **44**:265–70.

Querleu D, Leblanc E (1991) Laparoscopic pelvic lymphadenectomy in the staging of early carcinoma of the cervix. *Am J Obstet Gynecol* **164**:579–81.

Semm K (1983) Endoscopic appendectomy *Endoscopy* **15**:59–64.

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19
Vascular access and implantable vascular and peritoneal access devices

Paniti Sukumvanich
Gary L Goldberg

Introduction

Most patients with cancer will undergo multiple courses of chemotherapy and other intravenous infusions as a part of their management. Venous access can become compromised by the intravenous cytotoxic chemotherapies, transfusions, hyperalimentation and other fluids. In 1972, Cole and colleagues reported on the first surgically implanted vascular access device based on a modification of an arteriovenous fistula catheter for renal dialysis (Cole et al. 1972). This was later modified and made popular by Broviac and Hickman (Broviac et al. 1973, Hickman et al. 1979). A decade later, a completely implanted device known as the Port-a-Cath (PAC) was introduced (Ecolt et al. 1983). These devices have become more popular as a greater variety of chemotherapeutic options have become available to patients. The advantage of venous access ports includes fewer access failures with less access-related anxiety and pain (Bow et al. 1999). With the advent of intraperitoneal chemotherapy, Port-a-Cath devices became a means of obtaining intraperitoneal access. This chapter discusses the indications, techniques of insertion, complications and management of complications for these venous access devices.

Indications

The main indication for central venous access devices includes the need for venous access in patients undergoing prolonged chemotherapy especially in patients with poor venous access.
Port-a-Cath devices for use as intraperitoneal access devices are indicated in patients who are expected to undergo intraperitoneal chemotherapy.

Contraindications

Patients should not undergo venous access catheter placement in the presence of a current infection, such as bacteremia, septicemia or fungemia. Patients with clinically significant thrombocytopenia or coagulopathy should also not undergo the procedure without special consideration and preparations.

Anatomic considerations

Central venous lines can be accessed through a number of routes. The routes most commonly utilized are the internal jugular vein or the subclavian vein. The internal jugular vein is located within the supraclavicular fossa. The borders of the fossa are the clavicle inferiorly, the sternal and clavicular heads of the sternocleidomastoid muscle anteriorly and posteriorly respectively The internal jugular vein empties into the brachocephalic vein which is anterior and lateral to the common carotid artery and posterior to the artery is the apex of the lung. The subclavian vein is a continuation of the axillary vein which runs along the superior border of the pectoralis minor muscle to the level of the 1st rib. The lateral border of the 1st rib can be approximated by finding the area on the clavicle where it changes from a convex to a concave curvature (about two thirds of the distance from the head of the clavicle). It is important to note that there is no major vessel directly posterior to the clavicle lateral to the 1st rib. Thus, attempts at venous access lateral to this area will usually fail. At the lateral border of the 1st rib the subclavian vein begins and runs parallel to the 1st rib, posterior to the clavicle and ends at the medial border of the scalenus anterior muscle. The subclavian vein then merges with the internal jugular vein and forms the brachiocephalic vein. The subclavian artery though it runs parallel with the vein is separated by the scalenus anterior muscle.

Types of ports

Venous access catheters can be divided into two types. The first type consists of an externalized Hickman-type catheter. This type of catheter is similar to a central line catheter except that a portion of the catheter is tunneled subcutaneously and has an externalized access site. The second type of venous access catheter is a completely implanted device. The most common example is the Port-a-Cath. This device has a silicone and titanium reservoir site that is accessed through the skin.

Surgical procedure

Both types of access devices, the externalized Hickman-type and the internalized Port-a-Cath type are potential options for central venous access. However, internalized ports are recommended since they are easier to maintain than the externalized devices and they are more ‘patient-friendly’. It was assumed that the Hickman-type catheters had a higher rate of catheter-related infections but a randomized prospective trial did not bear this out (Mueller et al. 1992).

Preoperative evaluation and testing

1. Complete blood count, platelet count and coagulation profile.
2. Prophylactic antibiotics are not recommended. No data exist on the use of prophylactic antibiotics for central venous access device placement. There are limited data regarding the use of antibiotics in central venous catheters. Although possible reductions (Henrickson et al. 2000 Bock et al. 1990, Road et al. 1998) in infection rates have been reported, the emergence of resistant organisms is of concern and the use of prophylactic antibiotics is currently not recommended (HICPAC 1995).

Surgery

1. Prepare both sides of the neck and chest to the level of the xyphoid process should the attempt on the right side fail.
2. Have the arms tucked on the side of the insertion.
3. In obese patients, a roll of towel can also be placed between the shoulders to allow for easier access in the subclavian approach (Figure 1).

Venous access

Venous access can be obtained via either the internal jugular vein or the subclavian vein. The right

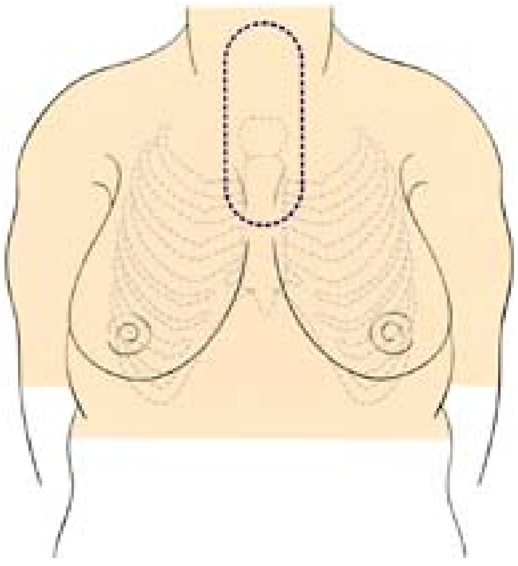

Figure 1

Positioning of patient with towel roll in place. The dotted area indicates where a roll of towel can be placed between the patient’s shoulder blades. This can help facilitate access to the subclavian vein in an obese patient.

subclavian vein is usually accessed as the initial choice. The most commonly used approach is the percutaneous technique. However, occasionally a cutdown procedure is required for access and the cephalic or internal jugular veins can be utilized. Cut-downs have the lowest risk of pnuemothorax.

Percutaneous (Seldinger) technique

Needle insertion

1. Local anesthesia using 1% lidocaine (lignocaine) at the site of either the internal jugular vein or the subclavian vein.
2. Set up the 16 gauge needle by lining the bevel of the needle with the numbers on the syringe. This will allow the surgeon to be aware of the direction of the bevel once the needle has been inserted.
3. Insertion into the vein should be done with the bevel pointing inferiorly (Figure 2).

Subclavian vein access

Traditional method of insertion

1. Insert the needle directly perpendicular to the skin about 0.5 cm from the edge of the clavicle two thirds from the head of the clavicle.
2. Once you have gone through the skin, angle the needle toward the subclavian vein underneath the clavicle by aiming for the sternal notch. The needle/syringe should be parallel to the chest wall as negative pressure is applied until there is

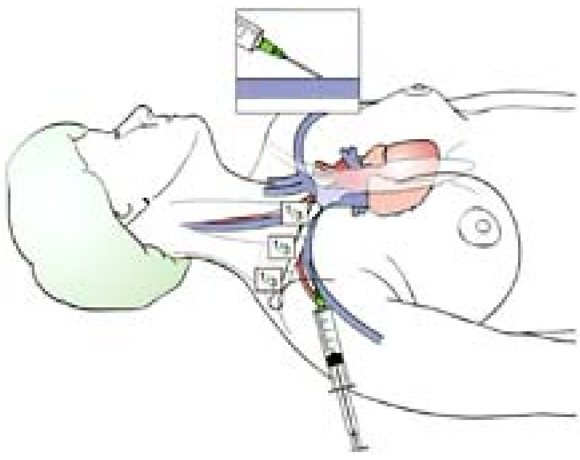

Figure 2

Subclavian venous access with the Seldinger technique. The 16 gauge needle should be inserted in an area that is two-third distal to the head of the clavicle with the bevel of the needle pointing down.

venous blood return. If there is no blood return on initial insertion, slowly withdraw the syringe.

Alternative technique

1. Squeeze the clavicle (two thirds from the head of the clavicle) with the index finger and thumb. Be sure you are grasping the entire clavicle.
2. Insert the needle at the lower edge of the thumb with bevel down. Once through the skin, aim the needle towards the sternal notch while pushing down on the needle with the left thumb. Negative pressure should be applied until there is venous blood return.

Internal jugular access
There are two approaches for accessing the internal jugular vein—the anterior and posterior approaches. The anterior or posterior portion of the name refers to whether or not the needle is inserted anterior or posterior to the sternocleidomastoid muscle.

1. *Anterior approach.* Locate the triangle that is formed by two heads of the sternocleidomastoid muscle and clavicle. First apply 1% lidocaine (lignocaine) to the apex of the triangle in order to anesthetize the skin. Insert the needle at the apex of the triangle, anterior to the muscle, aiming the needle towards the ipsilateral nipple at a 45–60° angle until the vein has been accessed. Be careful as to not aim too medially as there is a potential for puncturing the carotid artery.
2. *Posterior approach.* Local anesthesia with 1% lidocaine (lignocaine). Locate the sternocleidomastoid

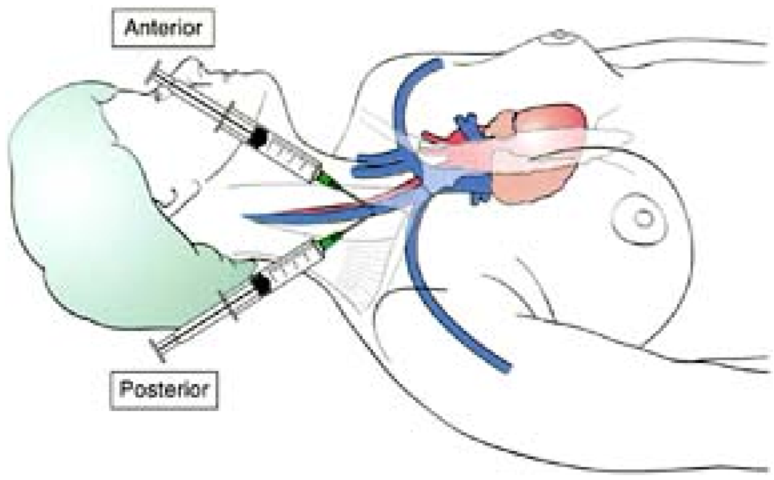

Figure 3

Internal jugular access with the Seldinger technique. The anterior approach involves insertion of a 16 gauge needle at the apex of the triangle that is formed by the two heads of the sternocleidomastoid muscle and the clavicle. In an obese patient where the apex of the triangle is hard to appreciate, the apex is approximately halfway between the sternal notch and the mastoid process.

muscle and insert the needle 3 finger-breadths above the clavicle and posterior to the sternocleidomastoid muscle. Aim the needle towards the suprasternal notch at a 45° angle to the horizontal plane (Figure 3).

Passing the guide wire

1. Once the subclavian vein has been accessed, rotate the bevel of the needle towards the heart (i.e. the numbers on the syringe should be facing the patient's heart). If the internal jugular vein is used, then no rotation of the needle is necessary.
2. Remove the syringe from the needle and gently thread the guide wire through the needle. Remove needle once the guide wire has passed into the vein without resistance. Minimal force should be used as injury to the vein or the heart can occur if undue force is applied. Care should also be taken not to leave the needle hub exposed for a long time as inspiration by the patient can lead to an air embolism.

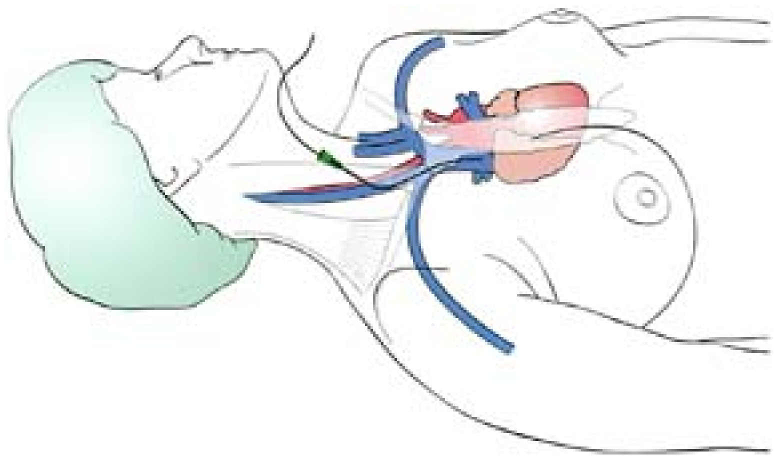

Figure 4

Passing the guide wire. It is important to perform this maneuver with very little force as there should be minimal resistance if the wire is going in the correct direction.

3. If PVCs are seen on the electrocardiogram (EKG) withdraw the wire until PVCs are no longer seen.
4. Fluoroscopy should be performed at this point to confirm the location of the wire.
5. Estimate the length of the catheter and cut with a pair of mayo scissors. The catheter should be long enough to go from the port site to the superior vena cava (Figure 4).

Dilating the skin incision/passing the catheter

1. Extend the skin incision with a no. 11 blade on either side of the guide wire. The incision should allow insertion of the port sheath without resistance.
2. Pass the inner dilator sheath over the guide wire. Pull back on the wire at this time to ensure the sheath is patent.
3. Remove the inner dilator sheath leaving the guide wire in place. Connect the inner and outer dilator sheaths and pass this over the guide wire. Again,

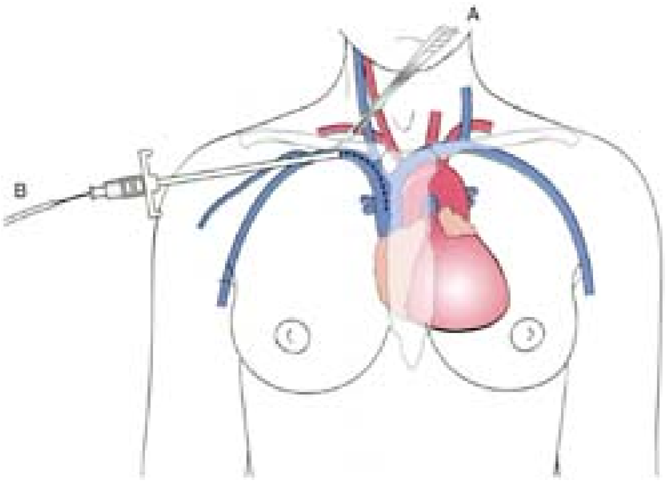

Figure 5

Dilating the skin incision and passing the catheter

pull back on the guide wire as the sheath is being inserted. Be sure to not completely pull out the guide wire.

4. Pull out the inner sheath with the guide wire in place.
5. Pass the premeasured catheter over the guide wire and then remove the guide wire.
6. Peel the sheath in half and slowly withdraw the outer sheath, stabilizing the catheter in place at the skin incision with a pair of forceps.
7. Access and flush the catheter with a weak heparinized saline via a blunt Huber needle to confirm venous access (Figure 5).

Cut-down technique

Venous access via the cephalic vein. A transverse skin incision is made at the acromial end of the clavicle. Dissect the fascia over the pectoralis muscle and identify the separation between the deltoid muscle and the pectoralis major. Within this groove is the cephalic vein. Retract the vein with a 2–0 silk and make a venotomy on the anterior surface of the vein. Cannulate with the catheter. Check the placement of the catheter by fluoroscopy. Once the position of the catheter tip is confirmed in the superior vena cava, tie the 2–0 silk in order to secure the position of the catheter and to maintain hemostasis (Figure 6A).

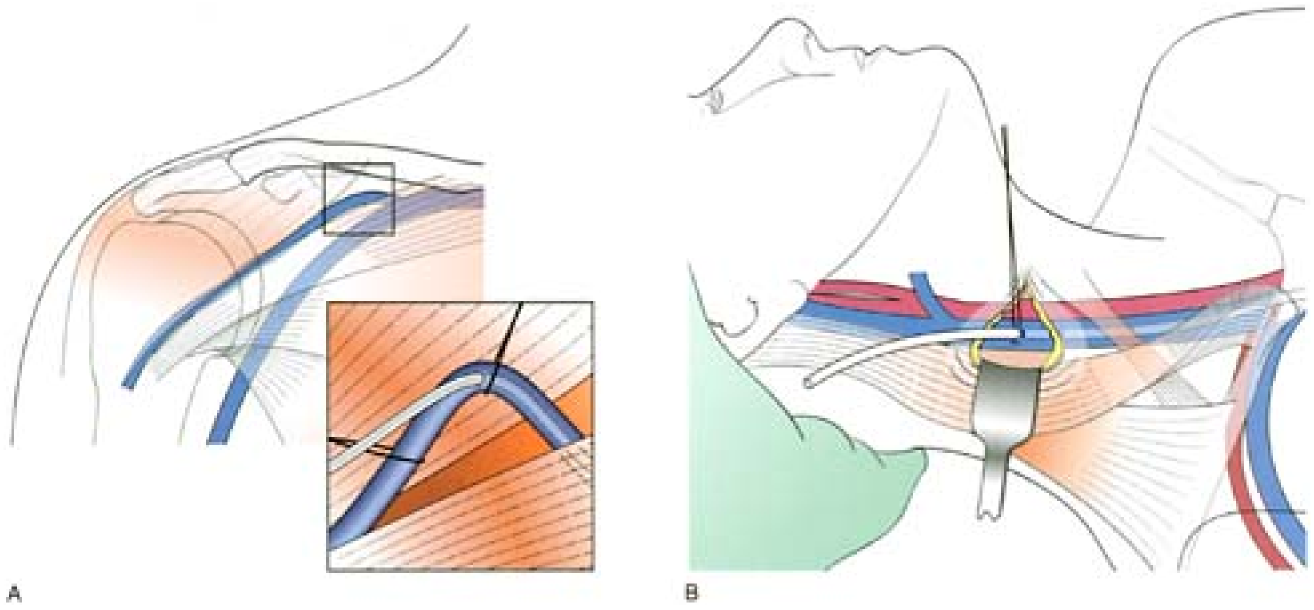

Figure 6

(A) Venous access via the cephalic vein using the cut-down (B) Venous access via the internal jugular using the cut-down technique technique

Internal jugular cut-down. A transverse skin incision is made 2 cm above the clavicle overlying the supraclavicular triangle. The dissection is performed to the level of the sternocleidomastoid muscle. Separate the muscle to expose the internal jugular vein. A 2–0 silk purse-string suture is placed in the internal jugular vein, followed by a venotomy. Once vein is cannulated with a catheter and the tip is in the correct position, tie the suture to secure the position of the catheter and to maintain hemostasis (Figure 6B).

Making the pocket for the port

1. The site of the pocket should be lateral enough to prevent kinking of the catheter by the clavicle after the port reservoir and catheter are connected. The site should not be too caudal as the port pocket should be on the anterior chest wall and not the breast tissue.
2. Incise the skin with a knife and dissect posteriorly towards the pectoralis major fascia.
3. Once the fascia has been located, dissect out the pocket for the port inferior to the skin incision. Make the pocket large enough to accommodate the port reservoir without difficulty. Ensure hemostasis in the pocket prior to fixation of the resevoir. (Figure 7).

Creating a tunnel for the catheter

1. Tunnel subcutaneously towards the cephalad incision. The tunnel should be under the fat and not directly under the skin. Tunneling too close to the skin will not properly conceal the catheter.

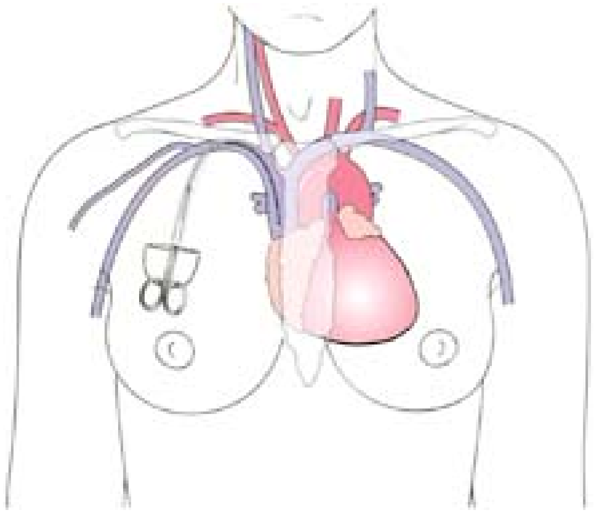

Figure 7

Making a pocket for the port

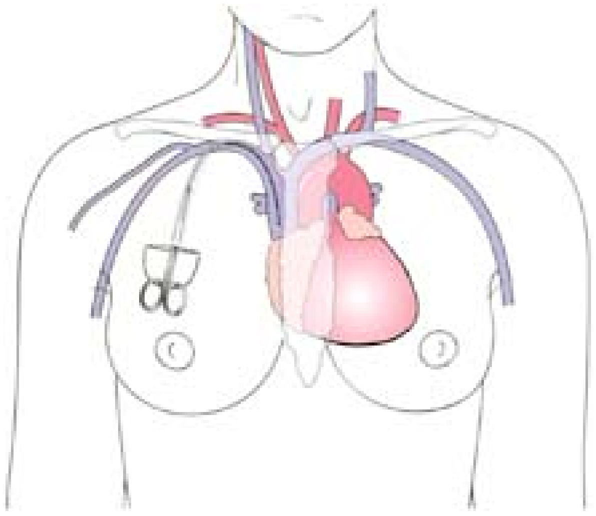

Figure 8

Creating a tunnel for the catheter.

2. Gently pull the catheter through the tunnel, taking care not to twist or kink the catheter at the insertion site.
3. Flush the catheter with weak heparinized saline using a blunt Huber needle to the confirm venous return (Figure 8).

Connecting the port to the catheter

1. Make sure the catheter is the appropriate length and trim as necessary.
2. Thread the locking device over the catheter.

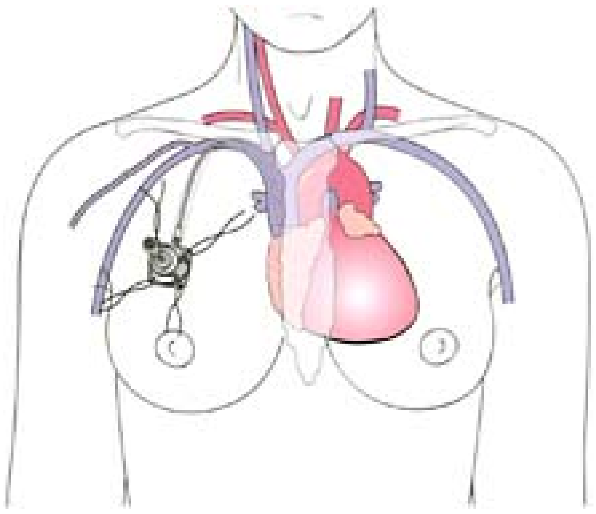

Figure 9

Connecting the port to the catheter

3. Connect the catheter to the reservoir and place in the pocket. Care should be taken not to puncture the catheter.
4. Check the placement of the catheter tip by fluoroscopy. The tip of the catheter should be in the superior vena cava and outside of the heart.
5. Deploy the locking device.
6. Access the port through the skin with a sharp Huber needle. After accessing, flush with 10 cc of heparinized saline. Leave the needle in place and suture the port in the pocket (Figure 9).

Checking placement of catheter

1. A chest X-ray should be obtained after the procedure to confirm position of the catheter and rule out potential complications associated with the placement.

- Pneumothorax may occur on the same or the contralateral side.
- The catheter tip should ideally be just outside the heart and parallel with the long axis of the vein. A good radiologic marker is the carina (Schuster et al. 2000).
- Hemothorax.

Peritoneal access device

1. Select the site for the peritoneal access device (Figure 10).
2. Once the site has been selected, make a vertical skin incision and enter the peritoneal cavity.
3. Create a subcutaneous pocket above the rectus fascia and on the rib cage about 3–4 cm in size and about 5–6 cm away from the vertical incision site.
4. Suture the reservoir to the fascia, and create a defect in the fascia about 2 cm away from the reservoir.
5. Grasp the catheter and pull it through the fascia and under the rectus muscle.
6. Place the catheter so that it transverses the peritoneal cavity.
7. Secure the catheter in place along the peritoneal cavity and close the fascial incision (Figure 10).

Maintenance and access of catheters

The purpose of routine maintenance of implanted catheters is to ensure venous access return and to prevent infection and thrombotic complications. Upper extremity deep vein thrombosis (DVT) in patients with central venous catheters is associated with pulmonary emboli in about 10–15% of cases (Monreal et al. 1994). The risk of upper extremity DVT in patients with implantable venous access devices is quite variable as most are thought to be asymptomatic (Monreal et al. 1996, De Cicco et al. 1997). One strategy to prevent catheter-related thrombosis is to use low-dose coumadin (1 mg/day). Such a low dose has little or no effect on the prothrombin time or activated partial thrombplastin time (Coccheri et al. 1999, Radclilte et al. 1999). In a prospective randomized trial, a coumadin dose of 1 mg per day has been shown to decrease the incidence of thrombosis from 37% to 10% without increasing hemorrhagic complications (Bern et al. 1990). However, care should be taken if mini-dose coumadin is given in patients on fluorouracil 5-based chemotherapy as this combination can lead to INR (international normalized ratio) elevation (Masci et al. 2003). Catheter tip occlusion is another frequent complication. One strategy used to reduce this complication is to flush the catheter regularly. In general, Hickman catheters are flushed once a day with heparinized saline (100 U of heparin/1 cc of saline). Although Port-a-Cath devices have usually been flushed once a month with heparinized saline, more recent data have shown that flushing once every three months is a viable option with a low rate of catheter tip thrombosis (Goldberg, pers. comm.). Routine flushing with heparinized saline has been shown to decrease thrombus formation at the catheter tip as well as catheter-related infection (Rack off et al. 1995, Randolph et al. 1998). This may be related to the role that thrombus formation plays in facilitating catheter colonization and subsequent infection (Gilon et al. 1998).
Meticulous sterile technique should always be used when ports are accessed. Access of Port-a-Cath devices should only be done with a none coring needle, such as a Huber needle. After accessing the port and confirming venous access, the port should be flushed with 10 cc of normal saline, followed by 5 cc of heparinized saline (100 U heparin/1 cc of saline).

Complications

Complications secondary to central venous access can be divided into intraoperative complications and postoperative (long-term) complications.
Intraoperative complications include pulmonary complications, such as pneumothorax, hemothorax and air embolism. Intraoperative cardiovascular complications include cardiac arrhythmia, cardiac tamponade, trauma to a major vessel or the right atrium, and hemorrhage.

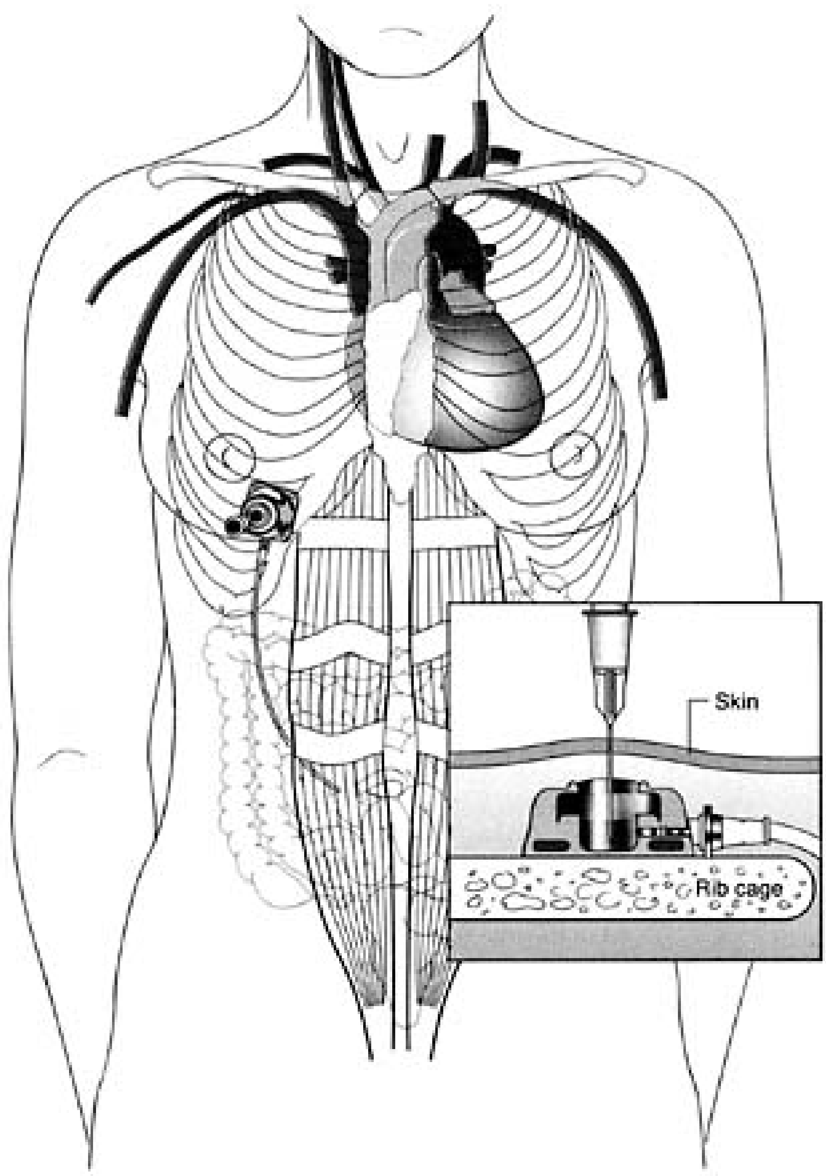

Figure 10

Placement of the peritoneal access device. The resevoir can be rolled up on the rib cage to provide a trim base while trying to access the device

Postoperative complications include infections of the exit site, tunnel infection and bacteremia. Mechanical complications, such as catheter breakage, catheter migration and catheter tip occlusions, may occur. Upper extremity venous thrombosis occurs in a relatively high number of cases (reported as high as 62%) (Hsuch et al. 2003).

The most common complications of peritoneal ports are infection of the port site and inability to flush or infuse the catheter. Table 1 outlines the more common complications of central venous catheters as well as their management strategies.

Table 1 Common complications and management of central venous catheters

Complications	*Incidence*	*Signs and symptoms*	*Management*
Pneumothorax	0.5–5%	Shortness of breath, hypoxia, chest pain, decreased breath sound on side with pneumothorax	If <30% pneumothorax seen on initial CXR and patient is relatively asymptomatic, repeat CXR in 4 hours, if no progression of pneumothorax and patient without symptoms, then observe. Repeat CXR in 12–24 h. If pneumothorax enlarges or if the patient develops symptoms, then place a small pigtail catheter. See protocol below (Loranga et al. 2000). If <30% pneumothorax with or without hypoxia, then place a small pigtail catheter with a Heimlich valve. Patient may be discharged home after insertion of pigtail. Have patient return in 24–48 h for a repeat inspiration/expiration CXR with the pigtail clamped. If no pneumothorax seen then pigtail can be removed. Placement of large chest tube is indicated for persistent or worsening pneumothorax.
Hemothorax	Rare	Shortness of breath, decreased breath sounds, chest pain, shoulder pain	If a hemothorax is visible on a CXR, a chest tube must be inserted to prevent a clotted hemothorax and associated restrictive pulmonary function.
Air embolism	Rare	Unstable vital signs, cardiac arrest	Air embolism is fatal only if more than 50–100 ml of air is aspirated. This is less of a risk in intubated patients since there is no negative pressure with inspiration.
Cardiac arrythmia	Common, rarely occurs postop	Palpitations, changes seen on EKG (PVCs, PACs or right bundle branch block)	If seen during procedure, this is secondary to catheter or guide wire presence in right atrium or ventricle. Right bundle branch blocks are seen with contact of the catheter with the right side of the ventricular septum. Treatment is to pull back on wire or catheter until EKG is normal. If present postop, then catheter should be pulled back and correctly placed and positioned.

Table 1 Common complications and management of central venous catheters

Complications	*Incidence*	*Signs and symptoms*	*Management*
Exit site infection	3–20%	Tenderness, erythema and swelling at port site. Incidence of infection was thought to be higher in Hickman-type catheters, however this was not seen in a randomized trial (Mueller et al. 1992:11)	The most common cause of infection is Gram-positive organisms such as *Staph. aureus*, *Staph. epidermidis*, or streptococcal species. Occasionally, Gram-negative organisms, such as *E. coli*, pseudomonal species, and klebsiella species, may be the pathogen. Polymicrobial infections with staphyococcal and pseudomonal species can also occur. Fungal infections may occur especially the candidal species. Rarer pathogens, such as *Rhodotorula glutinis* (a fungal species), *Chyrseobacterium indologenes*, and *Pseudallescheria boydii* have also been reported (Hsueh et al. 2003:16; Nulens et al. 2001:15; Perez et al. 1988:13). Port removal is not necessary as initial treatment (Olson 1987: et al. 381; Hiemenz et al. 1986:37). Blood cultures should be obtained from the port site and a peripheral site (about 50% of infections will yield a positive culture) (Muller et al. 1992:11). Complete blood count should be obtained to ascertain the patient's granulocyte count. Initial treatment is aimed at Gram-positive species with broad coverage for Gram-negative organisms, such as pseudomonas. Non-neutropenic patients should receive vancomycin (40 mg/kg/day) and gentamicin (5 mg/kg/day) given through the port. Neutropenic patients should receive zosyn/gent/ vancomycin given through the port. Treatment with the appropriate antibiotics should be given until WBC is normal, patient is afebrile and surveillance cultures are negative. Indications for PAC removal include: (1) unresolved, or worsening symptoms despite adequate antibiotic treatment; (2) persistent bacteremia after 72 h of appropriate antibiotic therapy; (3) recurrence or persistence of positive blood culture after 14 days of appropriate antibiotic therapy and persistent fungemia.
Tunnel infection	Not distinguished from above	Induration, erythema and tenderness over tunneled catheter	See treatment of exit site infection.
Bacteremia	Same as above	Fever, positive blood culture	See treatment of exit site infection.

Complications	*Incidence*	*Signs and symptoms*	*Management*
Catheter tip occlusion	1–22%	Inability to draw back blood or infuse chemotherapeutic agent	Initial strategies include: (1) changing the patient's arm or head position; (2) have patient perform a valsalva maneuver (in case the tip occlusion is secondary to the tip being up against the wall of the vein) (3) flushing with 5–10 mL of normal saline; (4) flushing with 3 mL of heparinized saline (300 U); (5) repeated attempts to aspirate blood. If all the above maneuvers fail then consider thrombolytic therapy. Urokinase can be used in the following manner. 1. 5000 U of reconstituted urokinase can be given through the port. After the urokinase instillation, inject the port with 1–2 mL of heparinized saline 2. Wait 15 min and re-attempt aspiration 3. If this fails, then repeat the above steps twice for a total of the 15 000 U of urokinase instillation 4. If this fails, then instill 40 000 U of urokinase into the port 5. After 12 h, another aspiration attempt can be performed.
Catheter fracture	Rare	Fairly rare event, most are asymptomatic and seen only on CXR obtained for inability to flush or draw from catheter (36%), pain/ swelling by supraclavicular region (29%), shoulder pain (12%), palpitations (7%), pectoral swelling (5 %), chest pain (5 %), 'swishing sound' during fluid infusion (2%)	Catheter fracture is thought to occur to secondary pinch-off syndrome where the catheter has been inserted too medially and is trapped (pinched) between the clavicle and the 1st rib. If the catheter fractures and embolus is suspected, CXR should be obtained. Prompt removal of catheter is necessary. This can be done through a transcutaneous approach via the femoral vein.
Venous thrombosis	1.5–62%	Progressive swelling of the arm or face. Most venous thromboses are asymptomatic, incidence of venous thrombosis in randomized studies where venograms were routinely performed whether or not patient has symptoms reveal an incidence of 38–62%	Anticoagulation should be started with heparin and switched over to coumadin. The duration of antiocoagulation is controversial. Given that these patients are hypercoagulable, a duration of 3–6 months seems appropriate. Several studies have treated these port-induced thromboses with the port in place without problems. It seems reasonable to leave the port in place while the patient is on anticoagulation therapy.

CXR, Chest-X-ray; EKG, electrocardiogram; PVC, premature reatricular contractions
PAC, Port-a-Cath; WBC, white blood cell count.

References

Bern MM, Lokich JJ, Wallach SR, et al. (1990) Very low doses of warfarin can prevent thrombosis in central venous catheters. A randomized prospective trial. *Ann Intern Med* **112**(6):423–8.

Bock SN, Lee RE, Fisher B, et al. (1990) A prospective randomized trial evaluating prophylactic antibiotics to prevent triple-lumen catheter-related sepsis in patients treated with immunotherapy. *J Clin Oncol* **8**(1):161–9.

Bow EJ, Kilpatrick MG, Clinch JJ (1999) Totally implantable venous access ports systems for patients receiving chemotherapy for solid tissue malignancies: A randomized controlled clinical trial examining the safety, efficacy, costs, and impact on quality of life. *J Clin Oncol* **17**(4):1267.

Broviac JW, Cole JJ, Scribner BH (1973) A silicone rubber atrial catheter for prolonged parenteral alimentation. *Surg Gynecol Obstet* **136**(4):602–6.

Coccheri S, Palareti G, Cosmi B (1999) Oral anticoagulant therapy: efficacy, safety and the low-dose controversy. *Haemostasis* **29**(2–3):150–65.

Cole JJ, Dennis MB, Hickman RO, et al. (1972) Preliminary studies with the fistula catheter—a new vascular access prosthesis. *Trans Am Soc Artif Intern Organs* **18**:448–51.

De Cicco M, Matovic M, Balestreri, et al. (1997) Central venous thrombosis: an early and frequent complication in cancer patients bearing long-term silastic catheter. A prospective study. *Thromb Res* **86**(2):101–13.

Ecoff L, Barone RM, Simons RM (1983) Implantable infusion port (Port-A-Cath). *Nita* **6**:406–8.

Gilon D, Schectes D, Rein AJ, et al. (1998) Right atrial thrombi are related to indwelling central venous catheter position: insights into time course and possible mechanism of formation. *Am Heart J* **135**(3):457–62.

Henrickson KJ, Axtell RA, Hoover SM, et al. (2000) Prevention of central venous catheter-related infections and thrombotic events in immunocompromised children by the use of vancomycin/ciprofloxacin/heparin flush solution: A randomized, multicenter, double-blind trial. *J Clin Oncol* **18**(6):1269–78.

Hickman RO, Buckner CD, Clift RA, et al. (1979) A modified right atrial catheter for access to the venous system in marrow transplant recipients. *Surg Gynecol Obstet* **148**:871–5.

HICPAC (Hospital Infection Control Practices Advisory Committee) (1995) Recommendations for preventing the spread of vancomycin resistance. *Infect Control Hosp Epidemiol* **16**:105–13.

Hiemenz J, Skelton J, Pizzo PA (1986) Perspective on the management of catheter-related infections in cancer patients. *Pediatr Infect Dis* **5**:6–11.

Hsueh PR, Teng LJ, Ho SW, et al. (2003) Catheter-related sepsis due to *Rhodotorula glutinis*. *J Clin Microbiol* **41**(2):857–9.

Laronga C, Meric F, Truong MT et al. (2000) A treatment algorithm for pneumothoraces complicating central venous catheter insertion. *Am J Surg* **180**(6):523–6 [discussion 526–7].

Masci G, Magagnoli M, Carnaghi C, et al. (2003) Minidose warfarin prophylaxis for catheter-associated thrombosis in cancer patients: can it be safely associated with fluorouracil-based chemotherapy? *J Clin Oncol* **21**(4):736–9.

Monreal M, Raventos A, Lerma R, et al. (1994) Pulmonary embolism in patients with upper extremity DVT associated to venous central lines—a prospective study. *Thromb Haemost* **72**(4):548–50.

Monreal M, Alastrue A, Rull M, et al. (1996) Upper extremity deep venous thrombosis in cancer patients with venous access devices—prophylaxis with a low molecular weight heparin (Fragmin). *Thromb Haemost* **75**(2):251–3.

Mueller BU, Skelton J, Callender DP, et al. (1992) A prospective randomized trial comparing the infectious and noninfectious complications of an externalized catheter versus a subcutaneously implanted device in cancer patients. *J Clin Oncol* **10**(12):1943–8.

Nulens E, Bussels B, Bols A, et al. (2001) Recurrent bateremia by *Chryseobacterium indologenes* in an oncology patient with a totally implanted intravascular device. *Clin Microbiol Infect* **7**(7):391–3.

Olson TA, Fisher GW, Lupo MC, et al. (1987) Antimicrobial therapy of Broviac catheter infections in pediatric hematology oncology patients. *J Pediatr Surg* **22**(9):839–42.

Perez RE, Smith M, McClendon J, et al. (1988) *Pseudallescheria boydii* brain abscess. Complication of an intravenous catheter. *Am J Med* **84**(2):359–62.

Raad II, Hachem RY, Abi-Said D, et al. (1998) A prospective crossover randomized trial of novobiocin and rifampin prophylaxis for the prevention of intravascular catheter infections in cancer patients treated with interleukin-2. *Cancer* **82**(2):403–11.

Rackoff WR, Weiman M, Jakobowski D, et al. (1995) A randomized, controlled trial of the efficacy of a heparin and vancomycin solution in preventing central venous catheter infections in children. *J Pediatr* **127**(1):147–51.

Randolph AG, Cook DJ, Gonzales CA, et al. (1998) Benefit of heparin in central venous and pulmonary artery catheters: a meta-analysis of randomized controlled trials. *Chest* **113**(1):165–71.

Ratcliffe M, Broadfoot C, Davidson M, et al. (1999) Thrombosis, markers of thrombotic risk, indwelling central venous catheters and antithrombotic prophylaxis using low-dose warfarin in subjects with malignant disease. *Clin Lab Haematol* **21**(5):353–7.

Schuster M, Nave H, Piepenbrock S, et al. (2000) The carina as a landmark in central venous catheter placement. *Br J Anaesth* **85**:192–4.

20
Gastrointestinal surgery

Eileen M Segreti
Charles Levenback

Introduction

The intestine is vulnerable to injury and obstruction as a result of involvement by gynecologic malignancies. The small and large intestine are frequently involved with metastases from epithelial ovarian cancer. The rectum may be invaded from locally advanced cervical or vaginal cancer. In addition to involvement at the time of diagnosis, the intestine may be adversely affected after successful treatment of gynecologic malignancies. The bowel may suffer consequences such as obstruction from adhesions, radiation enteritis, stricture or fistula. This chapter will focus on common surgical procedures performed on the gastrointestinal tract during the management of gynecologic malignancies. Laparoscopy for the management of bowel disorders in gynecologic oncology is an exciting alternative to traditional laparotomy. Advances in instrumentation have accelerated the use of minimally invasive surgery in gynecologic oncology surgery as well as general surgery Laparoscopy offers less blood loss, less postoperative pain, faster recovery, but usually longer operating times and often higher intraoperative costs. Laparoscopic surgical staplers, intracorporeal suturing devices, hand ports, unipolar and bipolar cautery, harmonic scalpel, LASER and hemoclips facilitate these procedures. Outcomes analysis will be important to evaluate the success and complications of this technique in gynecologic oncology patients. This chapter will focus on general open techniques with commentary as necessary to accommodate the laparoscopic approach.

Small bowel surgery

Indications

Small bowel resection is often necessary to remove obstructed, perforated, or tumor-infiltrated intestine. Small bowel may be obstructed at the time of primary diagnosis of ovarian cancer or manifest as a secondary recurrence of ovarian cancer. Endometriosis is also occasionally responsible for small bowel stricture or obstruction, particularly in the terminal ileum. If the obstruction is focal, surgical resection and reanastomosis is the preferable management approach. Similarly, for radiation-induced small bowel stricture, resection of the damaged segment is preferable; however if this is not feasible, a small bowel bypass may be necessary. Small bowel bypass may be necessary when damaged small bowel is densely adherent to a fibrotic and heavily irradiated pelvis. In addition, a bypass procedure may be considered to palliate an intestinal obstruction in a woman with refractory ovarian cancer and a short life expectancy.

Anatomic considerations

The small bowel begins just distal to the gastric pylorus and ends at the cecum. The duodenum is a C-shaped segment of small intestine that is about 25 centimeters long and curves around the head of the pancreas. The jejunum is approximately 2.5 meters long and separated from the duodenum by the ligament of Trietz. The distinction between the jejunum and the ileum is more gradual. The ileum is the most distal segment of the small bowel and is approximately 3.5 meters long. The small bowel is perfused by straight vessels that disperse into the anterior and posterior surfaces of the bowel. The straight vessels emerge from the arcades of the superior mesenteric artery. In the ileum the straight vessels are surrounded by fat, and the fat encroaches upon the bowel wall. In the jejunum, the vasa recta are more easily seen, as the mesenteric fat ends prior to reaching the jejunal serosa. The venous drainage of the small bowel is to the superior mesenteric vein which is a tributary of the portal vein. The autonomic nervous system, in conjunction with the gastrointestinal hormonal system, regulates peristalsis and bowel secretory action. The parasympathetic ganglia lie within the bowel wall, whereas the sympathetic ganglia lie close to the origin of the superior mesenteric artery.
The small intestine has four layers. They are the mucosa, the submucosa, the muscularis, and the serosa. The mucosa contains villi and crypts which greatly increase the absorptive surface area. The submucosa is a strong connective tissue layer important for structural integrity. It is especially vital to include

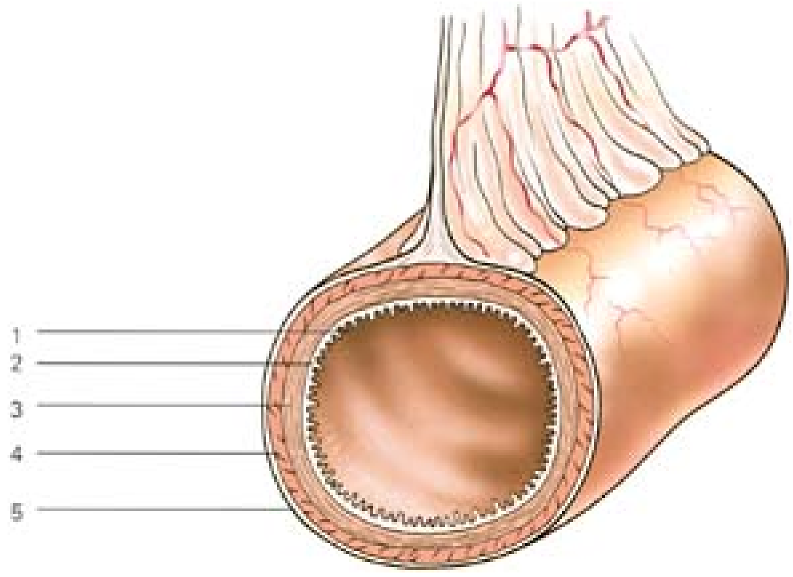

Figure 1

Layers of the small intestine
1 Mucosa
2 Submucosa
3 Inner circular muscle
4 Outer longitudinal muscle
5 Serosa

this layer during bowel reanastomosis. The muscularis consists of an inner circular layer and an outer longitudinal layer. The serosa is the outermost layer and is a continuation of the mesothelium that lines the peritoneal cavity (Figure 1).
The terminal ileum is the site of absorption of the fat-soluble vitamins, A, D, E and K, as well as vitamin B_{12}. Extensive resection of the terminal ileum will require vitamin supplementation.

Surgical procedures

Small bowel resection

To be successful, resection must completely remove the damaged or involved intestinal segment. Intestinal continuity must then be re-established using healthy ends of bowel that are approximated without tension while maintaining a good blood supply. Tissues should be handled gently, and a watertight anastomosis should be achieved. If not precluded by a complete or advanced small bowel obstruction, a mechanical and antibiotic bowel preparation should be administered to decrease the chance of infection or anastomotic breakdown.
There are several different means to affect a small bowel reanastomosis. Automatic gastrointestinal (GIA) staplers can be used, or the anastomosis can be entirely hand-sewn. The damaged or obstructed portion of the small bowel is identified. The vascular arcades are visualized by transillumination. Non-crushing intestinal clamps or Penrose drains can be used to occlude the

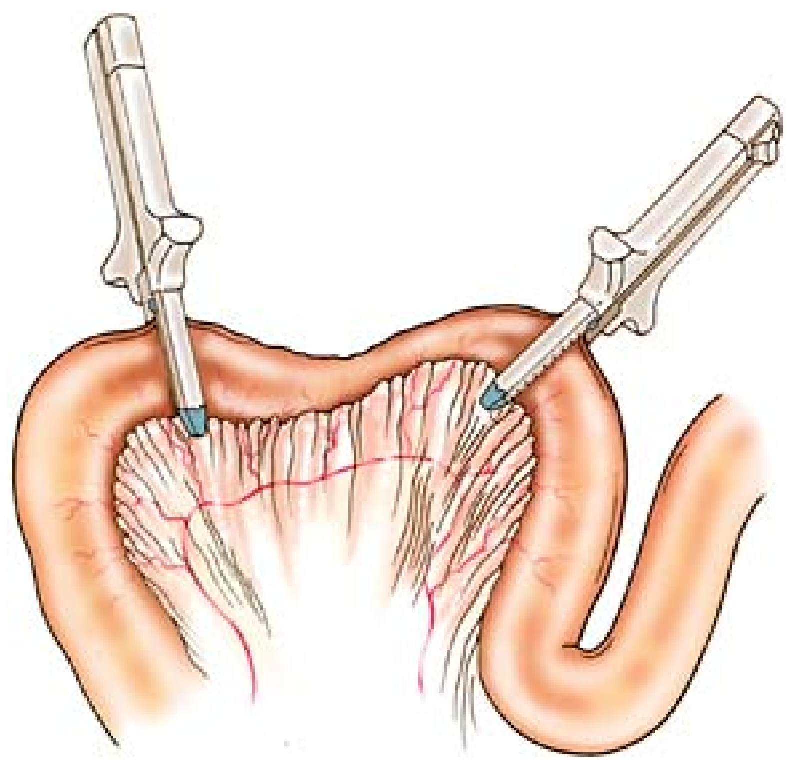

Figure 2

Positioning of clamps

bowel lumen on either side of the site of resection. A small defect is created in the mesentery proximal and distal to the affected bowel. Either a stapler or bowel clamps are used to isolate the abnormal section of small intestine. The stapler or clamps are oriented obliquely to maximize the mesenteric side of the bowel and minimize the antimesenteric side (Figure 2). This maneuver will also create a larger lumen thereby decreasing the chance of a subsequent stricture. The mesentery is scored with scissors or an electrocautery device, and the vessels are isolated between small clamps. The vessels are cut and secured with 2–0 suture. Alternatively, an LDS stapler can be used to secure the mesenteric vessels. Commonly, staplers are used to create a side-to-side, functional end-to-end, anastomosis. The ends of the small bowel are juxtaposed and inspected for viability. The tissue should be pink and not dusky. If there is any doubt as to bowel viability, the bowel is excised further until there is no question as to the quality of the bowel. The anastomosis must be tension-free. The loops are mobilized as necessary to relieve any tension. The antimesenteric borders are lined up in parallel. Stay sutures are placed 5–8 cm from the closed bowel ends along the antimesenteric border. The corners of the antimesenteric staple line are then excised (Figure 3). One arm of the GIA is then placed along the antimesenteric border of each limb of bowel and the

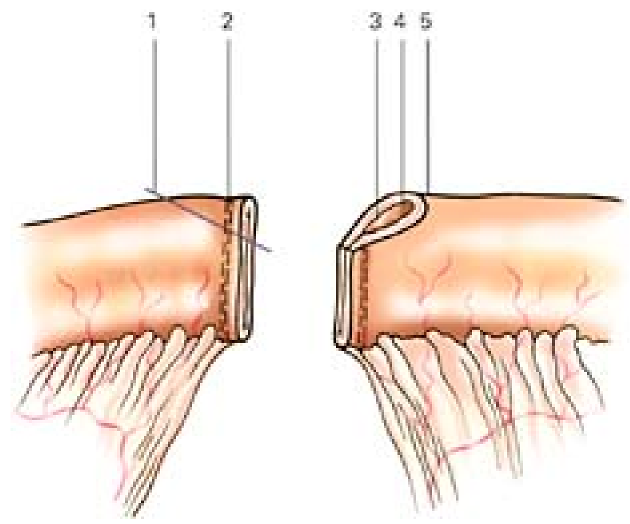

Figure 3

Preparation for anastomosis
1 Incision
2 Staple line
3 Bowel lumen
4 Mucosa
5 Serosa

stapler closed (Figure 4). Firing the stapler places two double rows of titanium staples, between which a knife cuts (Figure 5). The staple line is then inspected

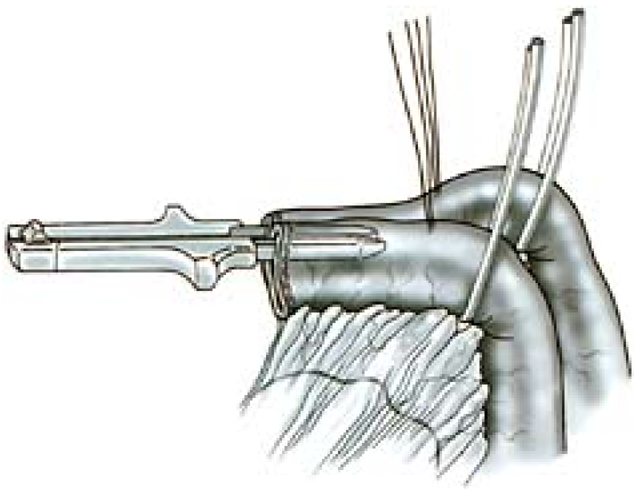

Figure 4

Positioning of stapler

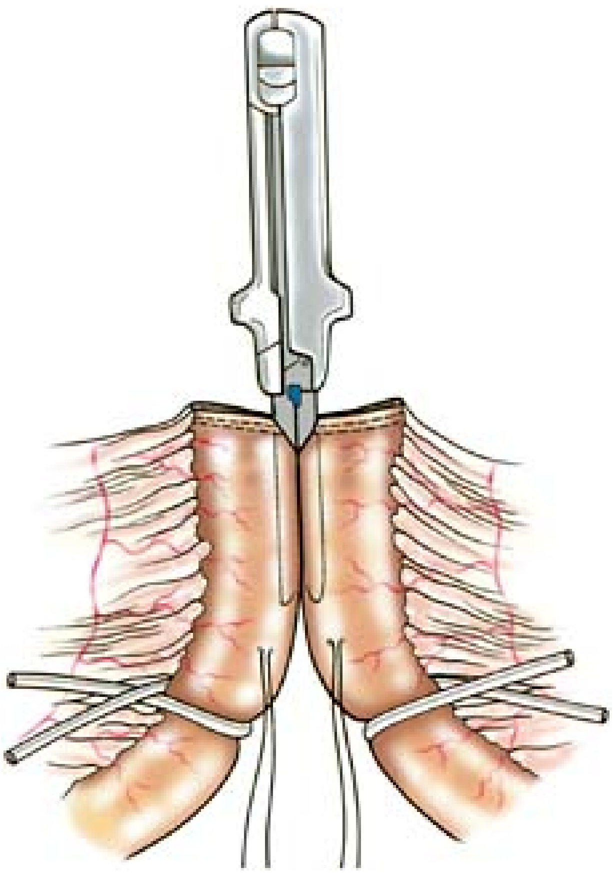

Figure 5

Stapling

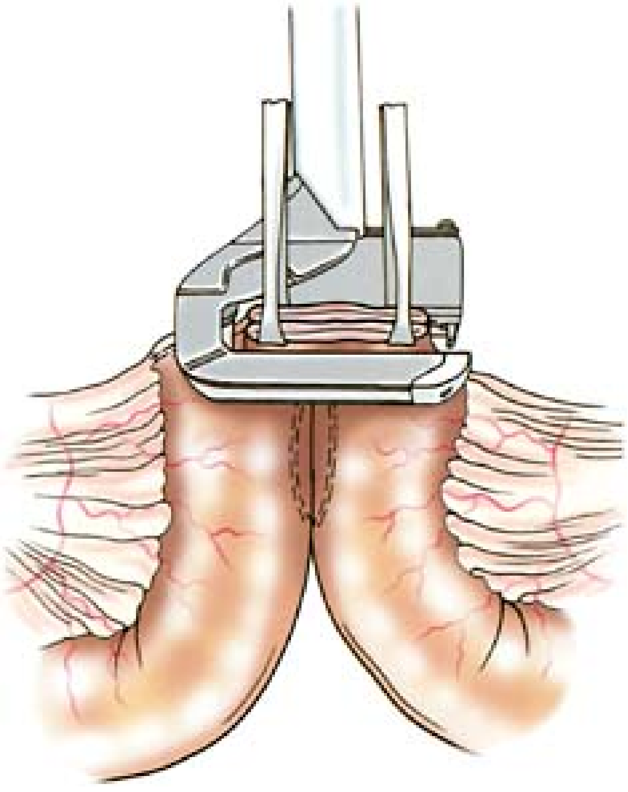

Figure 6

Positioning of thoracoabdominal stapler

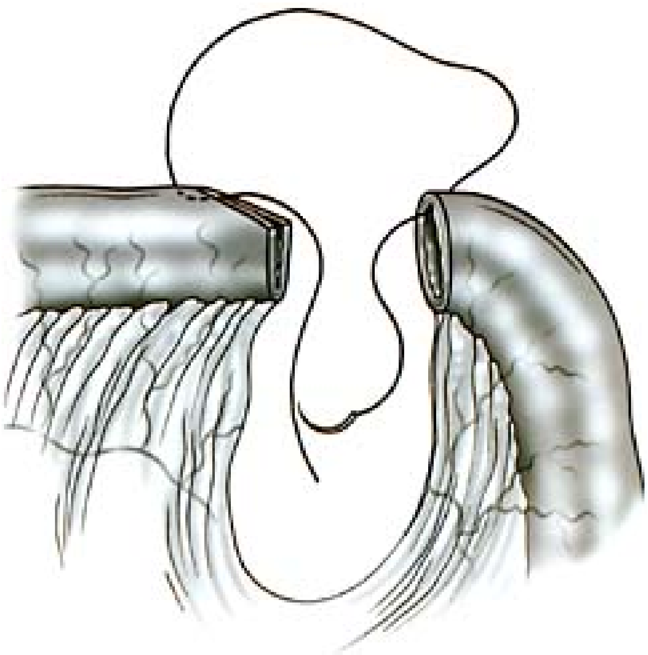

Figure 7

End-to-end anastomosis

for bleeding. Any bleeding area should be reinforced with an interrupted suture. Next, the remaining defect is grasped with Allis clamps and a thoracoabdominal (TA) stapler is set and fired to close the remaining enterotomy. The staple lines should overlap to prevent leakage at the anastomosis (Figure 6). Excess tissue above the TA device can be excised.

The small bowel can also be anastomosed end to end with a single or double layer of sutures. If the bowel lumens are of disparate sizes, a Cheatle slit can be made on the antimesenteric border of the smaller lumen

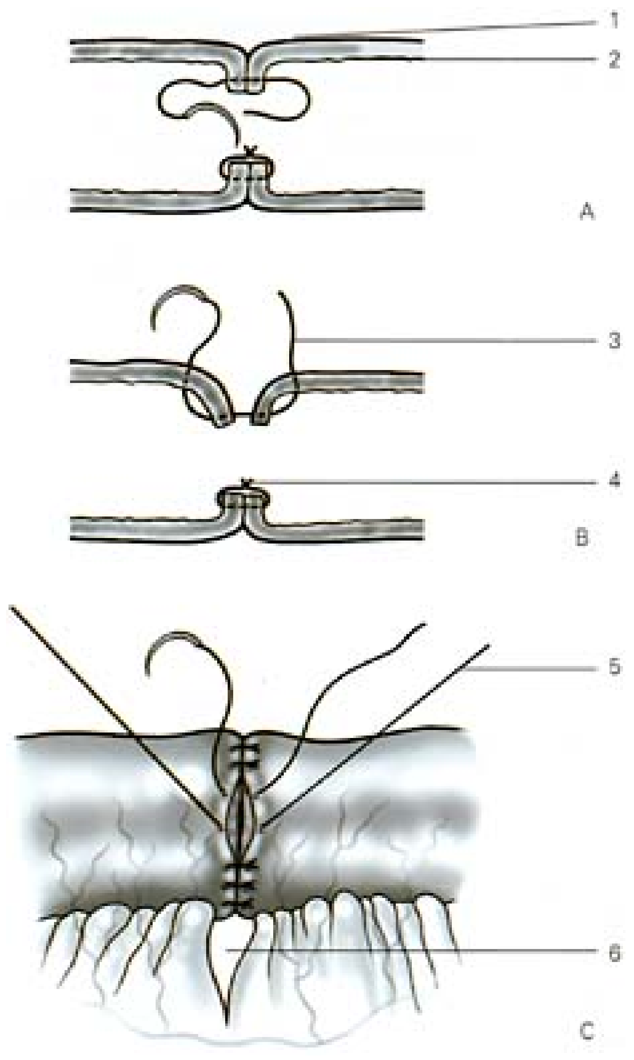

Figure 8

The Gambee technique
1 Serosa
2 Mucosa
3 Last suture
4 Lumen
5 Inverting suture held until all sutures in place
6 Defect to be dosed without vessel compromise

(Figure 7). If two layers are used, the inner layer is a continuous inverted layer of absorbable suture, and the outer layer is a series of interrupted inverting silk sero-muscular sutures. In a single layer closure, either continuous inverted or an interrupted inverted single-layer technique may be used (Gambee et al. 1956) (Figure 8). In the Gambee technique, 3–0 sutures are placed from the mucosa through the bowel wall to the serosa and back through, serosa to mucosa. The knots are tied on the mucosal side, and the sutures are placed 3 mm apart. Closure should be secure enough to prevent seepage of liquid. The mesenteric defect is then closed to prevent an internal hernia and subsequent bowel strangulation.

A diseased terminal ileum may require extensive resection with ileoascending or ileotransverse entero-colostomy in an effort to avoid an anastomosis in heavily irradiated tissues (Hoskins et al. 1987). An ileoileoenterostomy should probably be avoided within 10 cm of the cecum. The blood supply in this area may be compromised.

An alternative to small bowel resection is *small bowel bypass*, whereby an abnormal area of bowel is bypassed and a bowel anastomosis is created proximal to the abnormal area. This will allow intestinal contents to progress beyond an area of obstruction. A side-to-side enteroenterostomy is created, either with staplers or a double or single-layer suture technique (Figure 9).

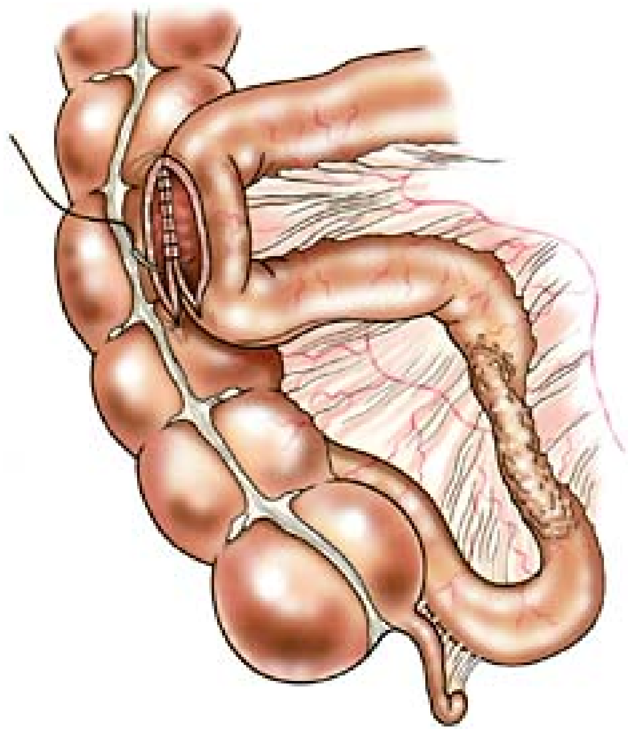

Figure 9

Side-to-side enterocolostomy

Alternatively, the bowel is divided proximally and distally to the damaged segment, and the damaged bowel is completely excluded from the intestinal stream. One end of the bypassed limb is brought up to the skin as a mucous fistula. A third option is to divide the bowel proximal to the damaged area and create an anastomosis distally. The mucous fistula may be incorporated into the inferior aspect of the incision. A disadvantage of bowel bypass, is that it may subsequently foster a blind loop syndrome. The blind loop syndrome is characterized by bacterial overgrowth with subsequent cramps, diarrhea, anemia and weight loss (Schlegel and Maglinte 1982). If a small bowel fistula is being bypassed, it is important to completely isolate this bowel from the intestinal stream.
Laparoscopic treatment of small bowel obstruction secondary to adhesive disease is possible in a subset of patients with two or fewer prior surgeries. There is a high conversion rate to open surgical repair as perforation as well as poor visualization have been reported (Wullstein 2003).

Large intestine surgery

Indications

Partial colectomy, rectosigmoid resection, colostomy and abdominal perineal resection are all utilized to treat gynecologic malignancies and occasionally endometriosis. These procedures may be integral to ovarian cancer debulking, treatment of radiation complications, or a component of pelvic exenteration for cervical, endometrial, vaginal or vulvar cancer. If the sphincter or distal rectum is damaged or involved with tumor, colostomy may be required to provide fecal continence. Stoma formation is required for either permanent or temporary fecal diversion. End colostomies are typically preferred for permanent stomas, as they are smaller and prone to fewer complications (Segreti et al. 1996). Loop colostomies are preferred when stomal closure is anticipated or a large bowel obstruction occurs secondary to advanced,

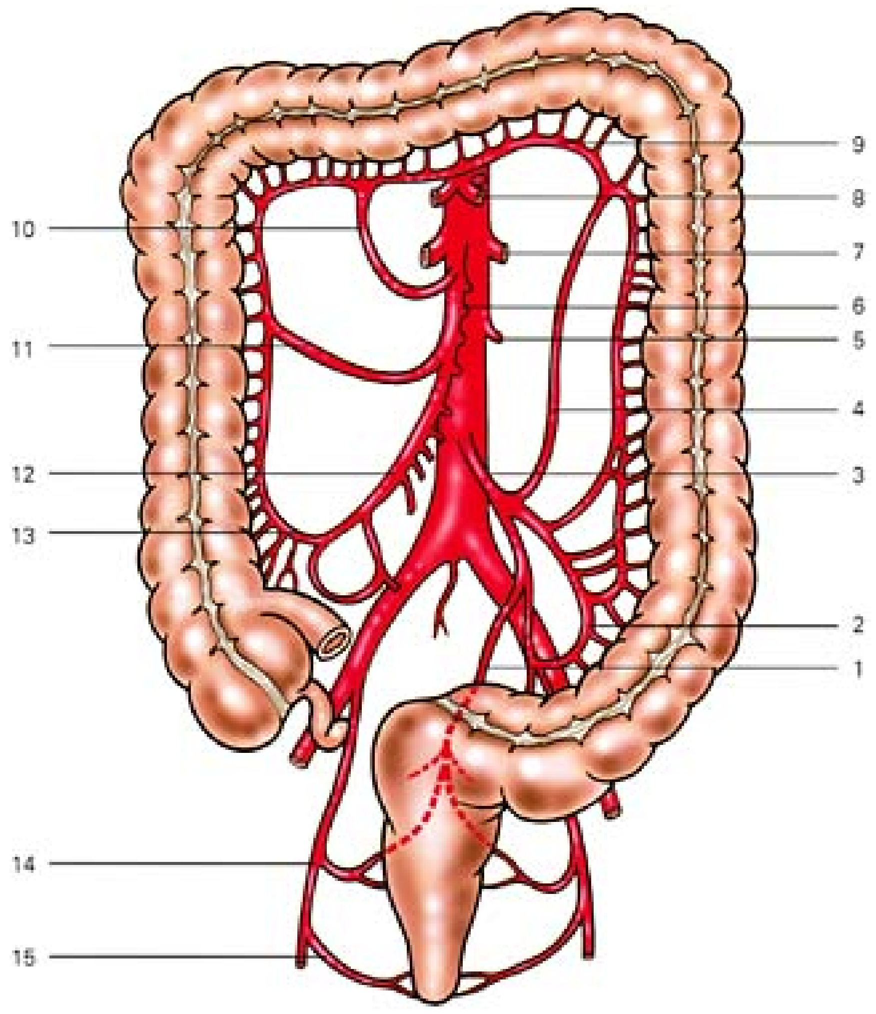

Figure 10

Blood supply to the colon and rectum
1 Superior rectal artery
2 Sigmoid artery
3 Inferior mesenteric artery
4 Left colic artery
5 Ovarian artery
6 Superior mesenteric artery
7 Renal artery
8 Celiac trunk
9 Marginal artery
10 Middle colic artery
11 Right colic artery
12 lleojejunal artery
13 lleocolic artery
14 Middle rectal artery
15 Inferior rectal artery

refractory ovarian cancer, and life expectancy is short. After a colostomy has served its purpose by allowing a distal anastomosis to heal or a fistula to be repaired, intestinal continuity is restored by closing the colostomy. Lastly, removal of the appendix may facilitate ovarian cancer debulking, urinary conduit construction, or serve as prophylaxis against future infectious or neoplastic complications.

Anatomic considerations

The blood supply to the colon and rectum is derived from branches of the superior mesenteric, inferior mesenteric, and the internal iliac arteries. The right colon is supplied by the ileocolic artery, the right colic artery, and a branch of the middle colic artery. The transverse colon is chiefly supplied by the middle

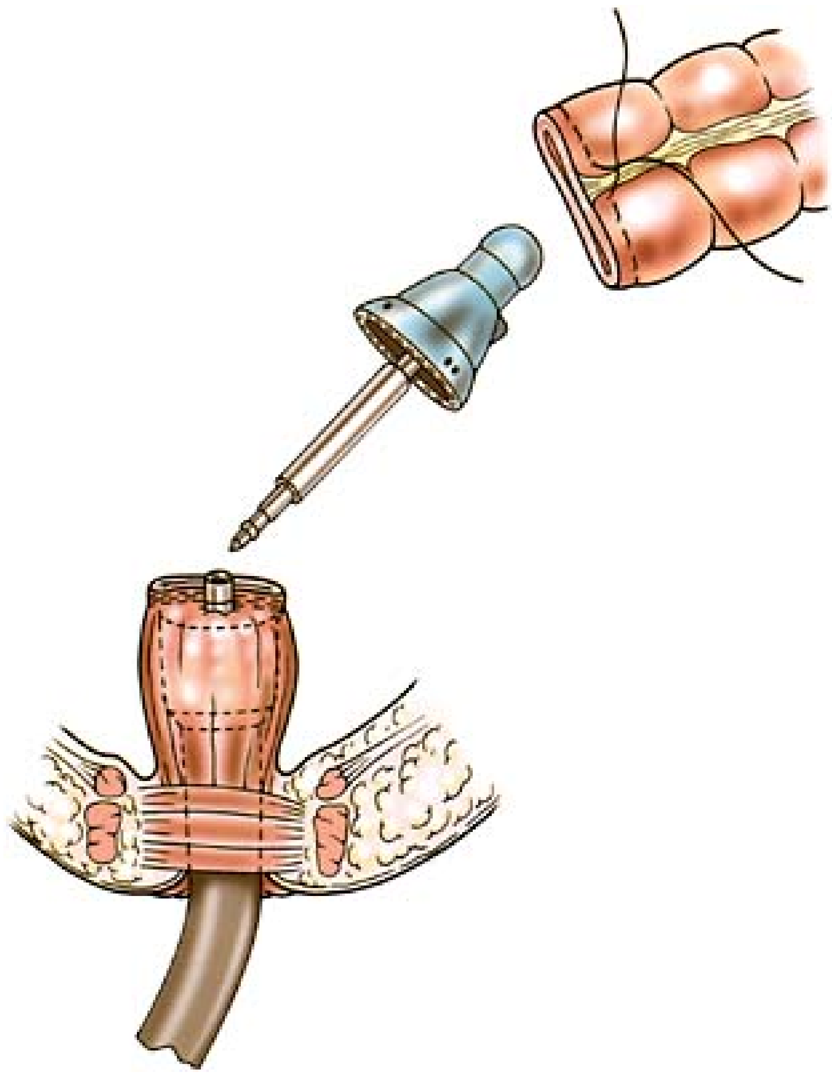

Figure 11

Positioning of purse-string suture

colic artery, but there is a communication with the inferior mesenteric arterial system via the marginal artery of Drummond. The inferior mesenteric artery supplies the colon from the splenic flexure to the proximal rectum. The inferior mesenteric artery branches into the superior rectal artery, the sigmoidal arteries, and the left colic artery. The distal rectum receives its blood supply from the paired middle and inferior rectal arteries, which originate from the internal iliac artery system (Figure 10).

The appendix is the embryologic continuation of the cecum. Its location is identified by the confluence of the three taenia of the cecum. The position of the appendiceal tip relative to the cecum may vary. The tip may be found lateral, medial or behind the cecum. The mesentery of the appendix passes behind the terminal ileum. The blood supply to the appendix is derived from the appendiceal artery, which is a branch of the ileocolic artery.

The nerves to the colon parallel the blood supply and consist of sensory afferent nerves, and the motor nerves from the autonomic system. The anal sphincter is under voluntary motor control. The colonic wall is more muscular than that of the small bowel. In addition, the longitudinal muscles are gathered in three places to form the taenia coli. The colon also has numerous fatty epiploica that hang from the taenia.

Operative procedure

The colon contains much more infectious material than the small bowel, and a thorough mechanical and antibiotic bowel preparation is very important prior to large bowel surgery. The principles of *large bowel resection and reanastomosis* are similar to those for small intestinal anastomosis and are based on the blood supply and the location of the pathologic seg-

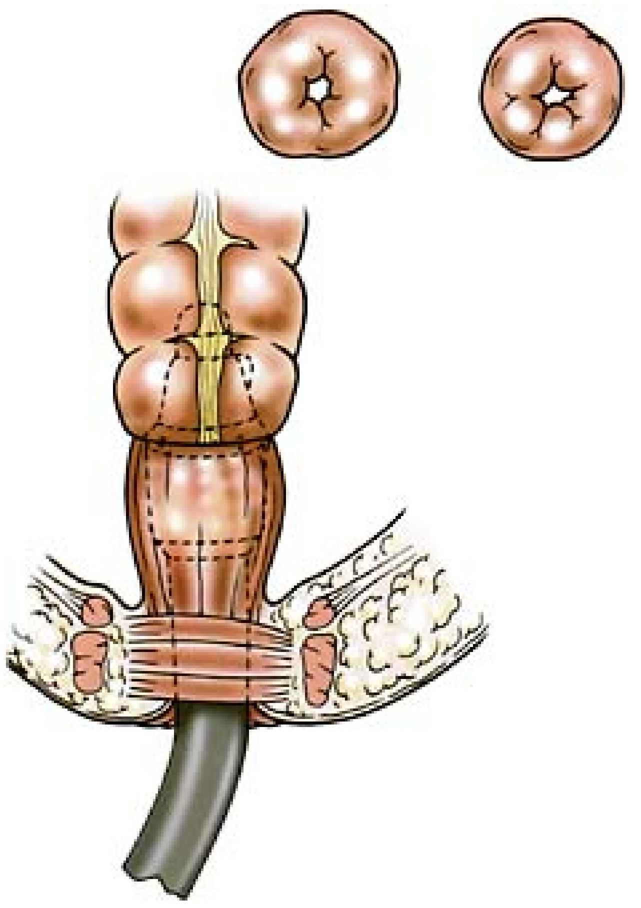

Figure 12

Two intact 'donuts' of tissue

ment. Resection and reanastomosis of the colon and proximal rectum are performed equally well with either a handsewn or stapled technique. For the distal rectum, the automatic end-to-end circular stapling device (EEA) has provided the ability to perform successful low and very low rectal anastomoses. Adequate mobility of the rectosigmoid must be achieved by incision along the lateral peritoneal reflection. The two ends of the bowel to be anastomosed must be mobile enough to lie adjacent to each other without tension. The largest EEA device that fits comfortably should be used. Sizers are available to measure the lumen. After resection of the diseased large bowel, a purse-string is placed around the proximal lumen. This is easily performed with the purse-string instrument and a straight needle. The purse-string suture is then secured around the anvil of the EEA instrument (Figure 11). The rectal

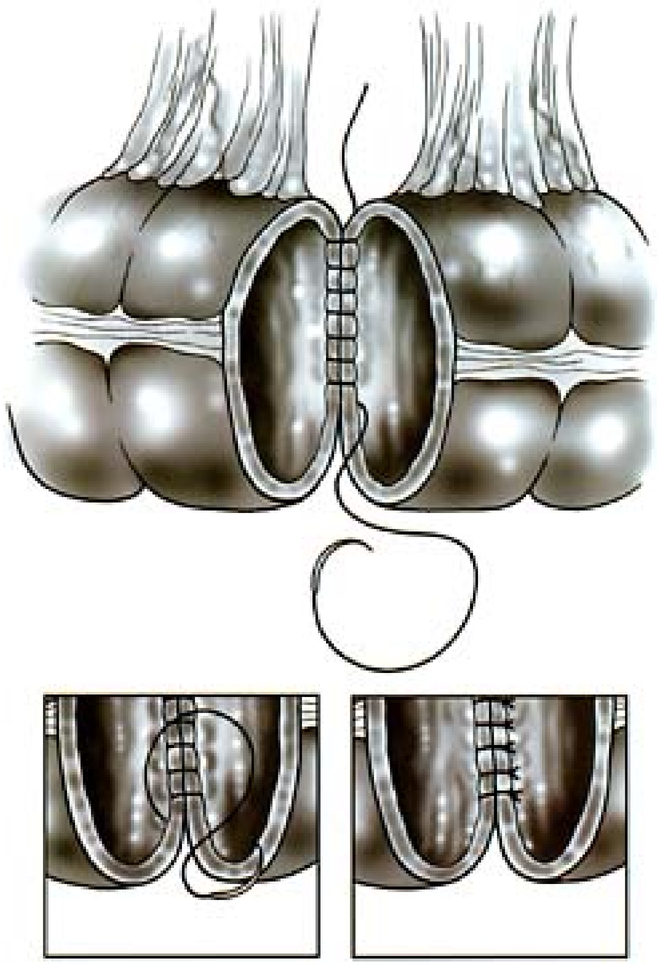

Figure 13

Single-layer anastomosis, with (inset left) continuous sutures and (inset right) interrupted sutures stump can similarly be circumscribed with a purse-string suture. Alternatively, a stapler can be used to close the rectal pouch. A trocar attached to the EEA is then used to puncture the closed rectal pouch at the site of the future anastomosis. The trocar is then removed, and the anvil shaft can be inserted into the EEA instrument. By turning the wingnut on the EEA handle, the two lumens are approximated. After releasing the safety, the handle is squeezed and two circular rows of staples are placed. A circular knife cuts the excess inverted tissue, and two 'donuts' are created. The wingnut is then turned in the opposite direction to open the instrument which is then withdrawn gently through the rectum. The two donuts should be inspected and be complete (Figure 12). A defect in one of the donuts is reason to redo or repair the anastomosis. The seal of the anastomosis can be tested by filling the pelvis with saline and injecting air into the rectum. Bubbles indicate an air leak that should be oversewn. One can also visually inspect the anastomosis with a sigmoidoscope.

Hand-sutured colonic anastomoses have classically been two layers in the tradition of Lembert and Halsted. The two-layer closure consists of a running inverted layer with 3–0 chromic or polyglactic acid suture, followed by an outer layer of interrupted 3–0 silk Lembert sutures. Recently, several investigators have reported using a one-layer inverting colonic closure with satisfactory results (Curley et al. 1988, Max et al. 1991, Ceraldi et al. 1993). One-layer closures are faster and less expensive than the two-layer closure and stapled closure respectively. The single-layer closure is performed with 3–0 or 4–0 polypropylene or polyglyconate suture using a double-armed needle. The suture is started at the mesenteric border of the bowel (Figure 13). The sutures are place from outside in, including a larger amount of serosa, muscularis and submucosa (approximately 5 mm) than mucosa (minimal) to affect mucosal inversion. The knot is secured outside the bowel lumen. Each end of the suture is then continued around to the antimesenteric border, spacing the stitches 3–4 mm apart. The sutures are then tied together.

The TA instrument can also be used to create an end-to-end anastomosis by triangulation (Figures 14–19). Three stay sutures are placed equidistantly on each limb of the bowel. One stay suture should be located at the level of the mesentery, and the other two stay sutures should be placed to form an equilateral triangle. The back wall is stapled first, and the mucosa is inverted. The second row of staples is placed to overlap the first row. The last row of staples is placed, and the mucosa is everted. The diameter of the lumen is palpated to ensure adequate size.

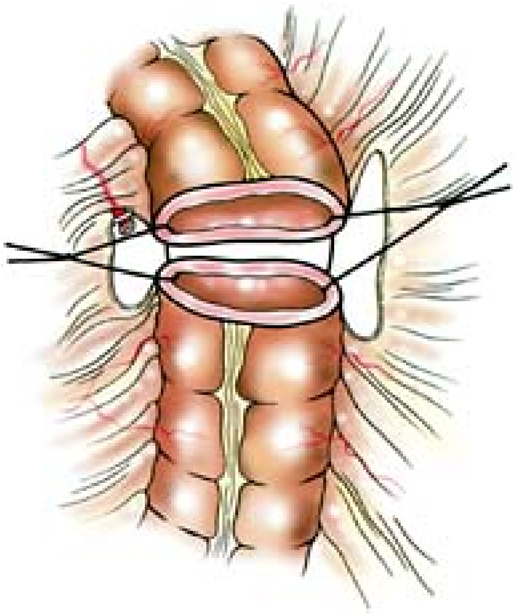

Figure 14

End-to-end anastomosis by triangulation

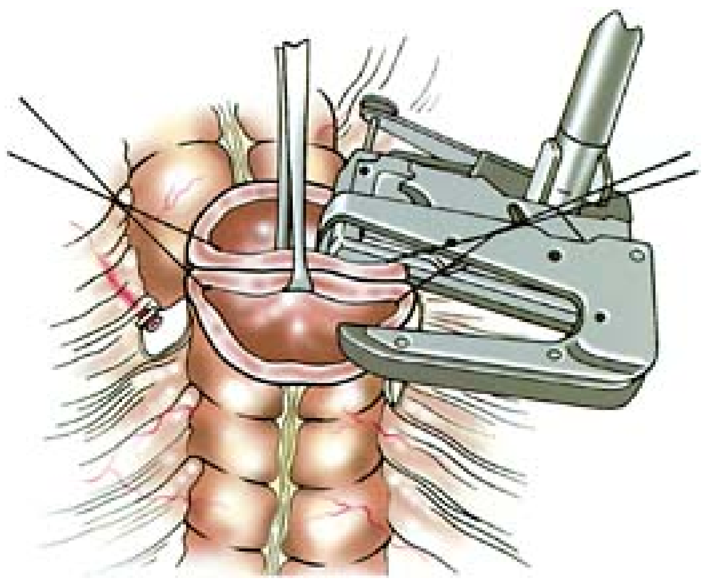

Figure 15

The posterior wall is stapled first

When *colostomy* formation is considered, a mechanical and antibiotic bowel preparation should be given preoperatively. The patient should consult an enterostomal therapist for preoperative teaching and evaluation of the abdominal wall for optimal stomal placement. Stomas should ideally pass through the rectus muscles and avoid abdominal wall folds or creases

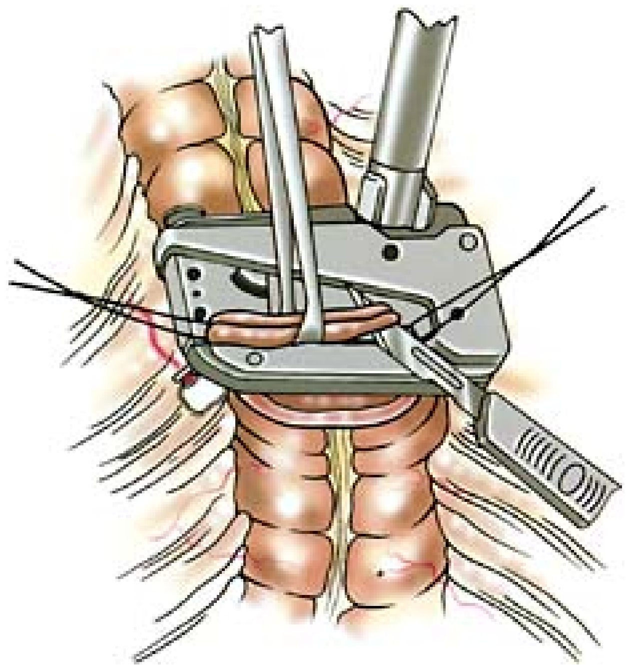

Figure 16

Excise the excess tissue

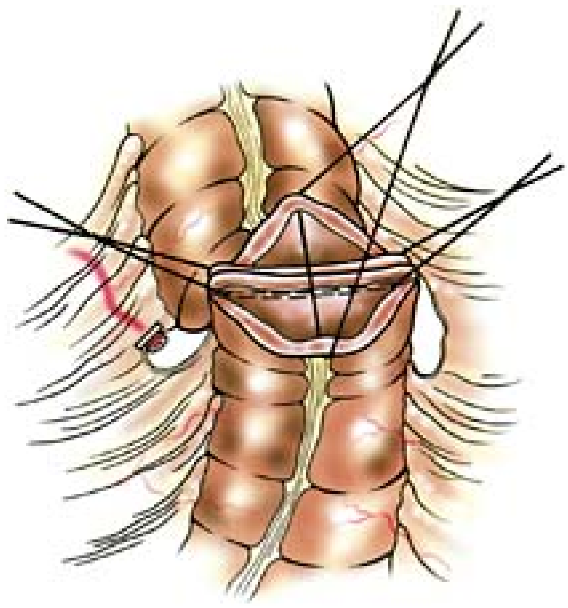

Figure 17

Place traction suture midway

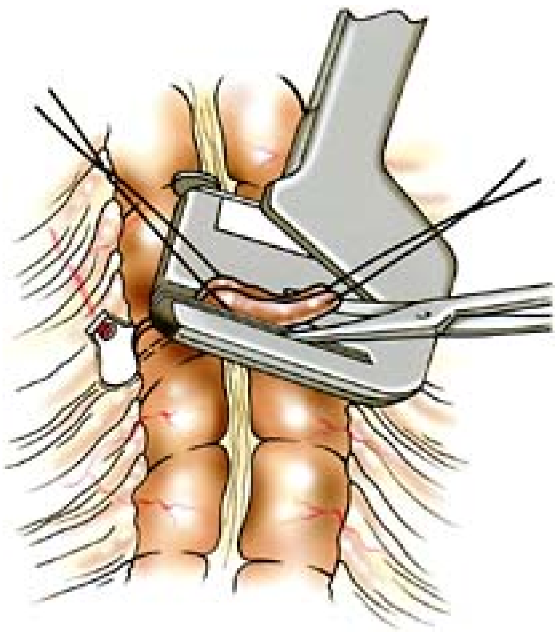

Figure 18

Excise redundant tissue after stapling

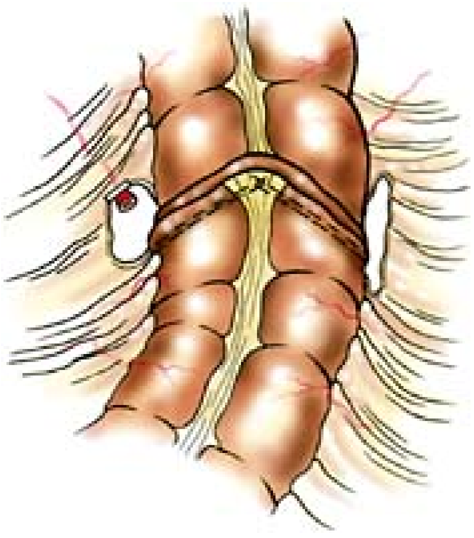

Figure 19

Completed reanastomosis

(Figure 20). The patient should be examined in both the sitting and standing position. Stoma placement in the waistline should be avoided.
A vertical laparotomy incision is helpful to provide adequate exposure. Prior to dividing the colon, the bowel is mobilized by dividing the lateral peritoneal

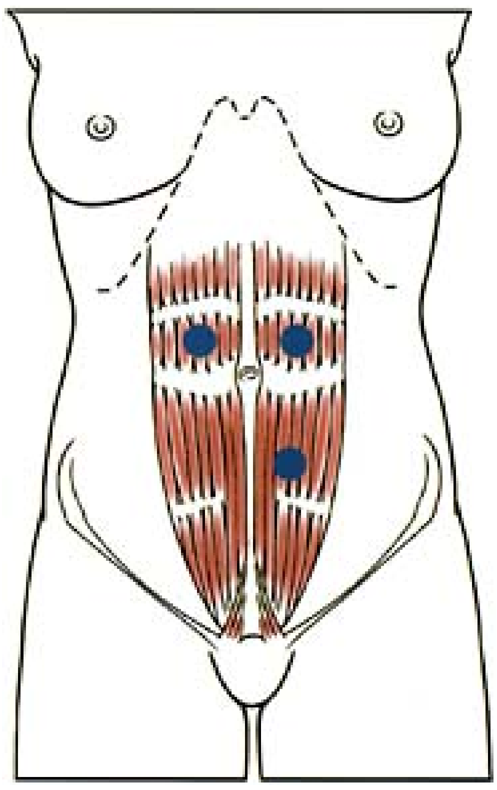

Figure 20 Ideal sites for stomas

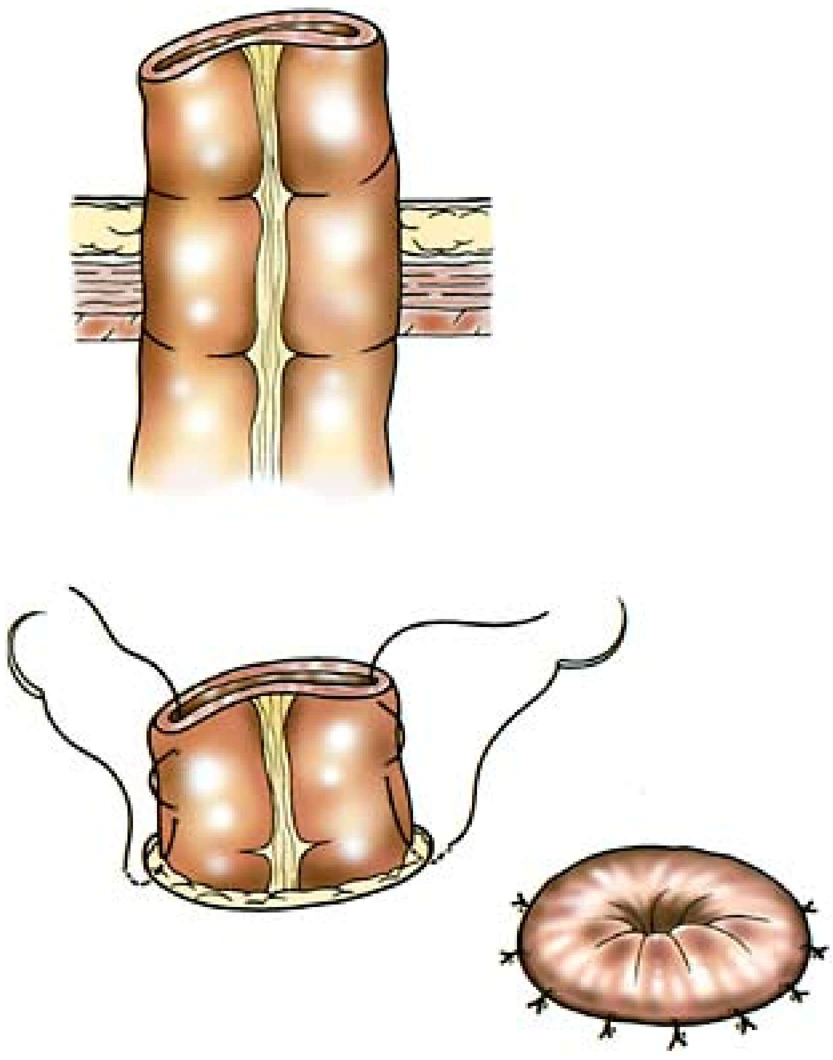

Figure 21

Maturation of the stoma in a ‘rosebud’ fashion

attachments. Adequate mobility must be achieved to provide a tension-free stoma. The distal bowel is resected or oversewn as a pouch. A 3 cm circular skin button is removed at the previously marked site. The subcutaneous tissues are bluntly separated. The anterior rectus sheath is incised in a cruciate fashion. The rectus muscles are split longitudinally with care taken to avoid the deep epigastric vessels. The peritoneum is then incised and two fingers are passed through the abdominal wall. The stapled bowel end is grasped with a Babcock clamp and brought through the stomal aperture. Care is taken to not twist the mesentery. Excess fat and mesentery are trimmed from the stoma. The mesentery can be fixed to the lateral peritoneum to prevent internal hernia. The abdominal incision is then closed. The staple line on the bowel is excised. The stoma is matured in a rosebud fashion by inserting the needle into the skin 1 cm from the stomal edge, then running it up the bowel serosa and muscularis for one or two stitches, exiting on the mucosal side and securing the knot over the mucocutaneous junction (Figure 21).

A *loop colostomy* may be situated at either the proximal or distal transverse colon. If a loop colostomy is performed for palliation of large bowel obstruction secondary to advanced, refractory ovarian cancer, one may choose the distal transverse colon to maximize colonic length. However, if the purpose is to create a temporary diverting colostomy while an anastomosis heals, the proximal transverse colon is usually preferred. A 10–12 cm transverse skin incision is made in the right or left upper quadrant. The fascia is incised transversely, and the rectus muscles are separated longitudinally. The peritoneal cavity is entered sharply. When a large bowel obstruction is present, the transverse colon is easily identified due to its dilatation. The adjacent omentum is dissected off the loop of colon. A defect is created in the mesentery to allow passage of a Penrose drain with which to lift and manipulate the colon. The fascial incision is then partially closed. A flat plastic bridge is passed through the mesenteric defect and secured to the skin with nylon suture. The skin incision, if larger than needed for the stoma, may be partially closed with skin staples or absorbable sutures. The colon is then opened either longitudinally along the taenia, or at a transversely oriented angle. The bridge may be removed in 7 to 10 days (Figure 22).

A *loop stoma is closed* by incising the skin adjacent to the mucocutaneous junction, elevating the stoma with Allis clamps, and dividing the filmy attachments to the subcutaneous tissues. The fascial edge is then identified, and the plane sharply developed between

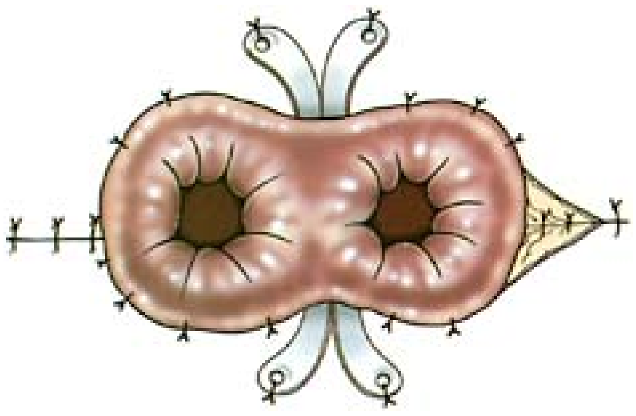

Figure 22

Use of a bridge in loop colostomy

the stoma and the fascial opening. The peritoneal adhesions are then lysed. The stomal edge can then be excised, and an extraperitoneal one- or two-layer closure can be performed. The loop is then dropped back into the peritoneal cavity and the fascia closed with delayed absorbable suture. The skin defect can be packed open and left to close secondarily, or alternatively staples can be used for immediate skin closure (Hoffman et al. 1993).

A faster option to close a loop colostomy is to use the TA stapler. After incising the mucocutaneous junction, the edges of the stoma are grasped with Allis clamps. The colostomy edges are held together to form a line perpendicular to the long axis of the bowel. This will allow the maximal lumen diameter. The stapler is fired, and the excess tissue is excised.

To *close an end stoma,* an exploratory laparotomy is usually required to identify the distal limb and create a large bowel anastomosis. Laparoscopy may alternatively be used and an extraperitoneal closure affected, if the distal limb is nearby and can be mobilized adequately. The end stoma is excised in a similar manner to that described for a loop stoma. The mucocutaneous junction of the distal end is excised. A large bowel anastomosis is performed similarly to that described in the previous section. Mesenteric defects are closed to prevent internal hernias.

Another option to palliate a large bowel obstruction is a colonoscopically placed endoluminal stent to acutely alleviate the obstruction. This may serve as a bridge prior to a definitive resection or as a pure palliative step in a poor operative candidate (Carter 2002).

Appendectomy is often performed during debulking surgery for ovarian cancer. Similarly, the appendix may be involved with endometriosis and require removal at the time of definitive treatment of severe endometriosis. Appendectomy is accomplished by isolating and ligating the blood supply to the appendix and closing or burying the stump of the appendix to prevent fecal spillage. If present, filmy adhesions from the appendix to the peritoneal surfaces are lysed. If the appendix is retrocecal, the cecum is mobilized by incising the peritoneal reflection. The appendiceal artery is isolated, doubly clamped, ligated and secured with 2–0 suture. The base of the appendix is then crushed between two straight hemostats. The specimen is excised between the hemostats, and the stump tied off with 2–0 suture (Figure 23). Alternatively, the unligated stump can be buried into the cecum with a Z-stitch or purse-string suture. Ligation of the stump, prior to burial into the cecum, may promote a mucocele or an abscess. Another

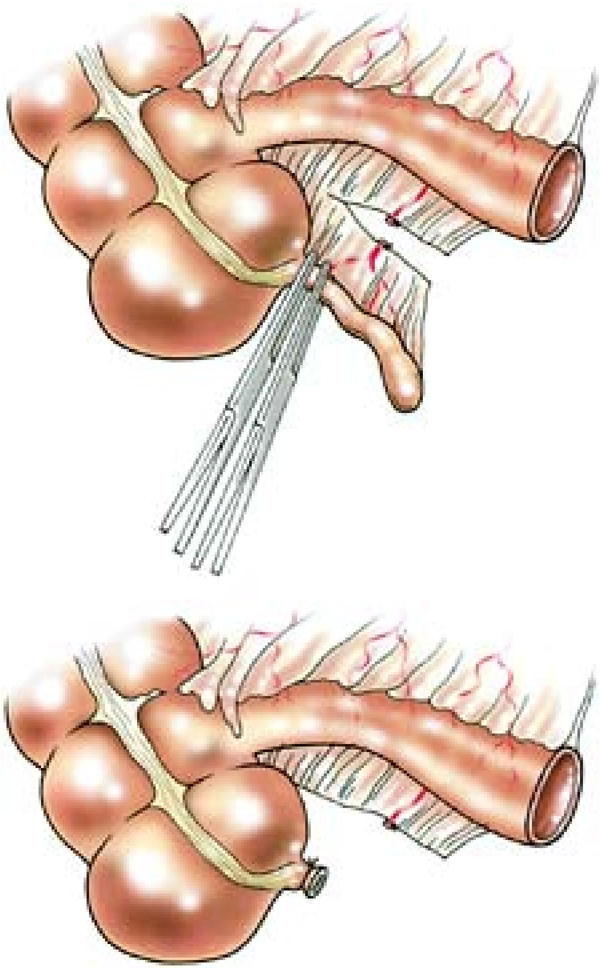

Figure 23

Use of hemostats in appendectomy

approach after dividing and securing the appendiceal artery is to remove the appendix using the GIA or the TA stapling device.

Enteral feeding and drainage procedures

Indications

Gastrostomy tubes are useful for drainage and for decompression of the stomach and the small bowel, if a prolonged ileus is anticipated. Patients with endstage ovarian carcinoma and small bowel obstruction may also benefit from palliative gastrostomy tube placement. In the postoperative setting, gastrostomy tubes may also be used for enteral nutrition.

Needle jejunostomy is a useful modality for providing enteral nutrition postoperatively. Tube jejunostomy is sometimes indicated to decompress or stent the small bowel.

Anatomic considerations

The blood supply to the stomach is derived from the celiac trunk. The greater curvature of the stomach is supplied by the right and left gastroepiploic arteries. The lesser curvature is supplied by the right and left gastric arteries. The right gastric artery and the right gastroepiploic artery are branches of the common hepatic artery. The left gastric artery is a branch of the celiac trunk, and the left gastroepiploic artery is a branch of the splenic artery. Routes of venous drainage include the gastric and the gastroepiploic veins as well as small tributaries of the esophageal veins.

Surgical procedure

Gastrostomy tubes can be placed percutaneously with endoscopic guidance or can be placed at the time of laparotomy. The stomach should be mobile enough to reach the anterior abdominal wall. At laparotomy, a Malecot gastrostomy tube is placed into the abdominal cavity via a left upper quadrant stab incision in the midclavicular line.

Two concentric purse-string sutures of chromic catgut are placed in the anterior stomach seromuscular wall approximately 1 cm apart. The electrocautery instrument is used to create an opening in the stomach through which the Malecot tube is placed into the stomach. The inner purse-string is tied first, then the outer purse-string, creating an inverted tunnel (Figure 24). Three to four interrupted 2–0 silk sutures are placed to approximate the stomach to the anterior abdominal wall. After the abdomen is closed, the tube is secured to the skin with a nylon suture. If the tube subsequently is dislodged, it can often be immediately replaced through the gastrocutaneous fistula.

Needle jejunostomy is a useful modality for providing enteral nutrition postoperatively (Figure 11). The technique entails creating an intramural tunnel in the jejunal wall, through which a catheter is placed into

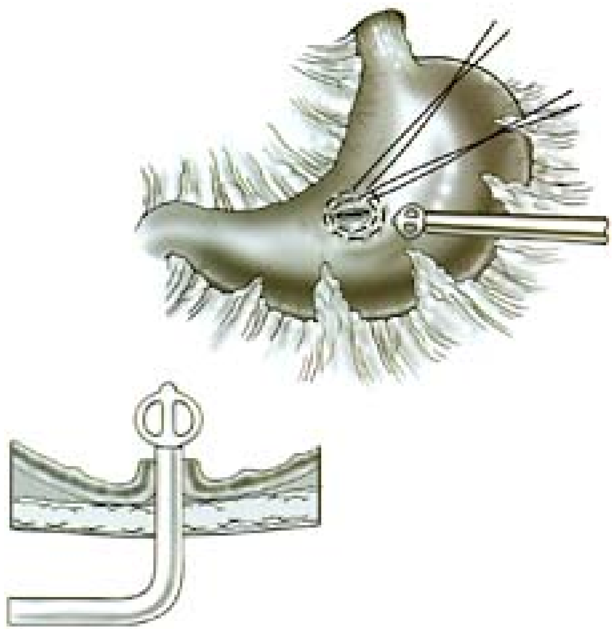

Figure 24

Gastrostomy tube placement

the lumen of the bowel. A purse-string suture 1 cm in diameter is placed but not tied in the antimesenteric side of the jejunum at least 12 cm from the ligament of Trietz. A mobile loop of jejunum that easily reaches the abdominal wall is chosen. A 2 inch long 14 gauge needle is inserted through the purse-string into the seromuscular layer for the entire length of the needle. The needle is then directed into the bowel lumen, and the feeding catheter and stylet are threaded through the needle. The needle is then removed. The catheter is advanced into the bowel for 20–25 cm. The stylet is then removed from the catheter. The purse-string suture is tied. Another 14 gauge needle is placed through the skin at an oblique angle similar to the angle of the catheter exiting from the bowel. The catheter is then pulled through the needle. The jejunum is then fixed to the anterior abdominal wall with 2–0 silk suture to prevent dislodgement of the catheter. Similarly the catheter is fixed to the skin to prevent kinking. Catheter position may be confirmed intraoperatively by injecting 10 cc of air and observing its passage into the jejunum. Radiographic confirmation of intraluminal tube placement can be performed with water-based contrast. A low-viscosity elemental amino acid diet is used to prevent clogging of the needle jejunostomy tube. When jejunal feeding is no longer necessary the tube is removed percutaneously

A Baker tube *jejunostomy* is inserted at laparotomy using a modified Stamm technique similar to that used for gastrostomy tube placement. The Baker tube is placed in the abdominal cavity through a stab wound in the abdominal wall. Two concentric pursestring sutures are placed in the antimesenteric edge of a mobile loop of jejunum. The balloon is inflated, and the tube is manually passed into the distal small bowel through the ileocecal valve and into the ascending colon. The small bowel is then situated in the peritoneal cavity to prevent obstruction. The purse-string sutures are tied to create an inverted tunnel. The bowel is secured to the parietal perineum with suture. If a Baker tube is used for decompression, making extra holes in the tube will facilitate drainage.

References

Carter J, Valmadre S, Dalrymple C, et al. (2002) Management of large bowel obstruction in advanced ovarian cancer with intraluminal stents. *Gynecol Oncol* **84**:176–9.

Ceraldi CM, Rypins EB, Monahan M, et al. (1993) Comparison of continuous single layer polypropylene anastomosis with double layer and stapled anastomoses in elective colon resections. *Am Surg* **59**:168–71.

Curley SA, Allison DC, Smith DE, Doberneck RC (1988) Analysis of techniques and results in 347 consecutive colon anastomoses. *Ann Surg* **155**:597–601.

Gambee LP, Garnjobst W, Hard wick CE (1956) Ten years' experience with a single layer anastomosis in colon surgery. *Am J Surg* **92**:222–7.

Hoffman MS, Gleeson N, Diebel D, et al. (1993) Colostomy closure on a gynecologic oncology service. *Gynecol Oncol* **49**:299–302.

Hoskins WJ, Burke TW, Weiser EB, et al. (1987) Right hemicolectomy and ileal resection with primary reanastomosis for irradiation injury of the terminal ileum. *Gynecol Oncol* **26**:215–24.

Max E, Sweeney WB, Bailey HR, et al. (1991) Results of 1,000 single-layer continuous polypropylene intestinal anastomoses. *Am J Surg* **162**:461–7.

Schlegel DM, Maglinte DDT (1982) The blind pouch syndrome. *Surg Gynecol Obstet* **155**:541–4.

Segreti EM, Levenback C, Morris M, et al. (1996) A comparison of end and loop colostomy for fecal diversion in gynecologic patients with colonic fistulas. *Gynecol Oncol* **60**:49–53.
Wullstein C, Gross E. (2003) Laparoscopic compared with conventional treatment of acute adhesive small bowel obstruction. *Br J Surg* **90**(9):1147–51.

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21
Urologic procedures

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Repair of ureteral injuries

Introduction

Ureteral injury occurs in 1–2% of all major gynecologic procedures. Pelvic irradiation, large pelvic tumors, endometriosis and the radicality of the procedures all increase the risk of damage. Ureteral obstruction can also occur as a result of any of the above processes, necessitating reimplantation. Theunderlying principles to be adhered to in repairing any post operative ureteral obstruction are:

1. Adequate vascular supply.
2. Adequate surgical exposure.
3. Gentle tissue handling.
4. Tension-free suturing.
5. Placing the minimum number of sutures.
6. Stenting to allow the repair to heal.

Indications

The nature and extent of the injury, the overall health of the patient and the underlying disease process must all be considered when deciding upon the type of procedure to be performed. Ureteroneocystotomy is the procedure of choice for injuries or obstruction within the pelvis at or below the level of the common iliac vessels. Bladder mobilization with a psoas hitch and/or bladder flap (Demel or Boari) may be required in order to yield a tension-free anastomosis. Ureteroneocystotomy is the preferred procedure where possible as the complication rate is lower than with ureteroureterostomy. Ureteroureterostomy is required for injuries to the abdominal portion of the ureter when the proximal portion will not reach the bladder directly.

Anatomic considerations

Vascular supply

Bladder
The bladder receives its blood supply mainly from the superior and inferior vesical arteries, both of which are branches of the anterior division of the hypogastric artery. The obturator, uterine and vaginal arteries may all also send branches to the bladder.

Ureter
The ureter takes its blood supply from branches of major vessels which it courses near. This includes the aorta as well as the renal, ovarian, iliac (common and internal), vesical and uterine vessels.

Nerve supply

Bladder
The bladder is innervated by the vesical plexus which carries efferent and afferent autonomic fibers, both sympathetic and parasympathetic. The plexus arises

from T11–L2 and courses through the base of the cardinal ligament.

Ureter

The renal (T9–T12), aortic (L1) and superior and inferior hypogastric (S2–S4) plexuses all contribute to the innervation of the ureter with autonomic fibers.

Muscles

Psoas

The psoas muscle originates from the anterior surface and lower borders of the transverse processes of the lumbar vertebral bodies and joins the iliac muscle to insert on the lesser trochanter of the femur. The muscle acts to flex the hip. It is innervated by fibers from L1–L3. Several important nerves are closely related anatomically to the psoas muscle. The iliohypogastric, ilioinguinal, lateral femoral cutaneous and femoral nerves all emerge from the lateral border of the muscle. The genitofemoral nerve arises anterolaterally and the obturator, accessory obturator and upper roots of the lumbosacral trunk all arise medially.

Operative procedure

Ureteroureterostomy

In cases of crush or similar injury, the injured ends of the damaged ureter are trimmed if necessary to reach viable bleeding tissues. This is generally not necessary for transection injuries. Each end is partially spatulated by making an incision of approximately 3–5 mm longitudinally in each ureter. These incisions should be 180° apart (Figure 1).

The ureter can be stented either by passing a stent through the injured ends towards both the bladder and the renal pelvis or by performing a cystotomy and passing a stent up through the ureter to the renal

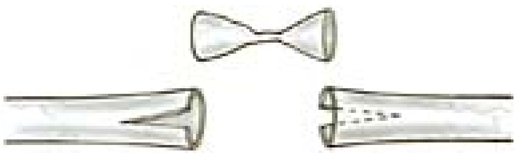

Figure 1

The injured segment is excised, ensuring that the ends to be approximated are well vascularized. Both ends are then spatulated to aid in preventing stenosis at the anastomosis site

Figure 2

Repair should be stented for at least two to three weeks. An intravenous pyelogram or pull-back ureterogram is recommended prior to stent removal to ensure patency of ureter

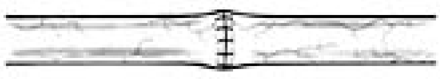

Figure 3

Ureteral repair is accomplished with four to six interrupted absorbable sutures

pelvis. This should be done before suturing the ureter. A closed suction drain should be placed in the operative field (Figure 2).

Interrupted 4–0 absorbable sutures (polyglycolic acid) are used to create the anastomosis. Care should be exercised to avoid tying the sutures too tightly or putting in too many sutures. Generally, four to six sutures are sufficient (Figure 3).

Ureteroneocystotomy with or without psoas hitch and bladder flap

In cases of crush injury or obstruction, ligate and divide the ureter as distally as possible, being mindful of the presence of fibrosis such as from radiation therapy. The distal stump is ligated with a permanent suture, such as 2–0 silk. If the ureter has been transected, the distal end should still be identified and ligated with a permanent suture. The proximal end is trimmed as necessary to ensure that the terminal ureter has adequate vascular supply to allow healing of the anastomosis. The ureter is also partially freed

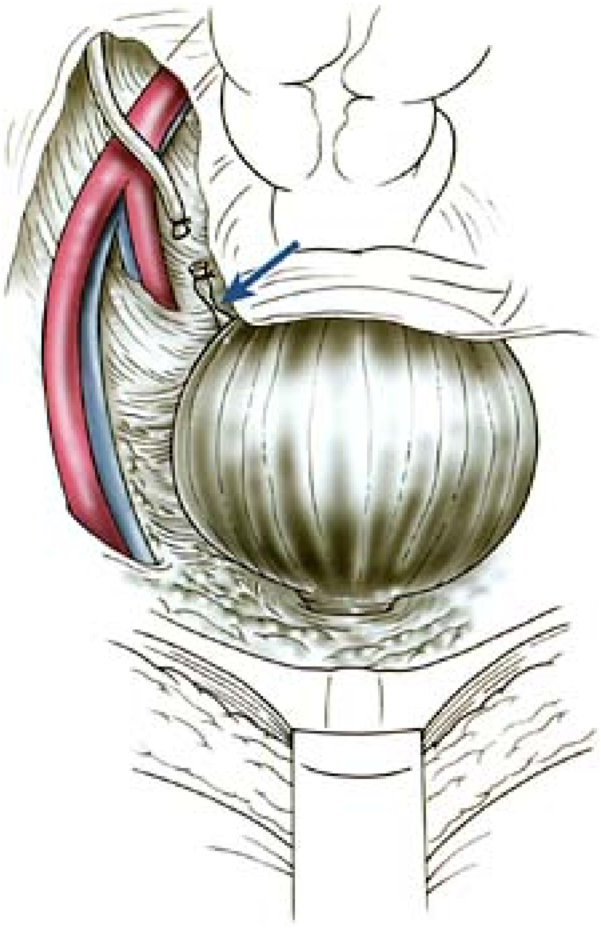

Figure 4

For ureteral injuries occurring in the pelvis, the ureter is divided and the distal end permanently ligated with non-absorbable suture

from its peritoneal attachments to provide mobility of the most distal segment. Care is taken to avoid disruption of the adventitial layer which carries the blood and nerve supply to the ureter (Figure 4).

If the ureter and the bladder can be placed in approximation without tension, then the surgeon may proceed with the anastomosis. Otherwise, an extending bladder flap may be necessary (see below).

A longitudinal extraperitoneal incision is made in the dome of the bladder. At the conclusion of the repair, this is closed transversely to take further tension off the anastomosis. A finger or a long, curved instrument is then placed in the bladder to indicate the posterolateral position on the bladder that most closely approximates to the ureter, and a cystotomy is made at this point. The ureter is then brought through the incision (Figure 5).

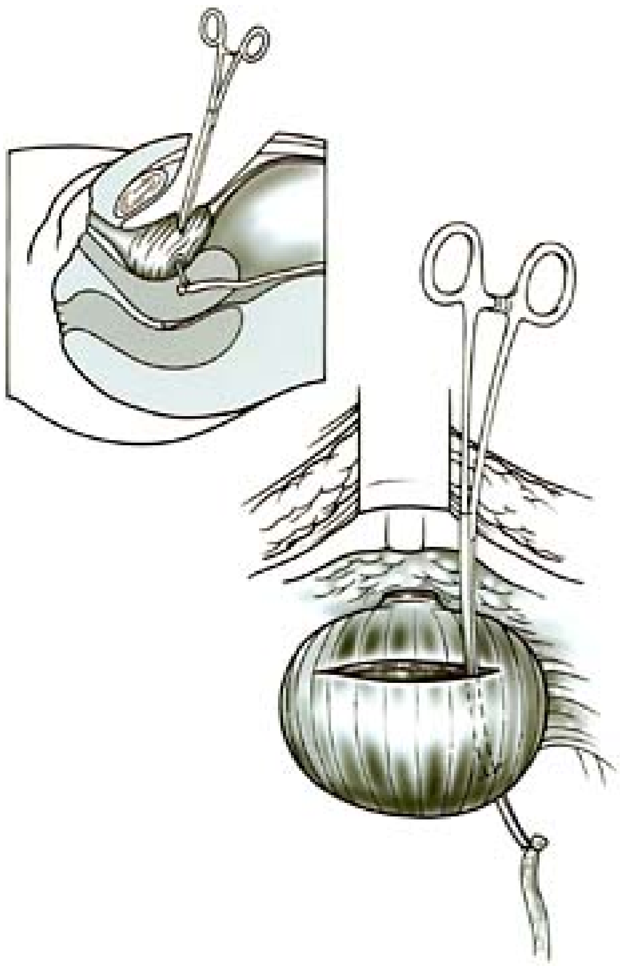

Figure 5

Working through an incision in the dome of the bladder, the ureter is brought through the bladder wall at a point that will ensure the most tension-free anastomosis

The ureter is spatulated by making two 5 mm longitudinal incisions 180° apart (Figure 6). The angles of the incisions are sutured using 4–0 absorbable sutures (polyglycolic-acid) which are tagged with the needles left on. A 28–30 cm, 7 or 8 Fr single or double J is then passed up the ureter towards the renal pelvis.

The anastomosis is performed using 4–0 absorbable interrupted sutures which include the full thickness of the ureter, but only the mucosa and submucosa of the bladder (Figure 7). Generally six sutures are required, including the previously placed angle sutures. The cystotomy is then closed and a closed suction drain is placed in the area of the anastomosis. Closure may be accomplished with a running 2–0 absorbable suture using through-and-through stitches. A second layer of 2–0 absorbable sutures may be placed incorporating the serosa and

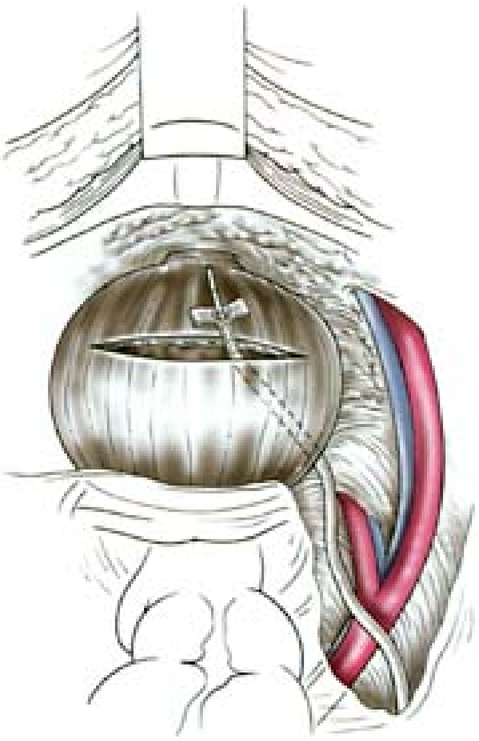

Figure 6

The ureter is spatulated and stented

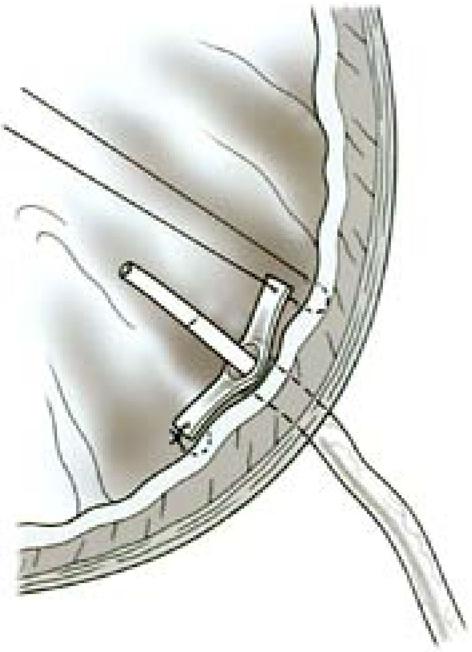

Figure 7

The anastomosis is created with interrupted absorbable sutures, full thickness through the ureter and partial thickness through the bladder

muscle but not the mucosa (Figure 8). Retrograde transurethral filling of the bladder should be performed to ensure a watertight seal. The ureteral stents may be removed in 2 weeks if a cystogram or intravenous pyelogram demonstrates ureteral patency and no leaks. A follow-up intravenous pyelogram is recommended after 1 month to confirm patency, especially in patients who have received prior radiotherapy.

If the ureter and bladder do not approximate easily then additional measures must be taken. Sufficient mobility of the bladder can often be obtained by developing the space of Retzius and dividing the anterior peritoneum and the lateral bladder attachments. The bladder can then be sutured to the psoas muscle to hold it closer to the ureter and to take up the tension that would other-

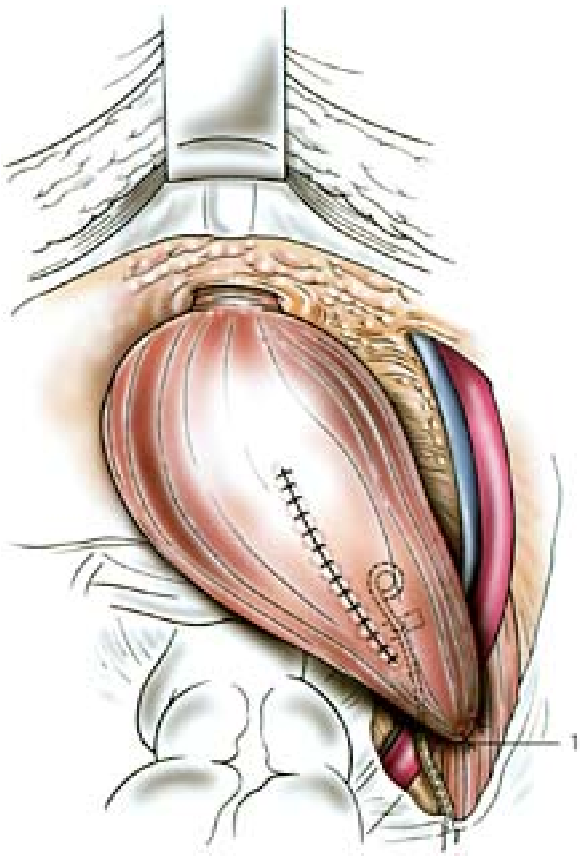

Figure 8

The cystotomy incision is closed. By making the incision transversely and closing longitudinally, the site of anastomosis can be brought closer to the ureter, thus relieving tension. A psoas hitch can then be performed (1; see text)

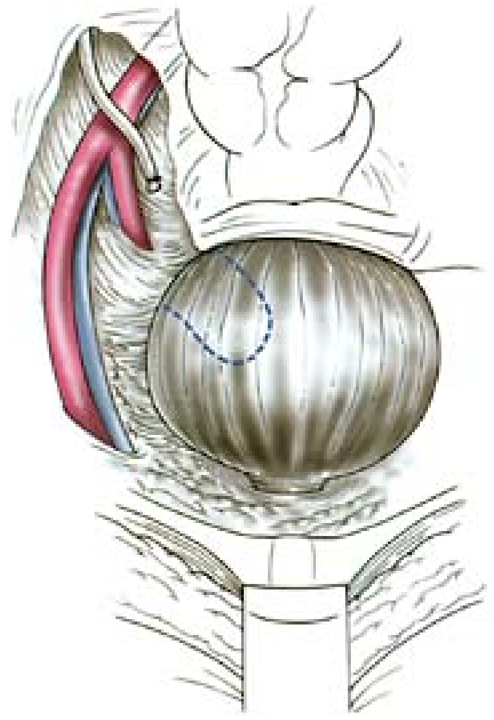

Figure 9

Boari flap: a U-shaped incision is made in the bladder

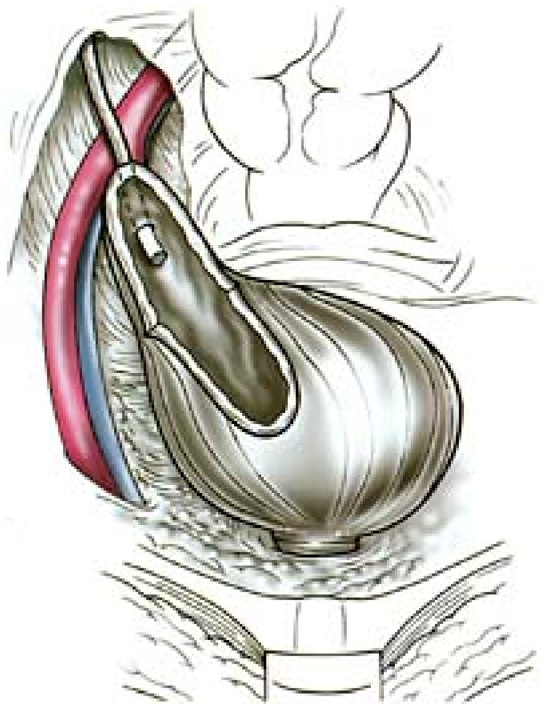

Figure 10

The flap is then 'unrolled' towards the undamaged ureter and the anastomosis performed.
Care must be exercised not to perform the anastomosis too close to the cut edge of the bladder

wise be exerted on the repair. Use 2–0 permanent suture, taking care to avoid damage to any of the nerves related to the psoas muscle.

In cases where still further mobility is required, an extending bladder flap such as those described by Boari (Figures 9–11) or Demel (Figures 12–14) may be used. The incisions are made and sutured as shown, resulting in the lengthening' of the bladder towards the ureter. Once this step is complete, the anastomosis is performed as described above.

Urinary diversion

Introduction

Urinary diversion was first described in the mid 1800s. Many different tissues and techniques have been employed, each with their own inherent

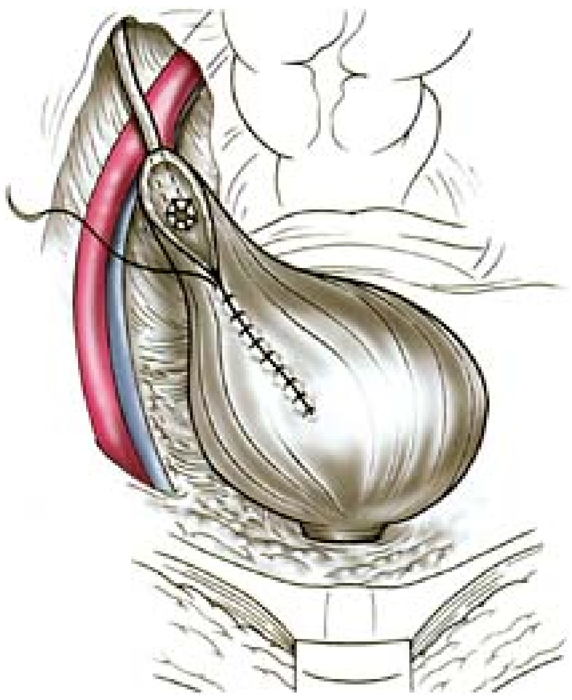

Figure 11

The flap is then closed. A psoas hitch may be performed to relieve any excess tension

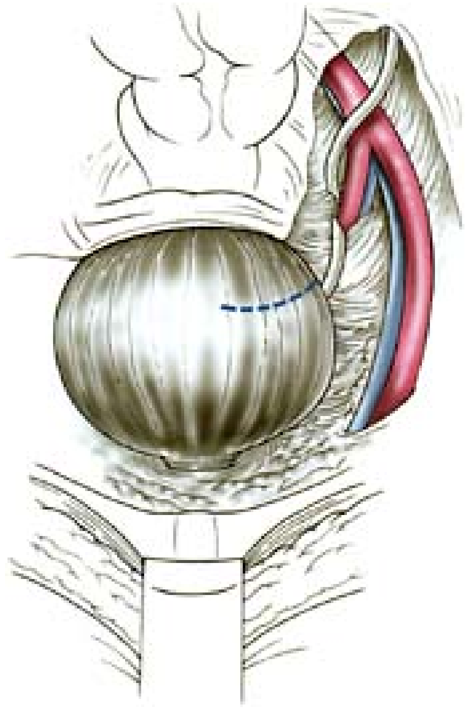

Figure 12

Demel flap: initial incision

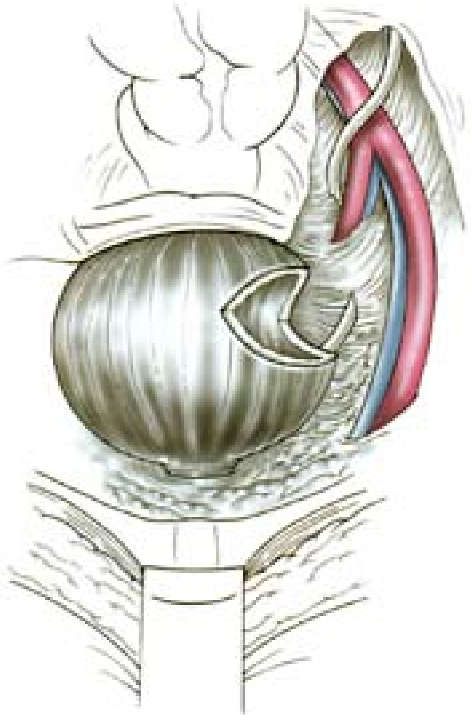

Figure 13

The bladder is opened and the lateral aspect brought into approximation with the injured ureter

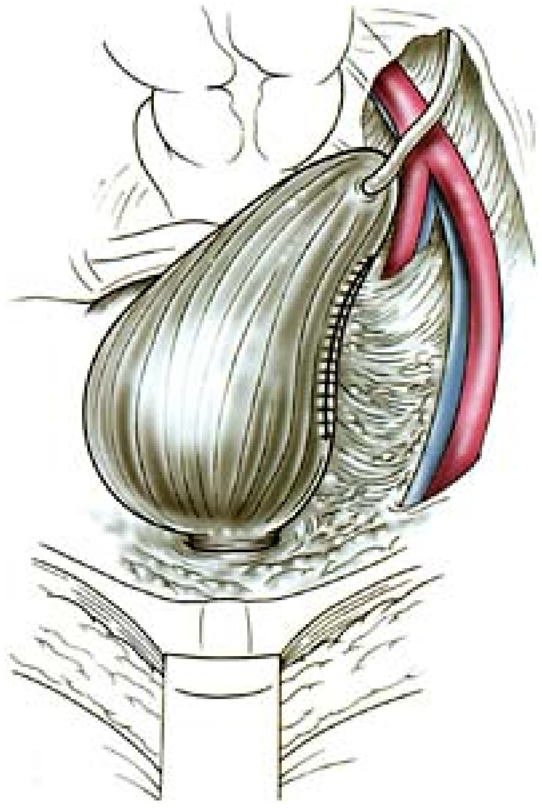

Figure 14

Anastomosis is performed and the bladder closed advantages and disadvantages. The major types now in use in gynecological practice are the intestinal conduits using either small or large bowel, and various versions of the ileocecal continent urinary reservoir.

Indications

In gynecology most urinary diversions are performed as part of the reconstructive phase of a pelvic exenteration or because of severe irradiation injury to the bladder. The type of diversion employed depends on the surgeon's preference, the patient's overall health, the prognosis and the patient's ability to perform the tasks necessary to catheterize a continent pouch.

The ileal conduit is the simplest diversion to perform. Care must be exercised in patients who have undergone radiotherapy as the vascular supply to the conduit may be compromised. The patient must also wear an appliance at all times.

Colonic conduits have the benefit that the segment may be taken from anywhere along the length of the colon. Anatomically, the sigmoid is the easiest part as it is ideally located for a urinary conduit. Like the ileum, however, it can be affected by prior radiotherapy. The transverse colon conduit avoids this problem, but because it is located in the upper abdomen, it is more difficult to perform the ureteral anastomoses.

Continent urinary reservoirs have the chief advantage that the patient is not required to wear an appliance continuously. The patient must be able to self-catheterize at least four times a day and irrigate the reservoir as needed. This can be particularly difficult for visually impaired, obese or elderly patients. The pouch is also more technically difficult and timeconsuming to construct.

Anatomic considerations

Vascular supply

Ileum

The ileum receives its vascular supply from the ileocolic artery, which is a branch of the superior mesenteric artery (SMA). Collateral circulation is from the right colic artery, which is also a branch of the SMA. The terminal ileum is at particular risk of vascular insufficiency owing to the fact that it is supplied by the terminal branches of the ileocolic artery and collateral circulation is poor.

Colon

The colon is supplied by branches of the superior and inferior mesenteric arteries (IMA). The right and middle colic arteries arise from the SMA and supply the right and transverse colons respectively up to the splenic flexure. The left colic and sigmoid arteries are branches of the IMA and supply the left and sigmoid colon respectively. Collateral circulation to the sigmoid is via the superior rectal artery, a branch of the IMA, which anastomoses with the middle and inferior rectal arteries, both branches of the hypogastric artery.

Nerve supply

Ileum

The ileum is innervated by the superior mesenteric plexus, which carries autonomic fibers from the vagus and thoracic splanchnic nerves.

Colon

The innervation of the colon is from the superior and inferior mesenteric plexuses, which carry autonomic fibers from the vagus, thoracic and lumbar splanchnic nerves.

Operative procedure

General considerations

Preoperative preparation should include a mechanical and antibiotic bowel preparation using a bowel cleansing solution such as Golytely (Schwarz Pharma, Inc., Milwaukee, WI, USA), and oral neomycin, erythromycin and an antifungal such as fluconazole. Perioperative antibiotics may also be required. A preoperative renogram should be performed to assess baseline renal function in all patients receiving a continent conduit and in any other patient whose renal function is in question.

Our preference is to stent all ureters prior to performing the anastomosis. This eliminates the risk of sewing the ureter closed or of disrupting the sutures, which can occur when stenting is performed after suturing. Stents are held in place by placing a 5–0 or 6–0 plain gut suture through the ureter and the stent approximately 2 cm from the junction of the ureter and pouch. We also study all stents radiographically

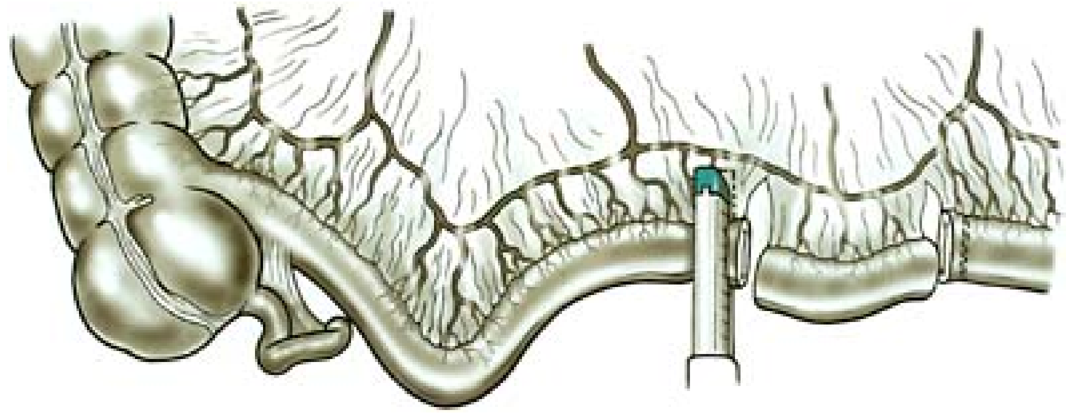

Figure 15

A segment of ileum is isolated sufficiently distant from the ileocecal junction to avoid the 'watershed' area

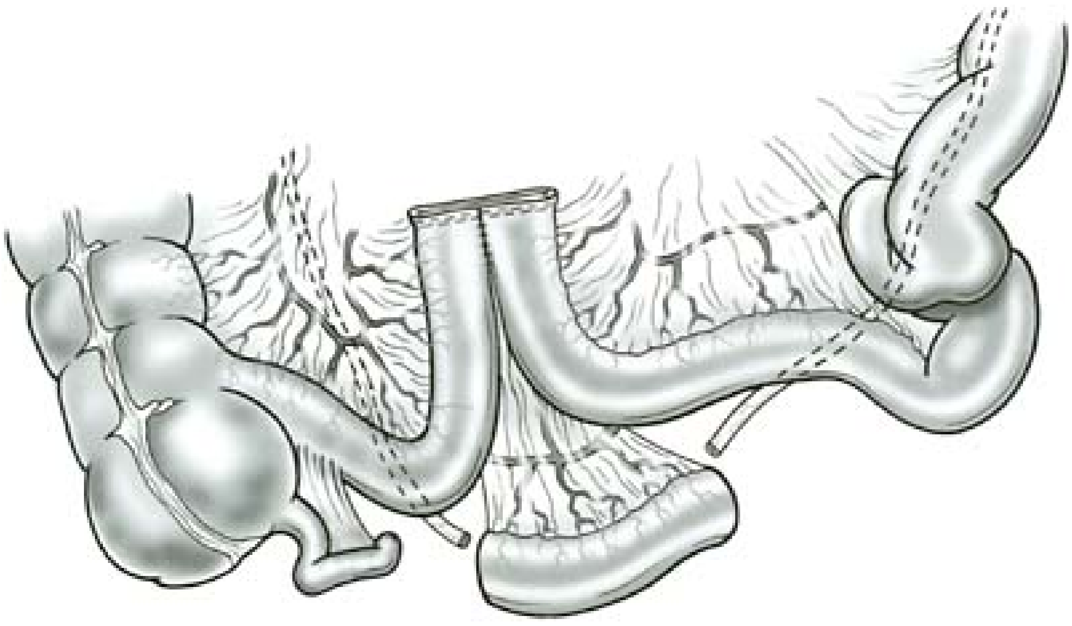

Figure 16

Bowel continuity is restored. The ureters are freed and brought through the retroperitoneum to the location of the conduit (generally, in the area of the sacral promontory)

prior to removing them. Retrograde 'stentograms' can demonstrate leaks if present and strictures can be identified with a pull-back study. We generally study with intent to remove stents 2–3 weeks postoperatively.

A closed suction drain (e.g. Jackson Pratt) is placed behind the pouch or conduit in the area of the ureteral anastomoses in all patients. The major benefit is in the detection of anastomotic leaks. The drain is removed at the same time as the ureteral stents.

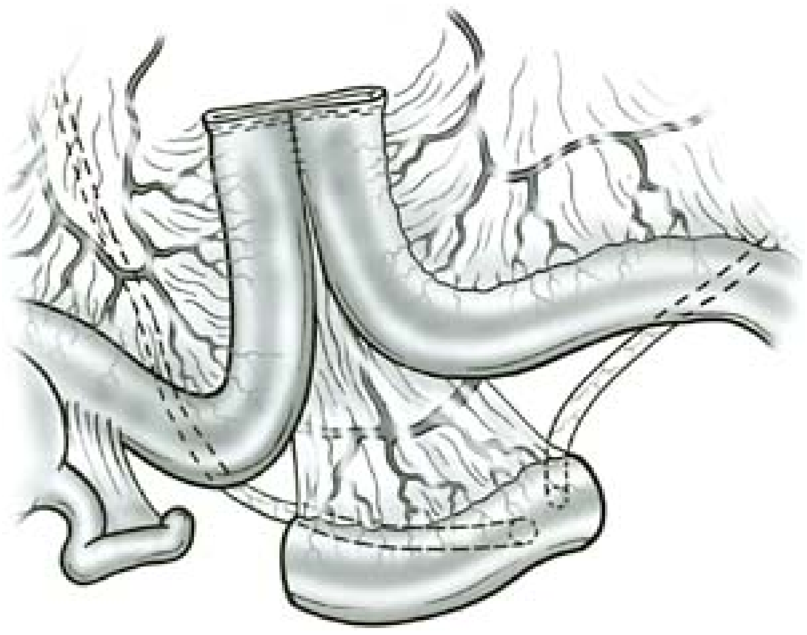

Figure 17

Ureteral anastomoses are performed about 2 cm from the closed end of the conduit

lleal conduit

The ileum is carefully inspected for the presence of radiation injury, if applicable. Where injury is present, a colonic conduit is preferred. The conduit can be as short as 4–6 cm or as long as 15 cm. Shorter conduits are less prone to electrolyte disturbances, but may make it difficult or impossible to perform tension-free ureteroileal anastomoses. The ileal segment is transected at both ends using an intestinal stapler. The distal end should be at least 10 cm from the ileocecal valve. An ileoileal anastomosis restores bowel continuity The mesentery is disrupted as little as possible (Figure 15).

The ureters are divided as far distally as is practical without involving diseased sections. The ureters and the conduit must be behind the ileal mesentery and the left ureter must be tunneled through the retroperitoneum behind the base of the sigmoid mesentery to bring it to the patient's right side (Figure 16).

The site for the anastomosis should be about 2 cm from the closed end of the conduit (Figure 17). A small (less than 1 cm) ellipse of tissue is removed from the wall of the ileum at the chosen site for the anastomoses. The ureteral ends are widened by first cutting them at an angle and then making a single longitudinal incision such that the ureteral opening corresponds to that in the bowel wall. Full-thickness sutures of 4–0 polyglycolic acid are used to perform end-to-side ureteroileostomies. Usually four to six sutures are sufficient (Figure 18). A stoma is then created with the distal end of the ileal

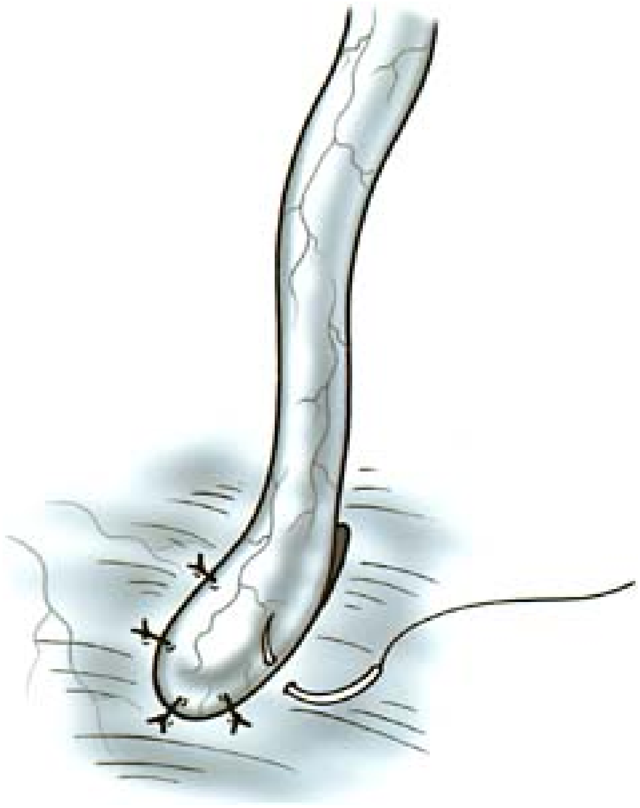

Figure 18

Detail of anastomosis. After removal of a small portion of the wall of the bowel the anastomosis is performed externally with full thickness, interrupted absorbable suture segment. The stoma is generally located in the right lower quadrant and is ideally marked preoperatively taking into consideration the type of appliance to be used, the patient's body habitus and the location of her belt line when standing. A circle of skin is excised, the subcutaneous fat is either spread apart with retractors or excised, and a cruciate incision is made in the fascia. The fibers of the rectus muscle are bluntly separated and the posterior sheath and peritoneum are incised. The stoma should admit one to one and a half fingers if it is of adequate caliber. The stoma is everted into a 'rosebud' raised slightly above skin level. The proximal end can then be sutured to the peritoneum overlying the sacral promontory.

An alternative technique is a modification of the Bricker ileal conduit that provides for tension-free ureteral anastomosis while better defining conduit length. Because ureteral anastomosis is performed after the stoma is matured, this technique also reduces post-anastomosis manipulation. While the technique is presented as a modification for ileal conduits, it has been used for colonic conduits as well. The terminal ileum is transected at about 10–15 cm proximal to the ileocecal valve using a stapling device. The proximal portion of ileum is mobilized so that the stapled end can be brought through the anterior abdominal wall to mature the conduit stoma. After maturing the stoma as previously described, the ileum is transected proximally after approximating the conduit to the ureters and assessing the appropriate length. The distal end of the Yankaur suction device is then manually inserted through the stoma and advanced into the proximal end of the conduit. The conduit wall is incised directly over the tip of the suction using an electrosurgical instrument. Gently advancing the Yankaur tip partially through this new aperture exposes the conduit mucosa. A single-J 70 cm ureteral stent of the desired size (7.0 to 8.5 French) is inserted through the Yankaur suction device and advanced into the ureter to the renal pelvis. A mucosa-to-mucosa ureteral anastomosis is performed using 4 to 5 interrupted stitches using a 4–0 delayed absorbable suture (Figure 19).

Colonic conduit

Colonic conduits are usually 15–20 cm in length. Since the colon will contract once isolated, a segment somewhat longer than desired should be selected. Bowel continuity can then be restored or a colostomy can be created if the distal colon is to be removed as part of an exenterative procedure. The mesenteric incisions should be of sufficient length to allow mobility of the conduit without interfering with the vascular supply to either the conduit or the remaining colon. The colonic anastomosis is performed anterior to the conduit. For a transverse colon conduit, the omentum must be dissected off the colon prior to isolating the conduit. The conduits should be isoperistaltic to prevent stasis, but can be constructed in an antiperistaltic fashion if anatomically necessary with no significant adverse effects. The ureteral anastomoses are performed with 4–0 interrupted absorbable mucosa-to-mucosa sutures in separate teniae. Again, four to six sutures usually suffice. The right ureter must be brought over to the left side retroperitoneally and behind the sigmoid mesentery (for a sigmoid conduit). The ureters are spatulated as described above for ileal conduits. The ureteral anastomoses should be staggered by 2–3 cm so that one is more proximal than the other.

A stoma is created with the distal end of the conduit. The stoma is usually on the left side, but it can be on the right if dictated by anatomical

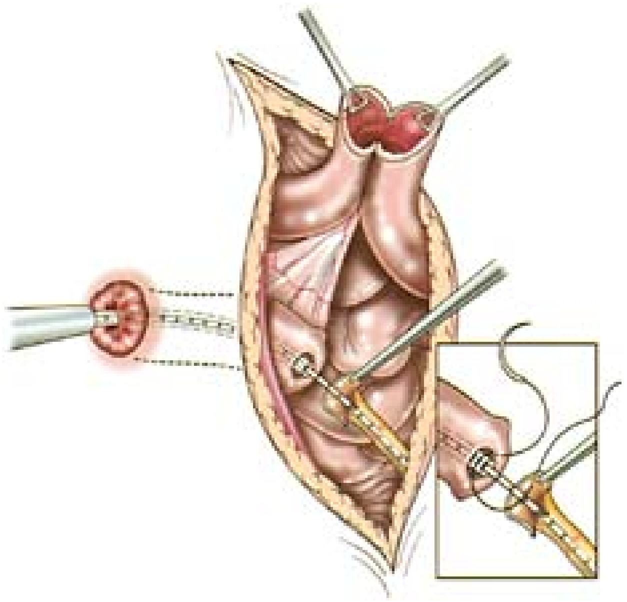

Figure 19

After isolating the distal end of the intestinal segment, a metal Yankaur suction catheter is advanced to the planned anastomotic site. A transmural incision is made over the end of the catheter with the electrosurgical instrument. The ureteral anastomosis is secured with interrupted 4–0 vicryl sutures. The catheter helps incorporate the seromuscular and mucosal layers as the needle is placed against and run along the metal catheter from outside to inside *(insert)*. A 7F 70 cm single J-stent is threaded through the catheter and passed directly into the ureteral lumen (Reproduced with permission from *Gynecologic Oncology*, Winter et al, Modified technique for urinary diversion with incontinent conduits)

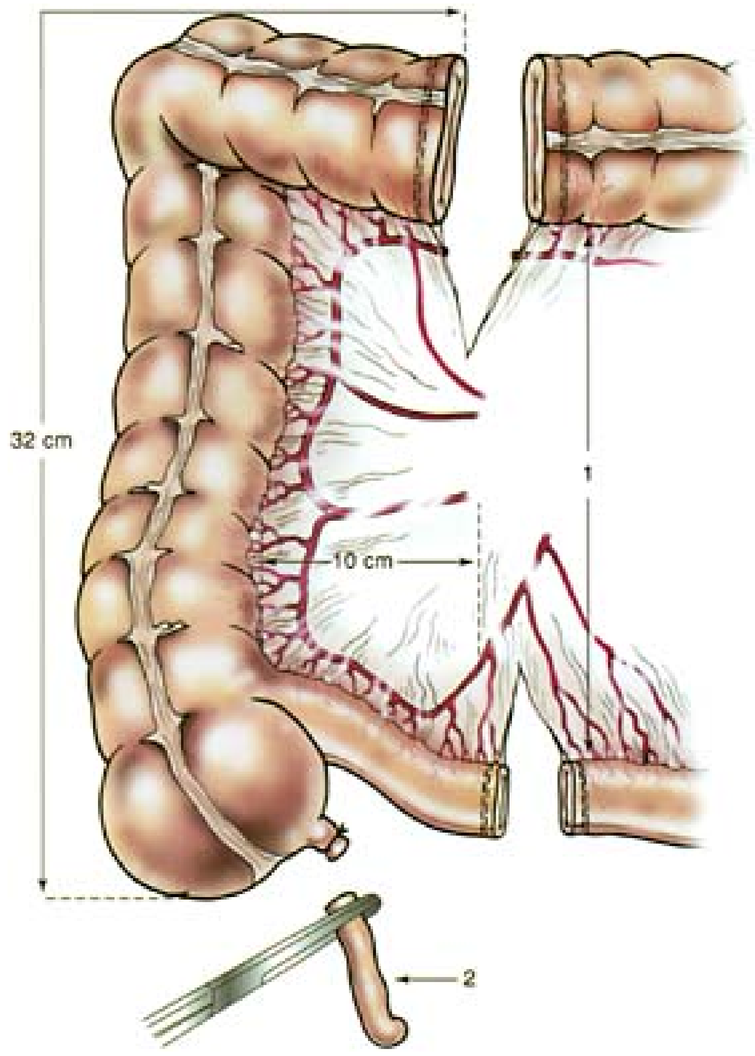

Figure 20

To begin a continent ileocecal reservoir the ileum is divided about 10 cm from the ileocecal valve and the colon is divided 32 cm from the cecum. If possible, this should be proximal to the middle colic artery. The appendix, if present, is removed
1 Anastomosis performed to restore bowel continuity
2 Appendectomy performed

concerns or if the patient has a colostomy as well. The stomal site must be larger than that for an ileal conduit and should admit at least two fingers. Finally, the proximal end is fixed to the psoas muscle with one or two interrupted permanent sutures.

Continent ileocolic reservoir

A 10 cm length of distal ileum and 32 cm of ascending and proximal transverse colon are isolated and mobilized. An ileotransverse enterocolostomy is performed in the standard fashion to restore bowel continuity. The appendix is removed at this time if it is present (Figure 20).

The colon is then folded on itself in a U configuration, bringing the transected end of the transverse colon in approximation to the cecum. Two interrupted stay sutures are used to maintain alignment of the colon. Electrocautery is used to make two small colotomies (2–4 cm) in the center of each segment of colon (Figure 21A and B).

A PolyGIA stapler (US Surgical, Norwalk, CT, USA) is then used to detubularize the colon. Each arm is passed into adjacent colon segments towards one end of the reservoir. Once the stapler is articulated and fired, a common lumen is created with two rows of absorbable staples on each side of the incision line created by the knife within the instrument (Figure 22A and B). A second instrument is then fired from this same point towards the opposite end of the reservoir, thus completing the detubularization process. The continence mechanism is constructed by tapering the ileum and reinforcing the ileocecal valve (Figure 23). A 14 Fr red rubber catheter is placed in the ileum. Allis clamps are placed along the anti-mesenteric border to create countertension and a gastrointestinal stapler is used to taper the ileal segment so that the inside diameter approaches that

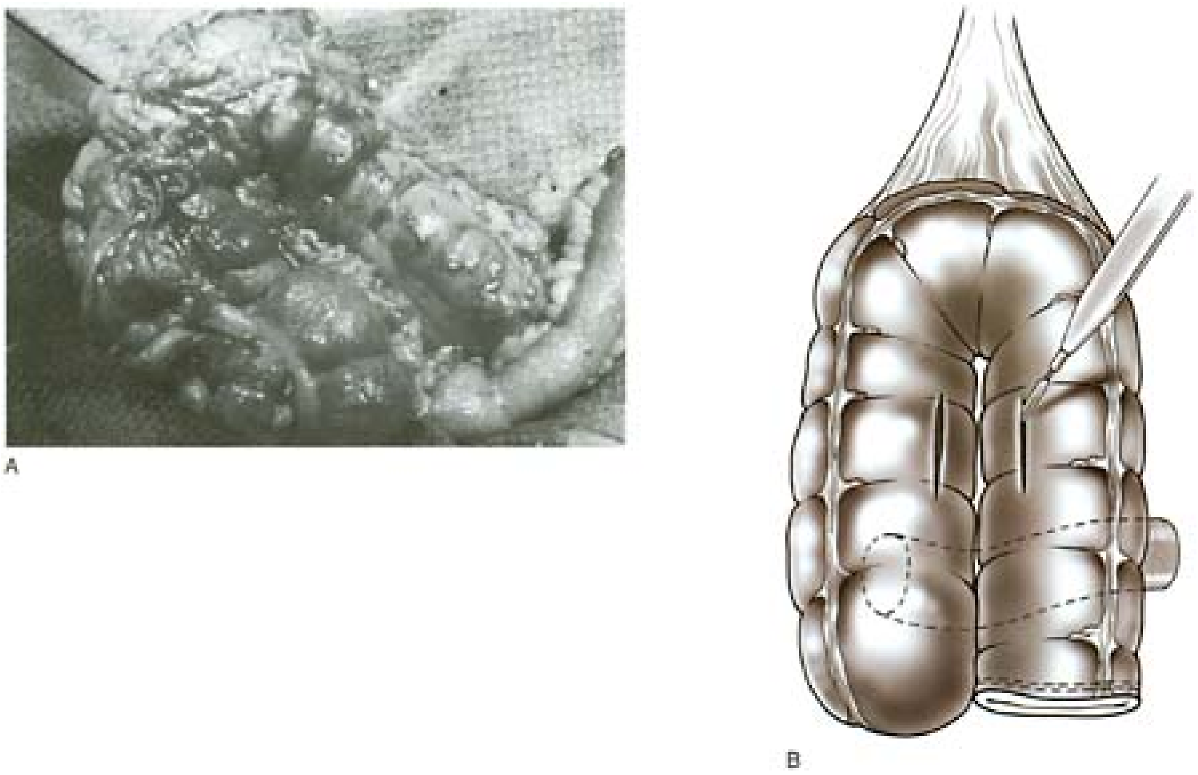

Figure 21

The colon is folded over on itself into a U as A and enterotomies are made (A) (B)

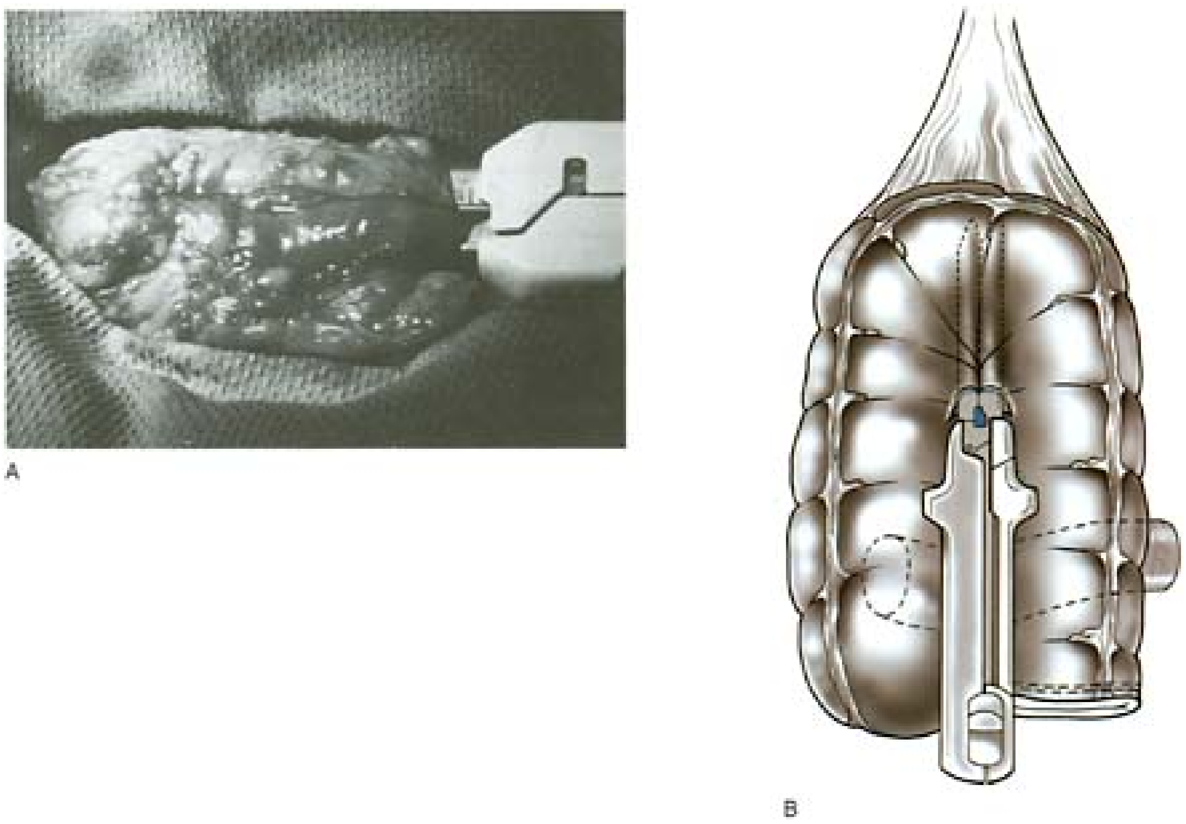

Figure 22

Detubularization is performed using a gastrointestinal stapler with absorbable staples. Two staplers are required, one towards each end of the conduit, as the staplers are not reloadable

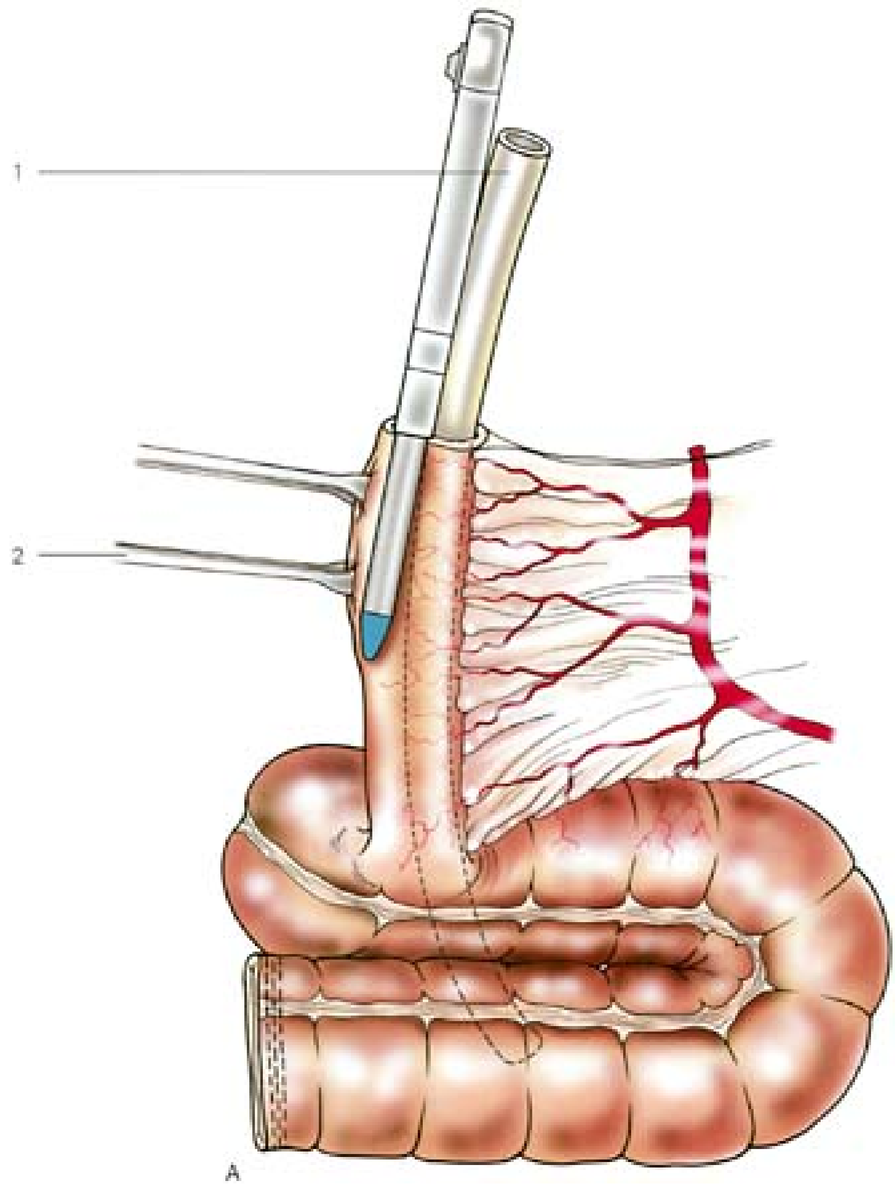

Figure 23

Using a standard gastrointestinal stapler, the ileal section is tapered over a Fr red rubber catheter
1 Rubber catheter
2 Allis clamp

of the catheter. More than one firing of the stapler may be required.
Two or three purse-string sutures of 2–0 silk suture are then placed at the level of the ileocecal valve. The sutures are placed through the serosa and muscularis layers, but not through the mucosa (Figure 24).
Working through the unified colotomy in the center of the pouch, the ureters are then anastomosed to the pouch (Figure 25). A long, curved instrument is passed through the colotomy into the pouch to the intended location of the anastomosis. A colotomy is made at this point and the ureter is then drawn into the interior of the pouch. The ureters are spatulated and anastomosed from within the pouch with mucosa-to-mucosa interrupted 4–0 delayed absorbable sutures, full thickness through the ureter and partial thickness through the bowel (mucosa and submucosa only). Externally, the serosa of the bowel and the adventitia of the ureters are sutured together in a similar fashion with two or three sutures. The left ureter must be brought to the right side retroperitoneally behind the sigmoid mesentery
Single J ureteral stents (7 Fr) are placed and fixed in position with a 5–0 or 6–0 plain gut suture which passes through the ureter and the stent approximately 2 cm from the junction of ureter and pouch. The stents are externalized through the anterior wall of the pouch and the abdominal wall, and the pouch

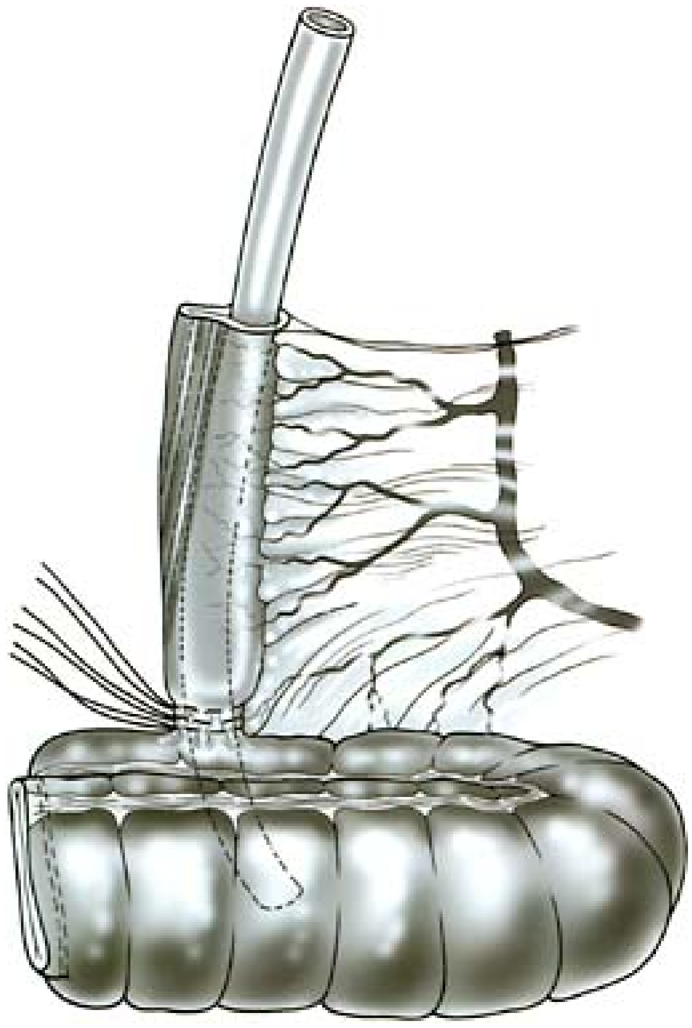

Figure 24

The ileocecal valve is reinforced with 2–3 purse-string sutures of non-absorbable suture such as silk

is fixed to the anterior abdominal wall with permanent sutures. The external end of the right stent can be cut at a right angle and the end of the left stent can be cut at a 45° angle for easy differentiation later. The 14 Fr red rubber catheter is exchanged for a triple-lumen Foley catheter of similar size. The Foley catheter is then left in place for 2 weeks until radiographic imaging confirms an intact system. At that stage the colotomy can then be closed with sutures or a TA-55 thoracoabdominal intestinal stapler. The ileum is also then externalized in the right lower quadrant. In some patients, the stoma can be placed in the umbilicus, which gives an excellent cosmetic result and makes catheterization easier as this is the thinnest portion of the abdominal wall. The continent stoma should not form a rosebud, but simply be everted flush with the skin. It is important that the course of the ileum be relatively straight to ease catheterization. A closed suction drain is placed behind the pouch and is removed with the ureteral stents. Postoperative pouch drainage via intermittent low-pressure wall suction and irrigation can be performed via the Foley catheter. It is essential to monitor input and output of the pouch and to irrigate the pouch gently with 30–50 mL of normal saline frequently—as often as every 2–4 hours—in the immediate postoperative period to prevent mucus build-up. If output is significantly less than input, an ultrasound scan of the pouch can be done to ensure that it has not become overdistended. Urine output is followed separately from

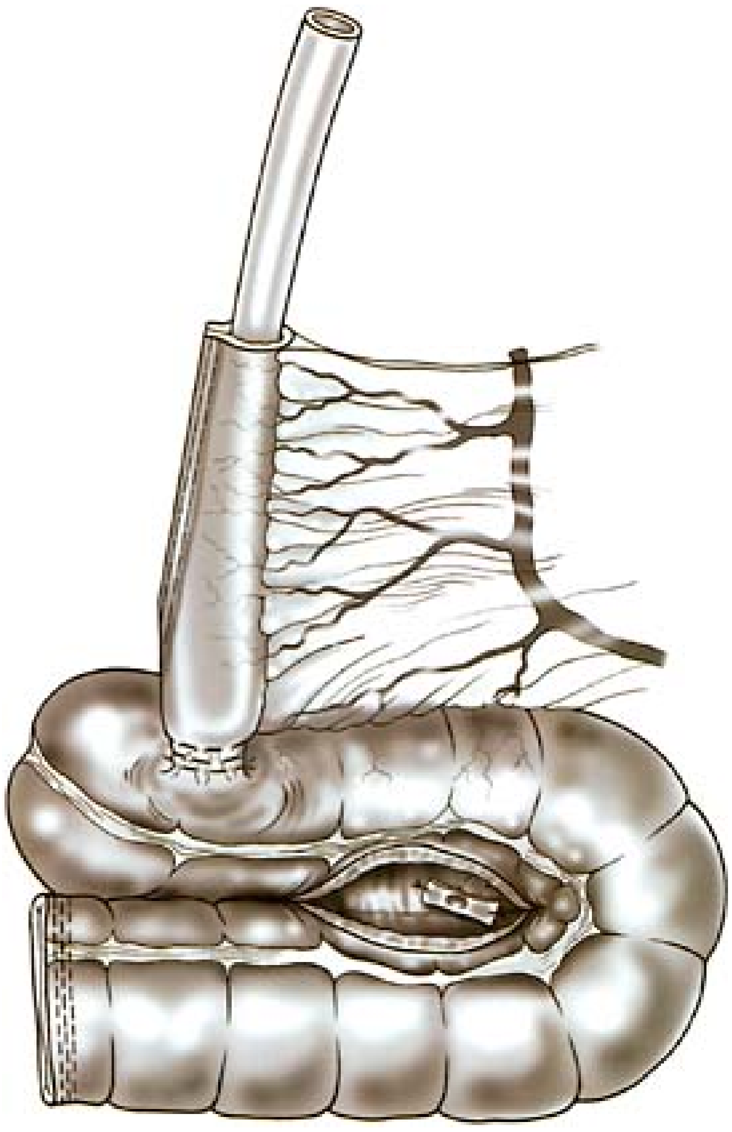

Figure 25

Working through the colotomy, the ureteral anastomosis is performed. After bringing the ureter through the wall of the conduit, the end is spatulated; interrupted absorbable sutures incorporating the full thickness of the ureter and partial thickness of the colon wall are used to performed the anastomosis

the stents which are connected to individual urimeters, carefully marked ‘left’ and ‘right’. The stents can also be irrigated with 10 mL of normal saline if urine output falls off. If there is no response to repeated irrigations, the stent should be studied radiographically to ensure proper placement and function. When the output decreases the pouch can be changed to gravity drainage, but the irrigations should continue at least four times a day with the irrigation fluid removed immediately.

A contrast study of the pouch and the ureters is performed about 2 weeks postoperatively If all is normal, the stents are removed and the patient is then taught self-catheterization which initially should be performed every 2–4 hours. The patient should also continue to irrigate the pouch at least four times a day to prevent mucus build-up.

Orthotopic neobladder

Orthotopic reconstruction has played a major role in the evolution of urinary diversion. It was first described in 1888 and later revisited in 1951. Advances in surgical techniques have improved the quality of life in women requiring radical cystectomy by allowing volitional, physiologic voiding. In the past 15 years, orthotopic neobladder surgery has emerged as an appealing alternative to the time-honored conduit for urinary diversion.

Indications

Orthotopic neobladder surgery is selected when radical cystectomy is required for primary and secondary cancer of the bladder. It is often performed in conjunction with pelvic exenteration. Although desirable for its physiologic features described above, the neobladder is contraindicated in several situations. Absolute contraindications include impaired renal function due to long-standing obstruction, chronic renal failure (serum creatinine 150–200 •mol/L) and hepatic dysfunction. Compromised intestinal function may also preclude neobladder surgery, particularly in the case of the presence of inflammatory bowel disease. In addition, the rhabdosphincter must be left intact following cystectomy, and the urethra must be free of tumor.

Previously, it was believed that removing the urethra at the time of cystectomy was necessary to obtain adequate margins. However, studies of cystectomy specimens have suggested that the urethra is free of tumor in the majority of cases where the bladder neck and proximal urethra are free of disease, and that skip lesions are rare. Therefore, intraoperative frozen section analysis of the surgical margin, including the proximal urethra, is necessary to determine candidacy of orthotopic diversion.

Anatomic considerations

Vascular supply

Bladder

The main blood supply to the bladder involves the superior and inferior vesical arteries, which are branches of the anterior division of the hypogastric artery. Branches of the obturator, uterine and vaginal arteries may also be involved.

Urethra

The urethra receives its blood supply from branchesof the pudendal and inferior vesical arteries.

lleum

The ileocolic artery, a branch of the superior mesenteric artery (SMA), is the main blood supply to the ileum. The right colic artery (also a branch of the SMA) supplies collateral circulation.

Colon

The colon is supplied by the superior and inferior mesenteric arteries (IMA). Arising from the SMA, the right and middle colic arteries supply the right colon and the transverse colon up to the splenic flexure. The left colic and sigmoid arteries are IMA branches that supply the left and sigmoid colon. The superior rectal artery, another branch of the IMA, anastomoses with the middle and inferior rectal arteries, supplying collateral circulation to the sigmoid colon.

Nerve supply

Bladder

The bladder is innervated by the vesical plexus, which arises from T11-L2 and travels through the cardinal ligament. The plexus carries efferent and afferent autonomic fibers, including sympathetic and parasympathetic innervation.

Urethra

The proximal urethra is innervated by the sympathetic fibers of the pelvic plexus which courses through the cardinal ligament. The distal two thirds of the urethra, including the rhabdosphincter, is innervated by branches of the pudendal nerve which course along the pelvic floor posterior to the levator muscles.

Ileum

The superior mesenteric plexus innervates the ileum. It carries autonomic nerve fibers from the vagus and thoracic splanchnic nerves.

Colon

The colon is innervated by the superior and inferior mesenteric plexuses, carrying autonomic fibers from the vagus, thoracic and lumbar splanchnic nerves.

Surgical procedure

When performing an orthotopic reconstruction, the radical cystectomy is modified to preserve the urethra and maintain the continence mechanism. This modification includes minimal dissection anteriorly to avoid disruption of the urethral innervation, as well as preserving the pubourethral suspensory ligaments. Any segment of the gastrointestinal tract may be used for the neobladder, provided it has the ability to reach the graft site without tension. However, the ileum has become a popular choice over the large bowel because it has less contractility and less reabsorption of urinary constituents.

The cystectomy is carried out in an anterograde fashion to the level of the vaginal apex, where a plane is created between the posterior bladder base (trigone) and vagina. The Foley catheter balloon may be palpated and used as an indicator of the urethrovesical junction. Dissection is then continued just distal to this point. Extensive dissection distally along the posterior urethra is avoided in order to prevent the disruption of pudendal innervation of the urethra and its musculofascial support of the anterior vagina.

After completion of the posterior dissection, a Satinski vascular clamp is placed across the bladder neck to prevent any tumor spillage from the bladder. While applying gentle traction, the proximal urethra is transected below the bladder neck and clamped. Frozen-section analysis of the proximal urethra is necessary to exclude the presence of tumor. Eight to ten urethral sutures are placed which will later be used to attach the urethra to the neobladder.

When small intestine is chosen for the bladder substitution, a 40–60 cm segment of ileum is isolated from the bowel. Ileal reanastomosis is performed to restore the integrity of the main portion of the bowel. (Figure 26a) The isolated ileum is detubularized along the antimesenteric border. At the end, where the ileourethral anastmosis will occur, the incision is curved toward the mesenteric border, spatulating the ileum (Figure 26b). The spatulated ileum is then folded

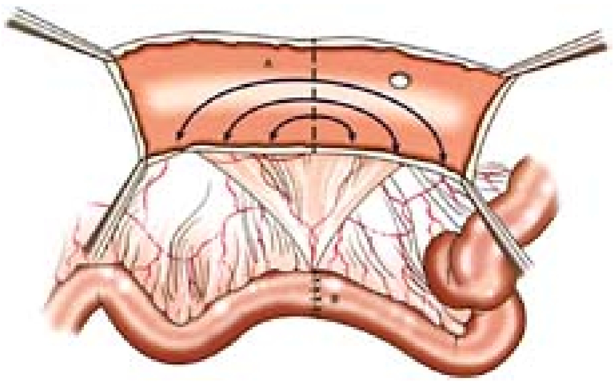

Figure 26

into a U-, S- or W- shaped reservoir (Figure 27a). The limbs of ileum are sutured together with running absorbable material to form a broad plate. An opening is made for the urethral reattachment in the caudal portion of the neobladder (Figure 26b).

Using the previously placed urethral sutures, the urethra is connected to the reservoir. These sutures, originally placed from inside to outside of the urethra, are sewn through the full thickness of the neobladder at the posterior margin of the ileourethral anastomosis. They are tied so that the knots lie within the lumen of the anastomosis (Figure 27b).

Two small openings are made in the wall of the neobladder lateral to the urethral implantation site. The ureters are reimplanted in an antirefluxing fashion (described previously in this chapter) with stent placement. The ileal plate is then folded to form a pouch and closed with running absorbable suture. To reduce tension on the anastomosis, the pouch is sutured to the pelvic fascia.

Various techniques to create a neobladder exist. Alternative approaches to the surgery described above use similiar techniques using other segments of the bowel. The distal 20cm of ileum and 15cm of cecum and ascending colon (MAINZ pouch) or 20–30cm of cecum and ascending colon may also be used. The selection bowel segment should be based on the ability to avoid tension on the completed anastomosis.

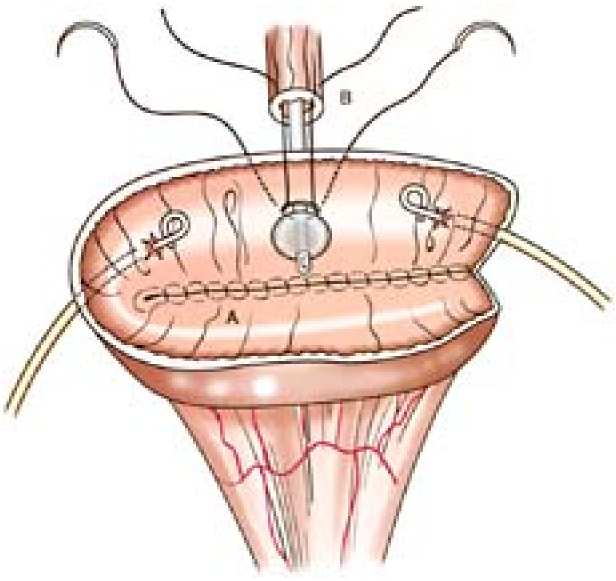

Figure 27

Acknowledgment

The authors would like to thank Dr William E. Winter for his contribution to this chapter.

References

Camey M (1990) Detubularized U-shaped cystoplasty (Camey 2). *Curr Surg Tech Urol* **3**:1–8.

Cosin JA, Carter JR, Paley PJ, et al. (1997) A simplified method for detubularization in the construction of a continent ileocolic reservoir (Miami pouch). *Gynecol Oncol* **64**:436–41.

Hartenbach EM, Saltzman AK, Carter JR, et al. (1995) Nonsurgical management strategies for the functional complications of ileocolonic continent urinary reservoirs. *Gynecol Oncol* **56**:127–8.

Kock NG, Nilson AE, Nilsson LO, et al. (1982) Urinary diversion via continent ileal reservoir: clinical results in 12 patients. *J Urol* **128**:469–75.

Penalver MA, Darwich EB, Averette HE, et al. (1989) Continent urinary diversion in gynecologic oncology. *Gynecol Oncol* **34**:274–88.

Rowland RG, Mitchell ME, Bihrle R, et al. (1989) Indiana continent urinary reservoir. *J Urol* **137**:1136–9.

Stein JP, Ginsberg DA, Skinner DG (2002) Indications and technique of the orthotopic neobladder in women. *Urol Clin North Am* **29**:725–34.

Symmonds RE (1976) Ureteral injuries associated with gynecologic surgery: prevention and management. *Clin Obstet Gynecol* **19**:623–44.

Thuroff JW, Alken P, Reidmiller H, et al. (1985) The MAINZ pouch (mixed augmentation ileum ‘n zecum) for bladder augmentation and continent diversion. *World J Urol* **3**:179_84.

Walsh PC, Retik AB, Starney TA, Vaughan ED. (1998) *Campbell’s urology*, Vol. 3, 7th edn. Philadephia: WB Saunders: 3201–14.

Wheeless CR Jr (1992) Recent advances in surgical reconstruction of the gynecologic cancer patient. *Curr Opin Obstet Gynecol* **4**:91–101.

Winter W (2002) Modified technique for urinary diversion with incontinent conduits. *Gynecol Oncol* **86**:351–53.

22
Fistula repair

Paul Hilton
Lucia M Dolan

Etiology and epidemiology

Urogenital fistulas may occur congenitally, but are most often acquired from obstetric, surgical, radiation and malignant causes. The same factors may be responsible for intestinogenital fistulas, although inflammatory bowel disease is an additional important etiologic factor here. In most developing countries over 90% of fistulas are of obstetric etiology, whereas in the UK and USA over 70% follow pelvic surgery.

Obstetric causes

The overwhelming proportion of obstetric fistulas in the developing world are complications of neglected obstructed labor. In the developed world, however, obstetric fistulas are associated with rupture of the uterus following previous cesarean section, or assisted vaginal delivery (Table 1). Obstetric factors leading to anovaginal or rectovaginal fistulas include an unrecognized fourth-degree tear or infection and breakdown of repair of a third-or fourth-degree tear.

Surgical causes

Genital fistulas may occur following a wide range of surgical procedures within the pelvis (Table 1). It is often supposed that this complication results from direct injury to the lower urinary tract at the time of surgery. Certainly, on occasions this may be the case; careless, hurried or rough surgical technique makes injury to the lower urinary tract much more likely. Of the 165 cases of urogenital fistulas referred to the author over a recent 10-year period, 117 were associated with pelvic surgery and 91 followed hysterectomy; of these, only 4(4%) presented with leakage of urine on the first day postoperatively. In other cases, it is presumed that tissue devascularization during dissection, inadvertent suture placement, pelvic hematoma formation or infection developing postoperatively results in tissue necrosis with leakage developing most usually 5–10 days later. Approximately 10–15% of postsurgical fistulas present late, between 10 days and 30 days after the procedure. Overdistension of the bladder postoperatively may be an additional factor in many of these latter cases. It has recently been shown that there is a high incidence of abnormalities of lower urinary tract function in fistula patients; whether these abnormalities antedate the surgery, or develop with or as a consequence of the fistula, is unclear. It is likely that patients with a habit of infrequent voiding, or those with inefficient detrusor contractility, may be at increased risk of postoperative urinary retention; if this is not recognized early and managed appropriately, the risk of fistula formation may be increased. Although it is important to remember that the majority of surgical fistulas follow apparently straightforward hysterectomy in skilled hands, several risk factors may make direct injury more likely (Table 2). Anovaginal and rectovaginal fistulas may also have a surgical etiology with vaginal hysterectomy, rectocele repair, hemorrhoidectomy low anterior resection and panproctocolectomy being commonly associated.

Table 1 Etiology of urogenital fistulas in two series, from the north of England, and from south-east Nigeria

Etiology	*NE England* (n=*165*) %	n	*SE Nigeria* (n=*2389*)* %	n
Obstetric				
Obstructed labor		1		1918
Cesarean section		5		165
Ruptured uterus		7		119
Forceps/ventouse		5		
Breech extraction		1		
Placental abruption		1		
Obstetric subtotal	12.1%	20	92.1%	2202
Surgical				
Abdominal hysterectomy		71		33
Radical hysterectomy		11		
Urethral diverticulectomy		12		
Colporrhaphy		2		35
Vaginal hysterectomy		4		25
TAH+colporrhaphy		1		
TAH+colposuspension		1		
LAVH		3		
Cytoplasty+colposuspension		2		
Colposuspension		1		
Sling		1		
Needle suspension		1		
Cervical stumpectomy		1		
Subtrigonal phenol injection		1		
Transurethral resection (TB)		1		
Lithoclast		1		
Unknown surgery in childhood			2	
Bowel surgery			1	
Suture to vaginal laceration				12
Surgical subtotal	70.9%	117	4.4%	105
Radiation	11.5%	19	0.0%	0
Malignancy	0.0%	0	1.8%	42
Miscellaneous				
Pessary		3		
Other foreign body		2		
Catheter-associated		2		
Trauma		1		11
Infection		0		7
Coital injury		1		22
Miscellaneous subtotal	5.4%	9	1.7%	40
Total	100.0%	165	100.0%	2389

* 2389 patients for whom notes were examined, out of total series of 2484 patients.
TAH, total abdominal hysterectomy; LAVH, laparoscopic assisted vaginal hysterectomy; TB, tuberculosis. (Reproduced from Hilton 2002, with permission).

Table 2 Risk factors for postoperative fistula

Risk factor	*Pathology*	*Example*
Anatomical distortion		Fibroids Ovarian mass
Abnormal tissue adhesion	Inflammation	Infection Endometriosis
	Previous surgery	Cesarean section Cone biopsy Colporrhaphy
	Malignancy	
Impaired vascularity	Ionizing radiation Metabolic abnormality Radical surgery	Preoperative radiotherapy Diabetes mellitus
Compromised healing		Anemia Nutritional deficiency
Abnormality of bladder function		Voiding dysfunction

Radiation

Injury to the gastrointestinal tract may arise following therapeutic radiation with the incidence of complications increasing when the radiation dose exceeds 5000 cGy. The obliterative endarteritis associated with ionizing radiation in therapeutic dosage proceeds over many years and may result in fistula formation long after the primary malignancy has been treated. Patients with a vesicovaginal fistula often have symptoms of radiation cystitis that improve on appearance of the fistula. Of the 19 radiation fistulas in the author's series, the interval between fistula development and radiotherapy ranged from 1 year to 30 years. The associated devascularization in the adjacent tissues means that ordinary surgical repair has a high likelihood of failure, and modified surgical techniques are required.

Malignancy

Excluding the effects of treatment, malignant disease itself may result in genital tract fistula. Carcinoma of cervix, vagina and rectum are the most common malignancies to present in this way. It is relatively unusual for urothelial tumors to present with fistula formation, other than following surgery or radiotherapy The development of a fistula may be a distressing part of the terminal phase of malignant disease; it is, nevertheless, one deserving not simply compassion, but full consideration of the therapeutic or palliative possibilities. Bilateral permanent nephrostomies may give continence when all else fails.

Inflammatory bowel disease

Inflammatory bowel disease is the most significant cause of intestinogenital fistulas in the UK, although these rarely present directly to the gynecologist. Diverticular disease can produce colovaginal fistulas and, rarely, colouterine or colovesical fistulas, with surprisingly few symptoms attributable to the intestinal pathology. It has been estimated that 2% of patients with diverticulosis will develop fistulas arising either through direct extension from a ruptured diverticulum or through erosion from a diverticular abscess. The possibility should not be overlooked if an elderly woman complains of feculent discharge or becomes incontinent without concomitant urinary problems. Pneumaturia and fecaluria are late presenting signs of a colovesical fistula. Crohn's disease appears to be increasing in frequency in the Western world, and a total fistula rate approaching 40% has been reported; in females the involvement of the genital tract may be up to 7%. Ulcerative colitis, unlike Crohn's disease, is not a transmural disease and therefore it is associated with only a small incidence of rectovaginal fistula.

In the author’s own series of rectovaginal fistulas, 65% are obstetric in origin, 21% relate to inflammatory bowel disease, 7% follow radiotherapy, and 7% are of uncertain cause.

Miscellaneous

Other miscellaneous causes of fistulas in the genital tract include infection (lymphogranuloma venereum, schistosomiasis, tuberculosis, actinomycosis, measles, noma vaginae), trauma (penetrating trauma, coital injury, neglected pessary or other foreign bodies) and catheter-related injuries.

Classification

There is no standardized or universally accepted method for describing or classifying fistulas although development of such a system has been recommended by the World Health Organization (WHO) International Consultation on Incontinence, to include location and size of the fistula, functional impact and quantification of the degree of vaginal scarring. Many different fistula classifications already proposed are based on anatomic site; often subclassified into simple fistulas (where the tissues are healthy and access good) or complicated fistulas (where there is tissue loss, scarring, impaired access, involvement of the ureteric orifices, or a coexistent rectovaginal fistula). Urogenital fistulas may be classified into urethral, bladder neck, subsymphysial (a complex form involving circumferential loss of the urethra with fixation to bone), midvaginal, juxtacervical or vault fistulas, massive fistulas extending from bladder neck to vault, and vesicouterine or vesicocervical fistulas. While over 60% of fistulas in the developing world are midvaginal, juxtacervical or massive (reflecting their obstetric etiology), such cases are relatively rare in Western fistula practice; 50% of the fistulas managed in the UK are situated in the vaginal vault (reflecting their surgical etiology). Rectovaginal fistulas are also classified according to anatomic site and relationship to the underlying anal sphincter.

Presentation

Fistulas between the urinary tract and the female genital tract are characteristically said to present with continuous urinary incontinence, with limited sensation of bladder fullness, and with infrequent voiding. Where there is extensive tissue loss, as in obstetric or radiation fistulas, this typical history is usually present, the clinical findings gross, and the diagnosis rarely in doubt. With surgical fistulas, however, the history may be atypical and the orifice small, elusive or occasionally completely invisible. Under these circumstances, the diagnosis can be much more difficult, and a high index of clinical suspicion must be maintained.

Ureteric fistulas have similar causes to bladder fistulas, and the mechanism may be one of direct injury by incision, division or excision, or of ischemia from strangulation by suture, crushing by clamp or stripping by dissection; the presentation may therefore be similarly variable. With direct injury leakage is usually apparent from the first postoperative day. Urine output may be physiologically reduced for some hours following surgery, and if there is significant operative or postoperative hypotension oliguria may persist longer. Once renal function is restored, however, leakage will usually be apparent promptly. With other mechanisms obstruction is likely to be present to a greater or lesser degree, and the initial symptoms may be of pyrexia or loin pain, with incontinence occurring only after sloughing of the ischemic tissue, from around 5 days up to 6 weeks later.

Investigations

If there is suspicion of a fistula, but its presence is not easily confirmed by clinical examination with a speculum, further investigation will be necessary to confirm or exclude the possibility fully. Even where the diagnosis is clinically obvious, additional investigation may be appropriate for full evaluation prior to deciding treatment. The main principles of investigation therefore are:

- to confirm that the discharge is urinary/fecal
- to establish that the leakage is extraurethral rather than urethral
- to establish the site of leakage
- to exclude other organ involvement.

Biochemistry and microbiology

Excessive vaginal discharge or drainage of serum from a pelvic hematoma postoperatively may simulate a urinary fistula. If the fluid is in sufficient quantity to be collected, biochemical analysis of its urea content in comparison with that of urine and serum will confirm its origin. Urinary infection is surprisingly uncommon in fistula patients, although urine culture should be undertaken (especially where there have been previous attempts at surgery) and appropriate antibiotic therapy instituted.

Dye studies

Although other imaging techniques undoubtedly have a role (see below), carefully conducted dye studies remain the investigation of first choice. Phenazopyridine may be used orally, or indigo carmine intravenously, to stain the urine and hence confirm the presence of a fistula. The identification of the site of a fistula is best carried out by the instillation of colored dye (methylene blue or indigo carmine) into the bladder through a catheter with the patient in the lithotomy position. The traditional ‘three swab test’ has its limitations and is not recommended; the examination is best carried out with direct inspection, and multiple fistulas may be located in this way. If leakage of clear fluid continues after dye instillation a ureteric fistula is likely, and this is most easily confirmed by a ‘two dye test’, using phenazopyridine to stain the renal urine and methylene blue to stain bladder contents.

Dye tests are less useful for intestinal fistulas, although a carmine marker taken orally may confirm their presence. Rectal distension with air via a sigmoidoscope may be of more value; if the patient is kept in a slight head-down position and the vagina filled with saline, the bubbling of any air leaked through a low fistula may be detected.

Imaging

Excretion urography

Although intravenous urography is a particularly insensitive investigation in the diagnosis of vesicovaginal fistula, knowledge of upper urinary tract status may have a significant influence on treatment measures applied, and should therefore be looked on as an essential investigation for any suspected or confirmed urinary fistula. Compromise to ureteric function is a particularly common finding when a fistula occurs in relation to malignant disease or its treatment (by radiation or surgery). Dilatation of the ureter is characteristic in ureteric fistula, and its finding in association with a known vesicovaginal fistula should raise suspicion of a complex ureterovesicovaginal lesion (Figure 1). While essential

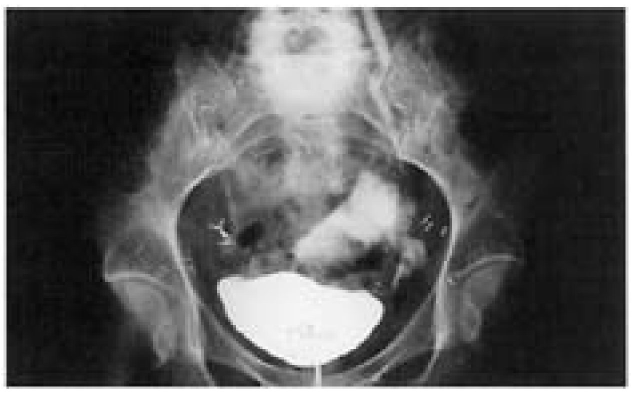

Figure 1

Intravenous urogram (with simultaneous cystogram) demonstrating a complex surgical fistula occurring after radical hysterectomy. After further investigation including cystourethroscopy, sigmoidoscopy, barium enema and retrograde cannulation of the vaginal vault to perform fistulography, the lesion was defined as a ureterocolovesicovaginal fistula

for the diagnosis of ureteric fistula, intravenous urography is not completely sensitive; the presence of a periureteric flare is, however, highly suggestive of extravasation at this site.

Retrograde pyelography

Retrograde pyelography is a more reliable way of identifying the exact site of a ureterovaginal fistula, and may be undertaken simultaneously with either retrograde or percutaneous catheterization for therapeutic stenting of the ureter.

Cystography

Cystography is not particularly helpful in the basic diagnosis of vesicovaginal fistulas, and a dye test carried out under direct vision is likely to be more sensitive. It may, however, occasionally be useful in achieving a diagnosis in complex fistulas or vesico-uterine fistulas.

Fistulography

Fistulography is a special example of the X-ray technique commonly referred to as sinography. For small fistulas a ureteric catheter is suitable, although if the hole is large enough a small Foley catheter may be used to deliver the radiopaque dye; this is particularly valuable for fistulas for which there is an intervening abscess cavity. If a catheter will pass through a small vaginal aperture into an adjacent loop of bowel its nature may become apparent from the radiological appearance of the lumen and haustrations, although further imaging studies are usually required to demonstrate the underlying pathology

Barium enema, barium meal and follow-through

Proctography may be used to identify the site of anovaginal or rectovaginal fistulas, although it has been suggested that vaginography has a higher sensitivity. Barium enema, barium meal or both may be required when a fistula is present above the anorectum. Aside from confirming the presence of a fistula, this allows evaluation of the intestinal condition and malignant or inflammatory disease may be identified.

Ultrasonography, CT and MRI

Ultrasonography, computerized tomography (CT) and magnetic resonance imaging (MRI) may occasionally be appropriate for the complete assessment of complex fistulas. Endoanal ultrasound scans and MRI are particularly useful in the investigation of anorectal and perineal fistulas and have been shown to have positive predictive rates of 100% and 92%.

Examination under anesthesia

Careful examination, if necessary under anesthesia, may be required to determine the presence of a fistula, and is deemed by several authorities to be essential for definitive surgical treatment. It is important at the time of examination to assess the available access for repair vaginally, and the mobility of the tissues. The decision between the vaginal and abdominal approaches to surgery is thus made; when the vaginal route is chosen, it may be appropriate to select between the more conventional supine lithotomy, with a head-down tilt, and the prone (reverse) lithotomy position with head-up tilt. This may be particularly useful in allowing the operator to look down onto bladder neck and sub-symphysial fistulas, and is also of advantage in some massive fistulas in encouraging the reduction of the prolapsed bladder mucosa. A rectovaginal examination may detect a rectovaginal fistula; probing of a perineal sinus with a fine metallic catheter may identify an anoperineal tract.

Endoscopy

Cystoscopy

Although some authorities suggest that endoscopy has little role in the evaluation of fistulas, it is the author’s practice to perform cystourethroscopy in all but the largest defects. Although in some obstetric and radiation fistulas the size of the defect and the extent of tissue loss and scarring may make it difficult to distend the bladder, nevertheless, much useful information is obtained. The exact level and position of the fistula should be determined, and its relationships to the ureteric orifices and bladder neck are particularly important. Most posthysterectomy fistulas are supratrigonal and located on the posterior bladder wall whilst postradiation fistulas usually involve the trigone and/or bladder neck. With urethral and bladder neck fistulas the failure to pass a cystoscope or sound may indicate that there has been circumferential loss of the proximal urethra, a circumstance which is of considerable importance in determining the appropriate surgical technique and the likelihood of subsequent urethral incompetence. The condition of the tissues must be carefully assessed. Persistence of slough means that surgery should be deferred, and this is particularly important in obstetric and postradiation cases. Biopsy from the edge of a fistula should be taken in radiation fistulas, if persistent or recurrent malignancy is suspected. Malignant change has been reported in a longstanding benign fistula, so where there is any doubt at all about the nature of the tissues, biopsy should be undertaken. In endemic areas, evidence of schistosomiasis, tuberculosis and lymphogranuloma may become apparent in biopsy material, and again it is important that specific antimicrobial treatment is instituted prior to definitive surgery.

Sigmoidoscopy and proctoscopy

Sigmoidoscopy and proctoscopy are important for the diagnosis of inflammatory bowel disease, which may not have been suspected before the occurrence of a fistula. The presence of air bubbles escaping from the vagina when it is filled with saline allows identification of the site of any fistula. Biopsy specimens of the fistula edge of any unhealthy looking area should always be obtained.

Preoperative management

Before epithelialization is complete an abnormal communication between viscera will tend to close spontaneously, provided that the natural outflow is unobstructed. Bypassing the sphincter mechanisms, for example, by urinary catheterization or defunctioning colostomy, may encourage closure.

Urogenital fistula

The early management is of critical importance, and depends on the etiology and site of the lesion. If surgical trauma is recognized within the first 24 hours postoperatively, immediate repair may be appropriate, provided that extravasation of urine into the tissues has not been great. The majority of surgical fistulas, however, are recognized between 5 days and 14 days postoperatively, and should be treated with continuous bladder drainage. It is worth persisting with this line of management in vesicovaginal or urethrovaginal fistulas for 6–8 weeks, since spontaneous closure may occur within this period.

Obstetric fistulas developing after obstructed labor should also be treated by continuous bladder drainage, combined with antibiotics to limit tissue damage from infection. Indeed, if a patient is known to have been in obstructed labor for any significant length of time, or is recognized to have areas of slough on the vaginal walls in the puerperium, prophylactic catheterization should be undertaken. Immediate management should also include attention to palliation and skin care, nutrition, physiotherapy, rehabilitation and overall patient morale. In women wishing to avoid surgery and where bladder drainage is unsuccessful other conservative treatments may be indicated when the vesicovaginal fistula is very small. Small series, and case reports have indicated success with fibrin glue, electrofulguration, laser ablation or combinations of these modalities; no large series, however, has confirmed their value.

Surgical fistula patients are usually previously healthy individuals who entered hospital for what was expected to be a routine procedure, and end up with symptoms infinitely worse than their initial complaint. Obstetric fistula patients in the developing world are social outcasts. Whatever the cause, these women are invariably devastated by their situation. It is vital that they understand the nature of the problem, why it has arisen, and the plan for management at all stages. Confident but realistic counseling by the surgeon is essential and the involvement of nursing staff or counselors with experience of fistula patients is also highly desirable. The support given by previously treated sufferers can also be of immense value in maintaining patient morale, especially where a delay prior to definitive treatment is required.

Intestinogenital fistula

In determining the most appropriate management consideration should be given to the underlying etiology of the intestinovaginal fistula. In patients with obstetric fistula, endoanal ultrasound should be performed to detect anal sphincter damage as the presence or absence of sphincteric injury may alter the choice of procedure. In patients with radiation rectovaginal fistulas or in those with inflammatory bowel disease preoperative anorectal manometry is necessary to assess rectal compliance. When rectal reservoir function is poor then there is unlikely to be a good response from local repair. For recurrent fistulas, radiation-induced fistulas, for those associated with active inflammatory bowel disease, or for ileo- or colovaginal fistulas, a preliminary defunctioning colostomy may be appropriate. However, for the majority of rectovaginal fistulas, defunctioning of the bowel is not required. Although surgeons vary in the extent to which they prepare the bowel prior to rectovaginal fistula repair, it is the author’s preference to carry out formal preparation in all cases of intestinogenital fistula, whatever the level of the lesion. A low-residue diet should be advised for a week prior to admission, followed by a fluid-only diet for 48 hours preoperatively. Polyethylene glycol 3350 (Klean Prep, Norgine Ltd, Harefield, Middlesex, UK), four sachets in 4 liters of water over a 4 hour period, or alternatively sodium picosulfhate (Picolax, Ferring Pharmaceuticals Ltd, Langley, Berks, UK), 10 mg repeated after 6 hours, is given orally on the day before operation. Bowel wash out should be carried out on the evening before surgery, and if the bowel content is not completely clear this procedure should be repeated on the morning of surgery.

General principles of surgical treatment

Timing of repair

Urogenital fistula

The timing of surgical repair is perhaps the single most contentious aspect of fistula management. While shortening the waiting period is of both social and psychological benefit to patients who are always very distressed, one must not trade these issues for compromise to surgical success. The benefit of delay is to allow slough to separate and inflammatory change to resolve. In both obstetric and radiation fistulas there is considerable sloughing of tissues, and it is imperative that this should have settled before repair is undertaken. In radiation fistulas, it may be necessary to wait 12 months or more. In obstetric cases, most authorities suggest that a minimum of 3 months should be allowed to elapse, although others have advocated surgery as soon as slough is separated.

With surgical fistulas the same principles should apply, and although the extent of sloughing is limited, extravasation of urine into the pelvic tissues inevitably sets up some inflammatory response. Although early repair is advocated by several authors, again most would agree that 10–12 weeks postoperatively is the earliest appropriate time for repair.

Pressure from patients to undertake repair at the earliest opportunity is always understandably great, but is never more so than in the case of previous surgical failure. Such pressure must however be resisted, and 8 weeks is the minimal time that should be allowed between attempts at closure.

Intestinogenital fistula

Similarly repair should be delayed until infection has been treated and until inflammation and induration has resolved to allow improved tissue handling. Some rectovaginal fistulas will heal spontaneously during this time. After a failed repair an interval of 3 months should be allowed before undertaking further repair surgery. When there is a coexisting urogenital fistula then rectovaginal fistula repair should be undertaken after and separately from urogenital fistula repair. In such cases, transverse colostomy may be used to temporarily divert feces away from the urogenital repair site until repair of the rectovaginal fistula. In patients with inflammatory bowel disease repair should be delayed until the disease is quiescent and sepsis treated.

Route of repair

Urogenital fistula

Many urologists advocate an abdominal approach for all fistula repairs, claiming the possibility of earlier intervention and higher success rates in justification. Others suggest that all fistulas can be successfully closed by the vaginal route. Surgeons involved in fistula management must be capable of both approaches, and have the versatility to modify their techniques to select that most appropriate to the individual case. Where access is good and the vaginal tissues sufficiently mobile, the vaginal route is usually most appropriate. If access is poor and the fistula cannot be brought down, the abdominal approach should be used. When the fistula lies close to the ureteric orifices and there is a risk of ureteric injury during repair then ureteric stenting may allow the vaginal approach. Alternatively, the need for ureteric reimplantation necessitates an abdominal approach. In the presence of a greatly reduced cystometric capacity, as often seen in postradiation fistulas, the need for concomitant cystoplasty necessitates an abdominal approach. Overall, more surgical fistulas are likely to require an abdominal repair than obstetric fistulas, although in the author’s series of cases from the UK, and those reviewed from Nigeria, two thirds of cases were satisfactorily treated by the vaginal route regardless of etiology.

Intestinogenital fistula

This will depend on the anatomical site of the fistula, number of previous repair attempts, surgeon’s preference, presence or absence of anal sphincter damage and presence or absence of intestinal or vaginal stenosis. In cases of colovaginal or enterovaginal fistulas laparotomy is usually required and recurrence rates are low because of mobilization of healthy tissue. In repairing rectovaginal fistulas then the current approaches include transperineal, transanal or transvaginal repair.

Instruments

All operators have their own favored instruments, although those described by Chassar Moir and Lawson are eminently suitable for repair by any route (Figure 2). The following are particularly useful:

- Series of fine scalpel blades on the no. 7 handle, especially the curved no. 12 bistoury blade
- Chassar Moir 30° angled-on-flat and 90° curved-on- flat scissors
- Cleft palate forceps
- Judd-Allis, Stiles and Duval tissue forceps
- Millin’s retractor for use in transvesical procedures, and Currie’s retractors for vaginal repairs
- Skin hooks to put the tissues on tension during dissection
- Turner-Warwick double-curved needleholder, particularly useful in areas of awkward access, and has the advantage of allowing needle placement without the operator’s hand or the instrument obstructing the view.

Dissection

Great care must be taken over the initial dissection of the fistula, and this stage should probably take as long

Figure 2

Fistula repair instruments

as the repair itself. The fistula should be circumcised in the most convenient orientation, depending on size and access. All things being equal a longitudinal incision should be made around urethral or midvaginal fistulas; conversely, vault fistulas are better handled by a transverse elliptical incision. The tissue planes are often obliterated by scarring, and dissection close to a fistula should therefore be undertaken with a scalpel or scissors. Sharp dissection is easier with countertraction applied by skin hooks, tissue forceps or retraction sutures. Blunt dissection with small pledgets may be helpful once the planes are established, and provided it takes place away from the fistula edge. Wide mobilization should be performed, so that tension on the repair is minimized. Bleeding is rarely troublesome with vaginal procedures, except occasionally with proximal urethro vaginal fistulas. Diathermy is best avoided, and pressure or under-running sutures are preferred.

Suture materials

Although a range of suture materials has been advocated over the years, and different opinions still exist, the author's view is that absorbable sutures should be used throughout all urinary fistula repair procedures. Polyglactin (Vicryl, Ethicon, Edinburgh, UK) 2–0 suture on a 25 mm heavy tapercut needle is preferred for both the bladder and vagina, and polydioxanone (PDS, Ethicon, Edinburgh, UK) 4–0 on a 13 mm round-bodied needle is used for the ureter; 3–0 sutures on a 30 mm round-bodied needle are used for bowel surgery, polydioxanone for the small bowel, and either polydioxanone or braided polyamide (Nurolon, Ethicon, Edinburgh, UK) for large bowel reanastomosis.

Surgical technique

Urogenital fistula repair

Dissection and repair in layers

Two main types of closure technique are applied to the repair of urinary fistulas: the classical saucerization technique described by Sims in 1852, and the much more commonly used dissection and repair in layers. Figures 3–8 demonstrate the latter form of repair in a posthysterectomy vault fistula. Tissue forceps or traction sutures are applied to bring the fistula more clearly into view, and obtain optimal access for repair. Infiltration with 1 in 200 000 adrenaline (epinephrine) helps to reduce bleeding, and may aid dissection by separating tissue planes to some degree. With small lesions it may be helpful to identify the fistula with a probe or Fogerty catheter, so that the track is not 'lost' after dissection. The fistula is then circumcised in a transverse elliptical fashion, using a no. 12 scalpel blade (Figure 3); this should start pos-

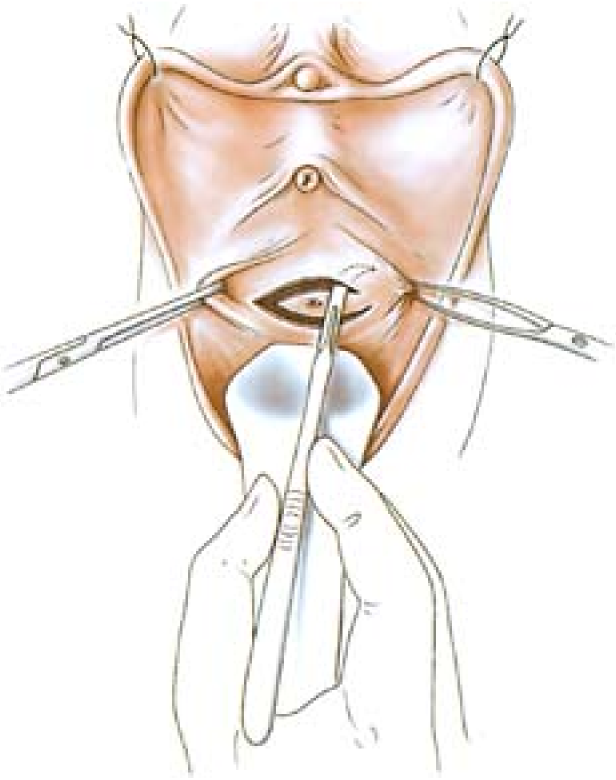

Figure 3

Traction sutures or tissue forceps allow the fistula to be brought into a more accessible position; the fistula is then circumcised in a transverse elliptical fashion, using a no. 12 scalpel blade

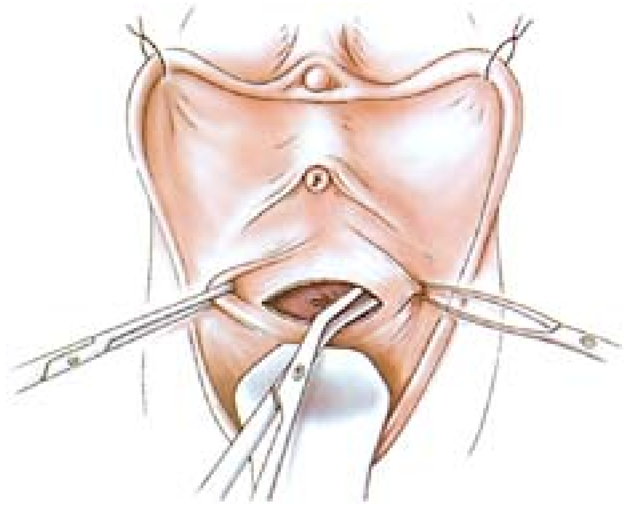

Figure 4

The dissection is then extended using scissors; the vaginal walls should be undermined so that the underlying bladder is mobilized for 1–2 cm beyond the fistula edge

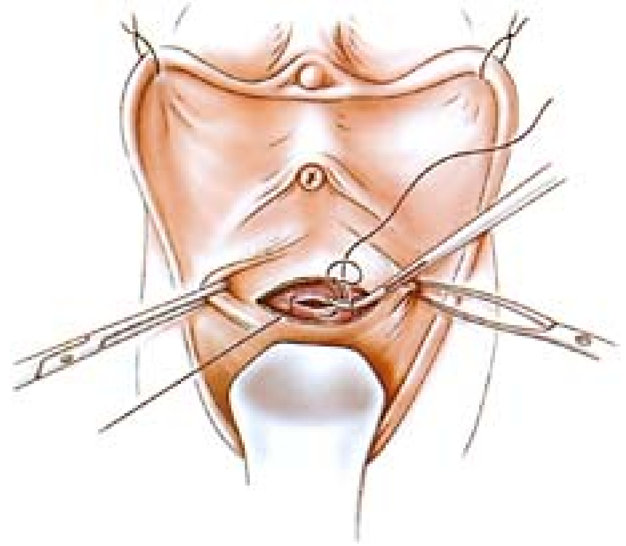

Figure 5

The repair is started at either end, working towards the midline, so that the least accessible aspects are sutured first

teriorly, and be completed on the anterior aspect. The dissection is then extended using scissors; Chassar Moir 30° angled-on-flat and 90° curved-on-flat scissors are particularly useful in this respect (Figure 4). The vaginal walls should be undermined so that the underlying bladder is mobilized for 1–2 cm beyond the fistula edge. The vaginal scar edge may then be trimmed, although most often it is simply inverted within the repair. Sutures must be placed with metic-

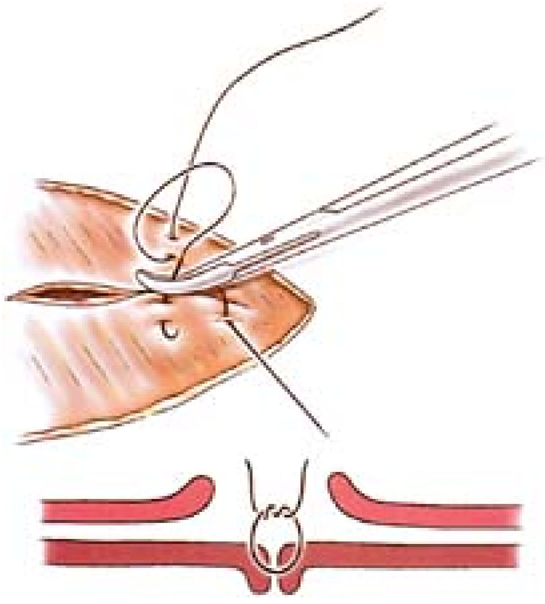

Figure 6

The first layer of sutures in the bladder inverts the bladder edges

ulous accuracy in the bladder wall, care being taken not to penetrate the mucosa which should be inverted as far as possible. The repair should be started at either end, working towards the midline, so that the least accessible aspects are sutured first. Interrupted sutures are preferred and should be placed approximately 3 mm apart, taking as large a bite of tissue as feasible. Stitches that are too close together, or the use of continuous or purse-string sutures, tend to impair blood supply and interfere with healing. Knots must be secure with three hitches, so that they can be cut short, leaving the minimum amount of suture material. With dissection and repair in layers the first layer of sutures in the bladder should invert the bladder edges (Figures 5 and 6); the second adds bulk to the repair by taking a wide bite of bladder wall, but also closes off dead space by catching the back of the vaginal flaps (Figure 7). After the repair has been tested, a third layer of interrupted mattress sutures is used to evert and close the vaginal wall, consolidating the repair by picking up the underlying bladder wall (Figure 8).

Saucerization

The saucerization technique involves converting the track into a shallow crater, which is closed without dissection of bladder from vagina using a single row of interrupted sutures (Figure 9). The method is only applicable to small fistulas, and perhaps to residual

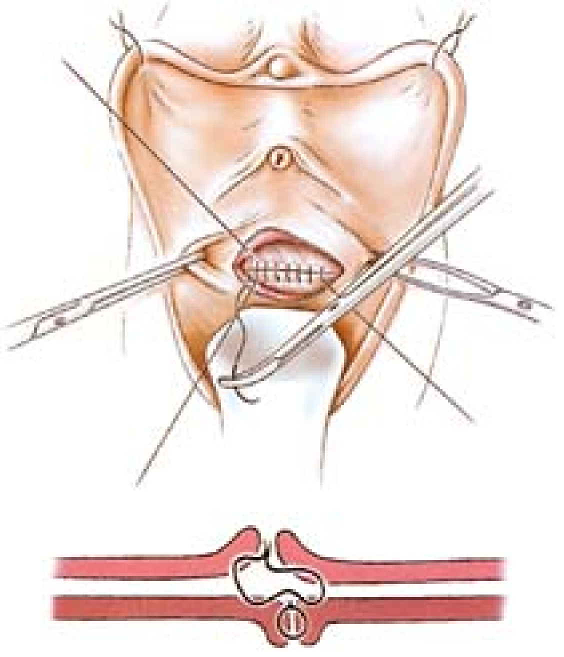

Figure 7

The second layer of sutures adds bulk to the repair by taking a wide bite of bladder wall, and closes off dead space by catching the back of the vaginal flaps

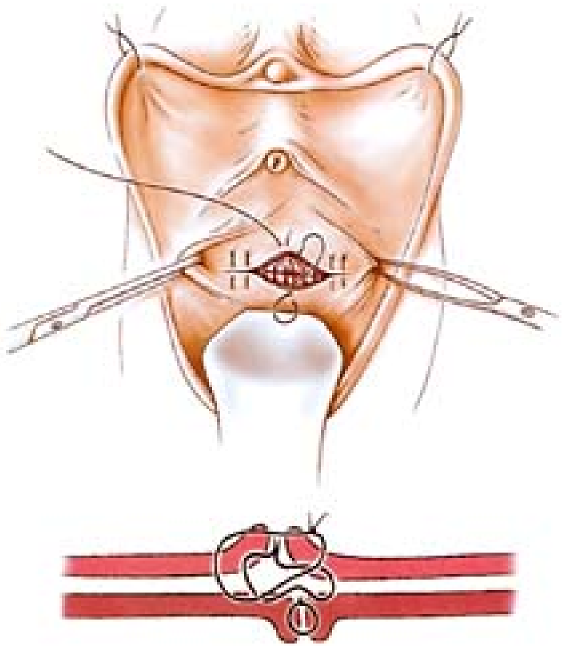

Figure 8

After the repair has been tested, a third layer of interrupted mattress sutures is used to evert and close the vaginal wall, consolidating the repair by picking up the underlying bladder wall

fistulas after closure of a larger defect; in other situations the technique does not allow secure closure without tension.

Vaginal repair procedures in specific circumstances

The conventional dissection and repair in layers as described above is entirely appropriate for the majority of midvaginal fistulas, although modifications may be necessary in specific circumstances. In juxtacervical fistulas in the anterior fornix, vaginal repair may be feasible if the cervix can be drawn down to provide access. Dissection should include mobilization of the bladder from the cervix. The repair should be undertaken transversely to reconstruct the underlying trigone and prevent distortion of the ureteric orifices; the second layer of the repair is used to roll the defect on to the intact cervix, for additional support (Figure 10).

Vault fistulas, particularly those following hysterectomy, can again usually be managed vaginally. The vault is incised transversely and mobilization of the fistula is

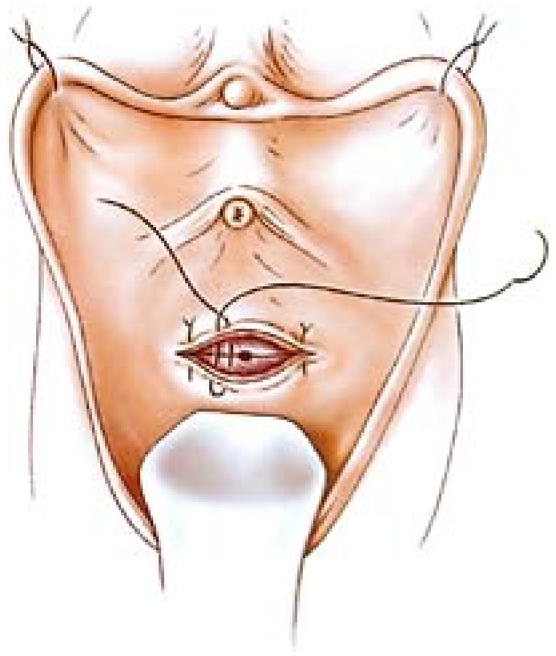

Figure 9

The saucerization technique involves converting the track into a shallow crater, which is closed without dissection of bladder from vagina using a single row of interrupted sutures

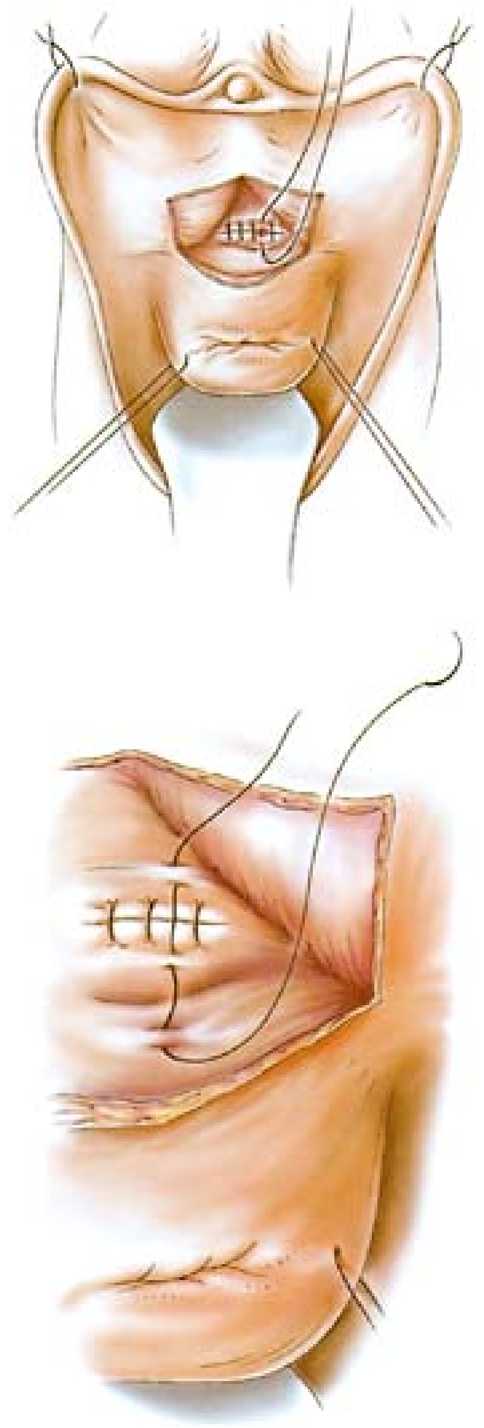

Figure 10

Vaginal repair of a juxtacervical fistula may be feasible if the cervix can be drawn down to provide access; dissection includes mobilization of the bladder from the cervix, and the repair should be undertaken transversely to reconstruct the underlying trigone and prevent distortion of the ureteric orifices. The lower diagram shows this in greater detail

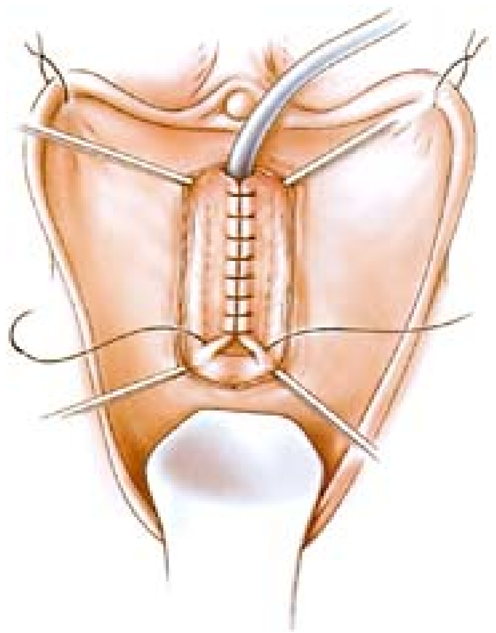

Figure 11

In urethral reconstruction a strip of anterior vaginal wall is constructed into a tube over a catheter

often aided by deliberate opening of the pouch of Douglas. The peritoneal opening does not need to be closed separately, but is incorporated into the vaginal closure.

With subsymphysial fistulas involving the bladder neck and proximal urethra as a consequence of obstructed labor, tissue loss may be extensive, and fixity to underlying bone a common problem. The lateral aspects of the fistula require careful mobilization to overcome disproportion between the defect in the bladder and the urethral stump. A racquet-shaped extension of the incision facilitates exposure of the proximal urethra. Although transverse repair is often necessary, longitudinal closure gives better prospects for urethral competence.

Where there is substantial urethral loss, reconstruction may be undertaken using the method described by Chassar Moir or Hamlin and Nicholson. After a U-shaped incision is made on the anterior vaginal wall, extending from the posterior edge of the fistula to the intended position of the external meatus, a strip of anterior vaginal wall is constructed into a tube over a catheter (Figure 11). Plication of muscle behind the bladder neck is probably important if continence is to be achieved. The interposition of a labial fat or muscle graft not only fills up the potential dead space, but provides additional bladder neck support and improves

Figure 12

([Figure 12](#)–14, colpocleisis procedure) In colpocleisis for the treatment of a radiation fistula by the vaginal route, the dissection should be commenced well away from the fistula edge, aiming to be in normally vascularized tissues as far as possible. Several rows of sutures may be required

Figure 13

A Martius labial fat graft may often be necessary to fill dead space

continence by reducing scarring between bladder neck and vagina. When intrinsic sphincter deficiency is present, continence has been reported in 87% when a rectus sheath sling is fashioned at the time of the flap repair and where the sling is positioned below the interposition graft separating it from the urethra. With very large fistulas extending from bladder neck to vault, the extensive dissection required may produce considerable bleeding. The main surgical difficulty is to avoid the ureters. They are usually situated close to the superolateral angles of the fistula, and if they can be identified they should be catheterized. Straight ureteric catheters passed transurethrally, or double pigtail catheters, may both be useful in detecting the intramural portion of the ureters internally; nevertheless, great care must be taken during dissection.

Radiation fistulas present particular problems, in that the area of devitalized tissue is usually considerably larger than the fistula itself. Mobilization is often impossible, and if repair in layers is attempted the flaps are likely to slough; closure by colpocleisis is therefore required (Figure 12–14). Some have advocated total closure of the vagina although it is preferable to avoid dissection in the devitalized tissue entirely, and to perform a lower partial colpocleisis converting the upper vagina into a diverticulum of the bladder. It is usually necessary to fill the dead space below this with an interposition graft (Figures 13 and 14).

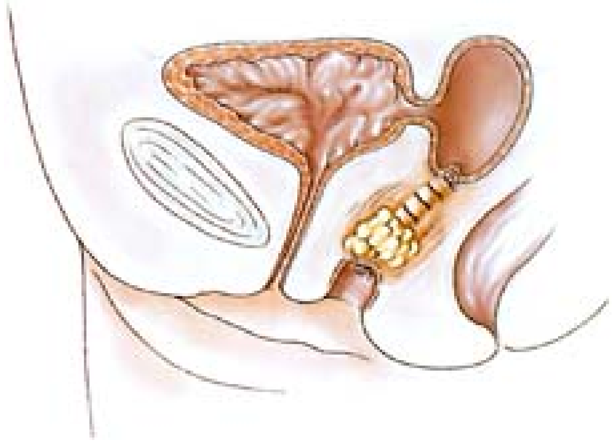

Figure 14

The vaginal or vulval skin is closed with interrupted sutures to cover the fat graft

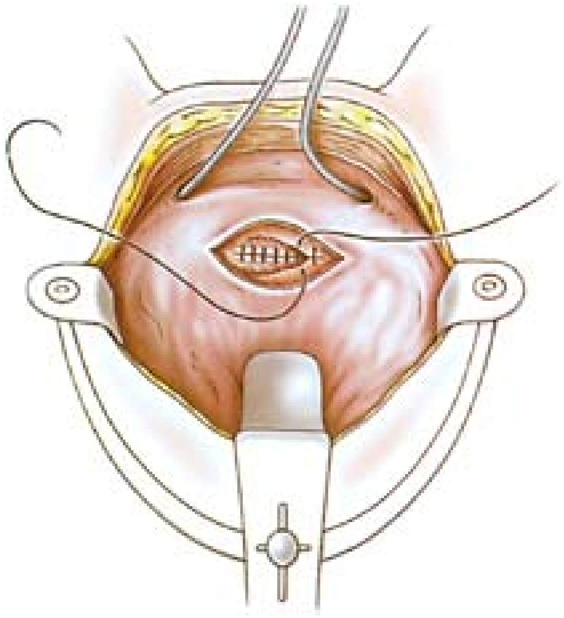

Figure 15

Transvesical fistula repair. After its mobilization from the overlying bladder wall, the vagina has been closed with a single layer of inverting interrupted sutures. The bladder is being closed with a similar layer of interrupted sutures, also picking up the vagina to close dead space. A continuous suture will be inserted into the urothelium for hemostatic purposes

Abdominal repairs

Transvesical repair

Repair by the abdominal route is indicated when high fistulas are fixed in the vault and are therefore inaccessible per vaginam. Transvesical repair has the advantage of being entirely extraperitoneal. It is often helpful to elevate the fistula site by a vaginal pack, and the ureters should be catheterized under direct vision. The technique of closure is similar to that of the transvaginal flap-splitting repair except that for hemostasis the bladder mucosa is also closed, using a continuous suture (Figure 15).

Transperitoneal repair

It is often said that there is little place for a simple transperitoneal repair, although a combined transperitoneal and transvesical procedure is favored by urologists and is particularly useful for vesicouterine fistulas following cesarean section. A midline split is made in the vault of the bladder; this is extended downwards in a racquet shape around the fistula

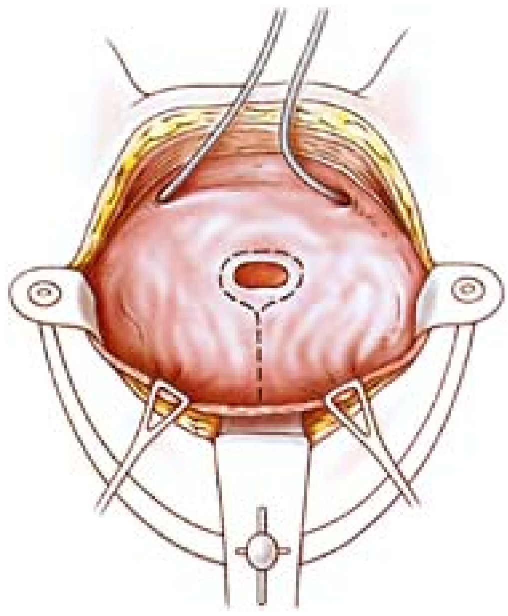

Figure 16

Transperitoneal transvesical repair. A midline split is made in the vault of the bladder, and is extended downwards in a racquet shape around the fistula

(Figure 16). The fistulous track is excised and the vaginal or cervical defect closed in a single layer (Figure 17). The bladder is then closed in one or two layers; either continuous or interrupted sutures may be employed. The interposition of an omental graft may also be considered if there is doubt over the integrity of the repair; this is also particularly appropriate when the technique is used for the repair of radiation fistulas.

Ureteric reimplantation

For ureteric fistulas not manageable by stenting, reimplantation is considered preferable to reanastomosis of the ureter itself, which carries a greater risk of stricture. Several techniques are described for ureteroneo-cystostomy, and the choice will depend on the level of the fistula and the nature of the antecedent pathology. For ureteric lesions within the pelvis, mobilization of the bladder from the opposite pelvic side-wall may be all that is required to allow reimplantation without tension. Otherwise the most widely used techniques are reimplantation using a psoas hitch (Figure 108), or the creation of a flap of bladder wall, the Boari-Ockerblad technique (Figure 19) (see further in Chapter 21). There are few lesions that are too high for these approaches, although where there is significant deficiency it may be necessary to perform an end-to-side anastomosis between the injured ureter and the

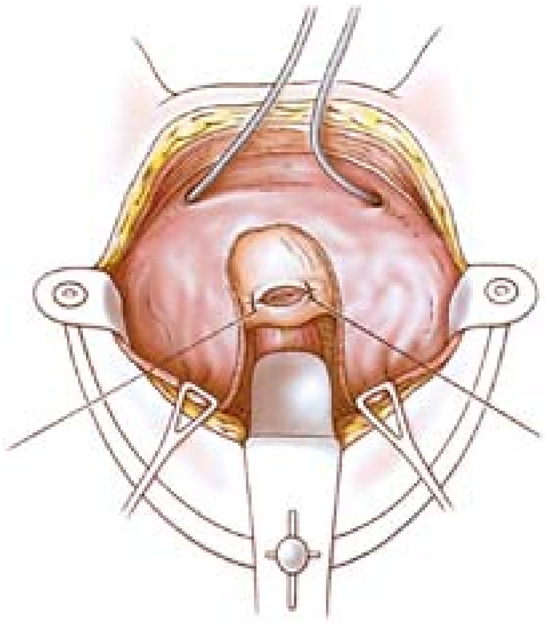

Figure 17

Transperitoneal transvesical repair. The fistulous track is excised and the vaginal or cervical defect closed in a single layer; the bladder is then closed in either one or two layers. An omental interposition graft may also be inserted, particularly when the technique is used for the repair of radiation fistula

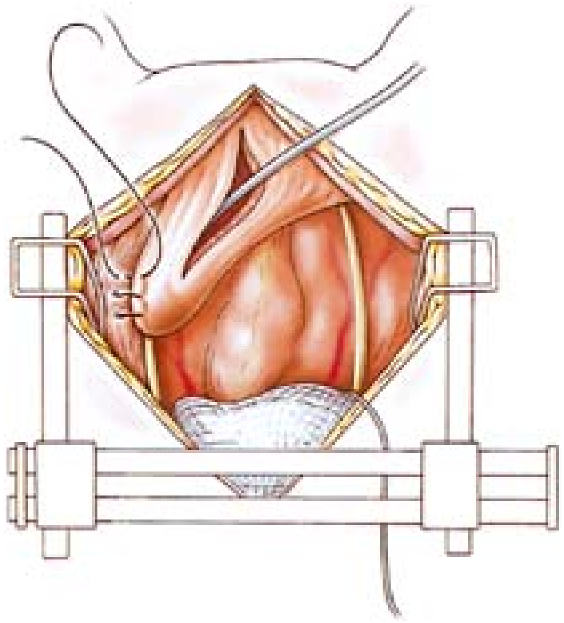

Figure 18

Ureteric reimplantations. Where the bladder cannot easily be mobilized sufficiently, a psoas hitch may allow reimplantation without tension

good contralateral ureter (i.e. a transureteroureterostomy), or to interpose a loop of small bowel.

Interposition grafting

Several techniques have been described to support fistula repair in different sites (see also Chapter 21). In each case, the interposed tissue serves to create an additional layer in the repair, to fill dead space, and to bring new blood supply into the area. The tissues used include:

- Martius graft—a vertical incision is made over the labium majus and a graft of labial fat and bulbocavernosus muscle fashioned by anterosuperior separation from the deep fascia (Colles fascia) over the urogenital diaphragm. Vascular supply is from the posterior labial branches of the internal pudendal artery. Good results are also seen when inferior separation is undertaken and the external pudendal vessels are preserved. The graft is passed subcutaneously to cover a vaginal repair; this is particularly appropriate to provide additional bulk

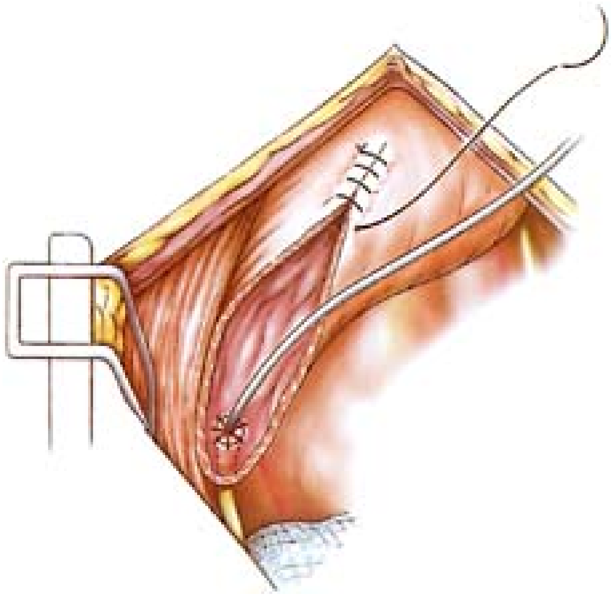

Figure 19

For high ureteric injury the Boari-Ockerblad technique may be appropriate, utilizing a flap of bladder wall to fill the deficiency in a colpocleisis and in urethral and bladder neck fistulas may help to maintain competence of closure mechanisms by reducing scarring (see Figure 13).

- Gracilis muscle passed either via the obturator foramen or subcutaneously is used as above (see Chapter 24).
- Omental pedicle grafts may be dissected from the greater curve of the stomach and rotated down into the pelvis on either the right or left gastroepiploic arteries; this may be used at any transperitoneal procedure, but has its greatest advantage in postradiation fistulas (see Chapter 13).
- Peritoneal flap graft is an easier way of providing an additional layer at transperitoneal repair procedures, by taking a flap of peritoneum from any available surface, most usually the paravesical area. The anterior vaginal wall is opened and after the fistula closed as described earlier, a peritoneal flap is created by dissecting posteriorly along the anterior vaginal wall to expose the edge of peritoneum in the anterior cul-de-sac. The peritoneal edge may then be mobilized from the posterior bladder wall and the flap tacked over the site of fistula closure. Cure rates of 97% and 96% are reported when Martius graft and peritoneal flap interposition respectively are used in cases of complex and/or failed vesicovaginal fistula.

Anal and rectovaginal fistula repair

Laying open of fistula track

An anoperineal fistula may be treated by laying open the tract using a diathermy probe and curetting to remove granulation tissue. Where there is an intersphincteric tract, it is laid open to the uppermost level by dividing the internal sphincter. If there is transsphincteric extension on the under surface of puborectalis, then the perianal skin should be incised at the external opening using fistula scissors and the granulation tissue curetted along the line of the tract.

Rectal advancement flap

This is indicated in cases of high transsphincteric anal fistulas. An Eisenhammer retractor is placed in the anus. A broad-based inverted U-shaped flap comprising rectal mucosa and muscularis is fashioned and separated from the internal sphincter muscle within the anal canal. The internal opening of the fistula tract is excised within the base of the flap (Figure 20) and the

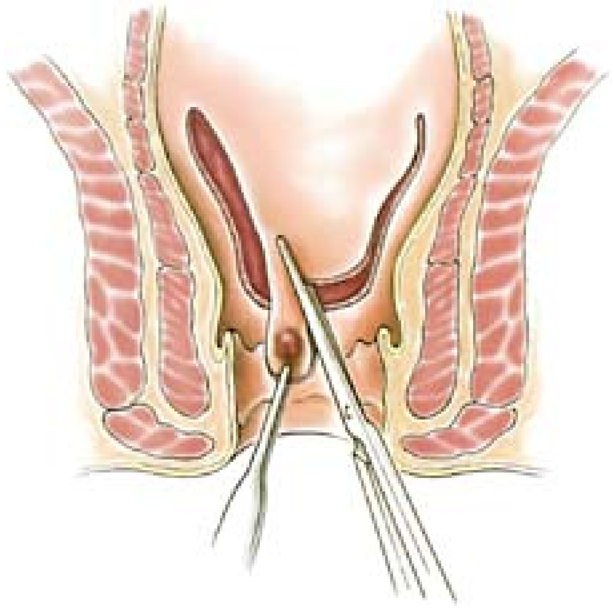

Figure 20

Rectal advancement flap. A flap of the whole thickness of rectal wall is fashioned, the internal opening excised, and the track curetted

tract opening into the internal sphincter is curetted. The external opening of the tract is laid open and curetted. The internal anal sphincter is repaired with interrupted polyglactin sutures. The flap is then held in the advanced position and beginning at the base and working towards the apex it is sutured around the margins with interrupted polyglactin sutures so that it comes to overlie the sphincter closure and advances to the mucocutaneous margin (Figure 21). The inter- or transsphincteric portion is left open to drain.

Transperineal

Conversion to third-degree tear. Although dissection and repair in layers is appropriate for lesions high in the vagina, most gynecologists when repairing fistula low in the vagina use the transperineal route and convert them into a ‘complete perineal tear’ during the course of dissection. This technique is suitable for incompletely healed third-or fourth-degree obstetric perineal lacerations. The patient is positioned in the lithotomy position and the skin bridge incising with a scalpel. The fistula tract and perineal scar are then excised and the vagina and rectum (close to the fistula) are separated from prerectal fascia sufficiently to allow closure without tension and from the anal sphincters. The cut ends of the external sphincter should be identified and secured with stay sutures;

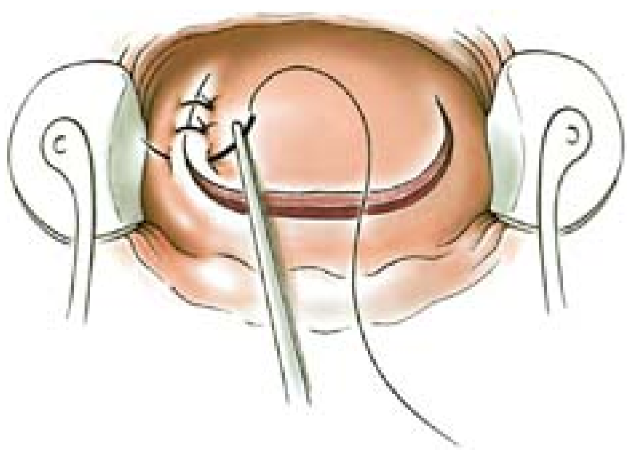

Figure 21

After mobilization of the flap, and closing the defect in the internal sphincter, the flap is sutured in place with interrupted 2/0 polyglactin or polydioxanone sutures

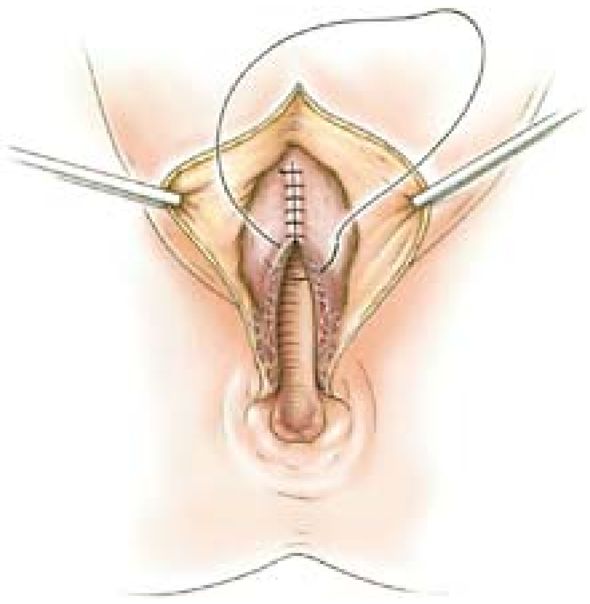

Figure 22

Repair of a low rectovaginal fistula. After the lesion has been converted into a ‘complete perineal tear’, the tissues are widely mobilized. The rectal wall is closed using a continuous suture

if disrupted, the ends should be sought by dissection into the pararectal tissues. Only when all layers are clearly dissected and identified should the repair commence.
The rectal mucosa is closed with either continuous or interrupted suture using 3–0 polyglactin or polydioxanone, commencing above the limit of the dissection. The second layer comprising muscularis (including the internal sphincter) and submucosa, is repaired with a series of Lembert sutures where the sutures do not enter the bowel lumen (Figure 22). An additional layer of sutures may be placed more superficially into the muscularis to help to create a zone of high presure within the rectum, although simply reconstructing the prerectal fascia over the rectal repair as an alternative is entirely appropriate. The external sphincter should then be repaired using 3–0 polydioxanone or prolene sutures. The conventional end-to-end technique with a series of vertical mattress sutures has been found to be unsatisfactory in many cases, and the overlapping repair technique developed by Parks is perhaps particularly appropriate where there is sphincter deficiency in addition to the fistula. The repair is accomplished by a series of interrupted sutures transfixing both layers of muscle, to achieve 2 cm overlap where possible (Figure 23). The superficial transverse perineal muscles are then reapproximated, and the vaginal wall is closed to the level of the hymenal ring, using continuous 2–0 polyglycolic acid. The perineal body may then be further built up using the medial fibers of the levator ani and bulbocavernosus muscles, before the perineal skin is closed. If interposition grafting is thought

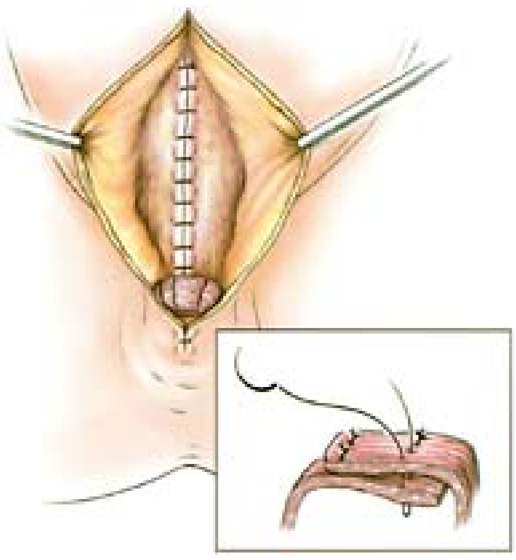

Figure 23

The ‘overlapping’ technique of sphincter repair to be necessary, the Martius graft is the most appropriate for use in low rectovaginal fistula repair.

Transverse transperineal

This is another transperineal method used for low rectovaginal fistulas when it is important to preserve sphincteric function such as in patients with Crohn's disease where it may be performed without the need for a defunctioning colostomy

The patient is placed in the dorsal lithotomy position and the tissues are injected with 1:200 000 adrenaline (epinephrine). A transverse incision is made in the skin across the perineal body above the anal sphincter and the perineal skin is mobilized in a cephalad direction by sharp dissection and extended laterally and superiorly around the fistula between the anterior rectal wall and posterior vaginal wall. Scar tissue is then excised from the vaginal opening of the fistula and the vaginal mucosa repaired longitudinally in two layers with interrupted sutures. Scar tissue from the fistulous opening at the rectal end is then excised and the rectal wall repaired transversely with interrupted sutures to invert the rectal mucosa followed by a second layer to imbricate and reinforce the first layer. The puborectalis muscle is then approximated in the midline with one or two interrupted sutures and the transverse perineii approximated with interrupted sutures. The skin is closed with interrupted sutures.

Transvaginal

This route offers the advantages of better access than the transanal route and avoidance of transection and repair of the anal sphincters. It does not, however, allow direct access to repair the rectal opening of the tract, the highest pressure end of the fistula and compared to some of the other procedures it may be complicated by inadequate tissue mobilization; vaginal narrowing and subsequent dyspareunia. The patient is placed in the lithotomy position and the fistula is identified with a probe. Infiltration with 1:200 000 adrenaline (epinephrine) is followed by circumferential incision of the fistula on the posterior vaginal wall and the fistula tract is excised to the rectal mucosa. The vaginal mucosa is then separated from the underlying prerectal fascia with fistula scissors and the rectum closed with a series of interrupted polyglactin sutures to invert the fistulous opening into the rectal wall. The vaginal mucosa is then closed in the usual way. When the tissues are devitalized, such as in radiation fistulas, the repair may be combined with tissue interposition as described earlier.

Transanal

The transanal approach is favored by coloproctologists and it is suitable for patients with low rectovaginal fistulas without fecal incontinence and with intact anal sphincters, although it may be combined with sphincteroplasty when there is sphincter involvement. It is not a suitable technique for radiation fistulas because of the lack of vascularized tissues. Dissection and repair in layers or rectal advancement flap, as described earlier, may be undertaken.

Advancement rectal sleeve procedure

This is a more complex alternative to the transanal advancement flap in which a circumferential incision is made from the mucocutaneous junction and extended circumferentially to the submucosa in a cephalad direction, to beyond the anorectal ring and supralevator space. The flap usually extends 7 cm in to the rectum with the base at least 4 cm cephalad to the fistula and is raised from the apex to the base with dissection commencing laterally and moving distally. The anterior rectal wall is then mobilized if necessary to the level of the peritoneal reflection and separated laterally from the submucosa and internal sphincter muscle so that it may be pulled down to the level of the dentate line without tension. The internal sphincter and submucosa are then approximated in the midline with interrupted polyglactin sutures. The rectal wall flap is advanced over the repaired area and unhealthy anorectal mucosa with the site of the fistula is excised. The flap margins are attached with interrupted 3–0 polyglactin sutures.

Transabdominal

The transabdominal route is often chosen when the rectum is ulcerated or stenotic following radiation. At laparotomy, the splenic flexure, left colon and sigoid colon and rectum are mobilized to the level of the levator hiatus and the diseased rectum is resected. A colonic reservoir is fashioned either as a J-pouch or as a coloplasty. In the frail or very elderly, colostomy may be the treatment of choice for radiation fistulas.

In patients with Crohn's disease affecting the rectum then proctectomy with colonic pull-through and delayed coloanal anastomosis may be the treatment of choice.

Postoperative management

Fluid balance

Nursing care of patients who have undergone urogenital fistula repair is of critical importance, and obsessional postoperative management may do much to secure success. As a corollary, however, poor nursing may easily undermine what has been achieved by the surgeon. Strict fluid balance must be kept, and an adequate daily fluid intake should be maintained until the urine is clear of blood. Hematuria is more persistent following abdominal surgery than vaginal procedures, and intravenous fluid is therefore likely to be required for longer in these patients.

Bladder drainage

Continuous bladder drainage in the postoperative period is crucial to success, and nursing staff should check catheters hourly throughout each day, to confirm free drainage and check output. Bladder irrigation and suction drainage are not recommended. Views differ as to the ideal type of catheter. The caliber must be sufficient to prevent blockage, although whether the suprapubic or urethral route is used is to a large extent a matter of individual preference. The author's usual practice is to use a 'belt and braces (suspenders)' approach of both urethral and suprapubic drainage initially, so that if one becomes blocked free drainage is still maintained. The urethral catheter is removed first, and the suprapubic retained, and used to assess residual volume, until the patient is voiding normally.

The duration of free drainage depends on the fistula type. Following repair of surgical fistulas, 12 days is adequate. With obstetric fistulas up to 21 days' drainage may be appropriate, and following repair of radiation fistulas 21–42 days are required. If there is any doubt about the integrity of the repair it is wise to carry out dye testing prior to catheter removal. Where a persistent leak is identified free drainage should be maintained for 6 weeks.

Mobility and thromboprophylaxis

The biggest problem in ensuring free catheter drainage lies in preventing kinking or drag on the catheter. Restricting patient mobility in the postoperative period helps with this, and some advocate continuous bed rest during the period of catheter drainage. If this approach is chosen patients should be looked on as being at moderate to high risk for thromboembolism, and prophylaxis must be employed (see Chapter 1).

Antibiotics

Antibiotic cover is advised for all intestinovaginal fistula repairs. If prophylactic antibiotics are not used at urogenital fistula repair, catheter urine specimens should be collected for culture and sensitivity every 48 hours; only symptomatic infection need be treated in the catheterized patient.

Bowel management

If patients are restricted to bed following urogenital fistula repair, a laxative should be administered to prevent excessive straining at stool. Following abdominal repair of an intestinovaginal fistula patients should either have a nasogastric tube inserted or be restricted to nil by mouth until they are passing flatus; the majority prefer the latter approach. Once oral intake is allowed, or following vaginal repair of a rectovaginal fistula, a low-residue diet should be administered until at least postoperative day 5. Some authorities advocate total parenteral nutrition throughout the first week postoperatively for all intestinovaginal fistulas. Enemas and suppositories should be avoided, although a mild aperient, such as dioctyl sodium (docusate sodium), is advised to ease initial bowel movements.

Subsequent management

On removal of catheters most patients will feel the desire to void frequently, since the bladder capacity will be functionally reduced after being relatively empty for so long. In any case it is important that the bladder does not become overdistended, and hourly voiding should be encouraged and fluid intake limited. It may also be necessary to wake patients once or twice during the night for the same reason. After discharge from hospital, patients should be advised to gradually increase the period between voiding, aiming to achieve a normal pattern by 4 weeks postoperatively. Tampons, pessaries, douching and penetrative sex should be avoided until 3 months postoperatively.

References

Bladou F, Houvenaeghel G, Delpero JR, et al. (1995) Incidence and management of major urinary complications after pelvic exenteration for gynecological malignancies. *J Surg Oncol* **58**:91–66.

Blaivas JG, Heritz DM (1996) Vaginal flap reconstruction of the urethra and vesical neck in women: a report of 49 cases. *J Urol* **155**(3):1014–17.

Chassar Moir J (1967) *The vesico-vaginal fistula*, 2nd edn. London: Bailliere.

Eilber KS, Kavaler E, Rodriguez LV, et al. (2003) Ten-year experience with transvaginal vesicovaginal fistula repair using tissue interposition. *J Urol* **169**(3):1033–6.

Elkins TE, DeLancey JO, McGuire EJ (1990) The use of modified Martius graft as an adjunctive technique in vesicovaginal and rectovaginal fistula repair. *Obstet Gynecol* **75**(4):727–33.

Emmert C, Köhler U (1996) Management of genital fistulas in patients with cervical cancer. *Arch Gynecol Obstet* **259**:19–24.

Evans LA, Ferguson KH, Foley JP, et al. (2003) Fibrin sealant for the management of genitourinary injuries, fistulas and surgical complications. *J Urol* **169**(4):1360–2.

Hamlin R, Nicholson E (1969) Reconstruction of urethra totally destroyed in labour. *Brit Med J* **2**:147–50.

Hawley P, Burke M (1985) Anal sphincter repair. In: Henry M, Swash M, eds. *Coloproctology and the pelvic floor. Pathophysiology and management.* London: Butterworth: 252–8.

Hilton P (1997) Debate: Post-operative urogenital fistulae are best managed by Gynaecologists in specialist centres. *Br J Urol* **80**(suppl 1):35–42.

Hilton P. (1998) The urodynamic findings in patients with urogenital fistulae. *Brit J Urol* **81**:539–42.

Hilton P (2002) Urogenital fistulae. In: Maclean A, Cardozo L, eds. *Incontinence in women—proceedings of the 42nd RCOG Study Group.* London: RCOG: 163–81.

Hilton P. 2000 Bladder drainage. In: Stanton S, Monga A, eds. *Clinical Urogynaecology.* London: Churchill-Livingstone: 541–50.

Hilton P Ward A. (1998) Epidemiological and surgical aspects of urogenital fistulae: a review of 25 years experience in south-east Nigeria. *Int Urogynecol J & Pelvic Floor Dysfunct* **9**:189–94.

Huang WC, Zinman LN, Bihrle W, 3rd (2002) Surgical repair of vesicovaginal fistulas. *Urol Clin North Am* **29** (3):709–23.

Hudson CN (1968) Malignant change in an obstetric vesicovaginal fistula. *Proc Roy Soc Med* **61**(12):1280–1.

Jonas U, Petri E (1984) Genitourinary fistulae. In: Stanton S, ed. *Clinical gynecologic urology.* St Louis: Mosby: 238–55.

Kelly J, Kwast B (1993) Epidemiologic study of vesicovaginal fistula in Ethiopia. *Int Urogynecol J* **4**:278–81.

Kiricuta I, Goldstein A (1972) The repair of extensive vesicovaginal fistulas with pedicled omentum: a review of 27 cases. *J Urol* **108**:724–7.

Kodner IJ, Mazor A, Shemesh EI, et al. (1993) Endorectal advancement flap repair of rectovaginal and other complicated anorectal fistulas. *Surgery* **114**(4):682–9.

Lawson J (1972) Vesical fistulae into the vaginal vault. *Br J Urol* **44**:623–31.

Lawson J (1978) The management of genito-urinary fistulae. *Clin Obstet Gynecol* **6**:209–36.

Lawson L, Hudson C (1987) The management of vesico-vaginal and urethral fistulae. In: Stanton S, Tanagho E, eds. *Surgery for female urinary incontinence.* Berlin: Springer: 193–209.

Lee R, Symmonds R, Williams T (1988) Current status of genitourinary fistula. *Obstet Gynecol* **71**:313–19.

Morita T, Tokue A (1999) Successful endoscopic closure of radiation induced vesicovaginal fistula with fibrin glue and bovine collagen. *J Urol* **162**(5):1689.

Parks A, McPartlin J (1971) Late repair of injuries of the anal sphincter. *Proc Roy Soc Med* **64**:1187–9.

Saclarides TJ (2002) Rectovaginal fistula. *Surg Clin North Am* **82**(6):1261–72.

Smith A, Daneshgari F, Dmochowski R, et al. (2002) Surgical treatment of incontinence in women. In: Abrams P, Cardozo L, Khoury S, Wein A, eds. *Incontinence; 2nd WHO international consultation on incontinence.* Plymouth: Health Publications: 823–63.

Stoker J, Rociu E, Schouten WR, et al. (2002) Anovaginal and rectovaginal fistulas: endoluminal sonography versus endoluminal MR imaging. *Am J Roentgenol* **178**(3):737–4l

Sultan AH, Kamm MA, Hudson CN, et al. (1994) Third degree obstetric and sphincter tears: Risk factors and outcome of primary repair. *BMJ* **308**:887–91.

Waaldijk K (1989) *The surgical management of bladder fistula in 775 women in northern Nigeria.* [MD thesis]: University of Amsterdam.

Wiskind AK, Thompson JD (1992) Transverse transperineal repair of rectovaginal fistulas in the lower vagina. *Am J Obstet Gynecol* **167**(3):694–9.

White A, Buchsbaum H, Blythe J, et al. (1982) Use of the bulbocavernosus muscle (Martius procedure) for repair of radiation-induced rectovaginal fistulas. *Obstet Gynecol* **60**(1):114–18.
World Health Organization (1989) *The prevention and treatment of obstetric fistulae: a report of a technical working group.* Geneva: WHO.
Wall L, Arrowsmith S, Briggs N, et al. (2002) Urinary incontinence in the developing world: the obstetric fistula. In: Abrams P, Cardozo L, Khoury S, Wein A, eds. *Incontinence; 2nd WHO international consultation on incontinence.* Plymouth: Health Publications 893–936.
Yeates W (1987) Uretero-vaginal fistulae. In: Stanton S, Tanagho E, eds. *Surgery for female urinary incontinence.* Berlin: Springer: 211–17.
Zacharin R (1988) *Obstetric fistula.* Vienna: Springer.

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23
Treatment of vascular defects and injuries

Karl A Illig
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Introduction

The pelvis and groin contain a complex web of blood vessels. Given the magnitude of resection often needed when treating pelvic malignancies, it is not uncommon to be faced with the need to address major vascular issues. These fall into three general categories: inadvertent injuries requiring repair; planned resection as part of tumor excision, requiring reconstruction; and caval interruption to prevent pulmonary embolism.

It should be remembered that preservation of life through control of hemorrhage takes priority over preservation of blood flow to the limbs.

Indications

The primary indication for vascular repair is, of course, a vascular injury Major blood vessels may at times need to be resected along with the specimen as part of en bloc extirpation. Not every defect requires reconstruction, however.

The aorta and common and external iliac arteries form the blood supply to the legs, and must always be reconstructed if the limb is to remain viable. If direct reconstruction is not possible, an 'extra-anatomic' (femoral-femoral or axillary-femoral) bypass can be constructed to preserve limb blood flow.

Venous bleeding can be much more serious than arterial bleeding, primarily because the thin walls and prodigious tributaries make control and repair difficult. Collateral drainage, also, is rich. These two concepts suggest that virtually any vein, including the cava, can be ligated if absolutely necessary. At times a venous reconstruction will be required, but urgency is less than after ligation of arterial structures.

Anatomic considerations

The two hypogastric (internal iliac) arteries and the inferior mesenteric artery (IMA) together supply blood flow to the pelvis, including the buttocks, left colon, and terminal spinal cord. It is a near-absolute requirement that at least one of these three vessels be preserved. The IMA is frequently the least important source of pelvic blood flow; every effort should be made, however, to preserve at least one hypogastric artery. Within these guidelines, essentially any other vessel can be ligated with impunity.

The anatomy of the lower abdominal, pelvic and groin vasculature is illustrated in Figures 1 and 2.

Remember that arteries are thick-walled, resistant to

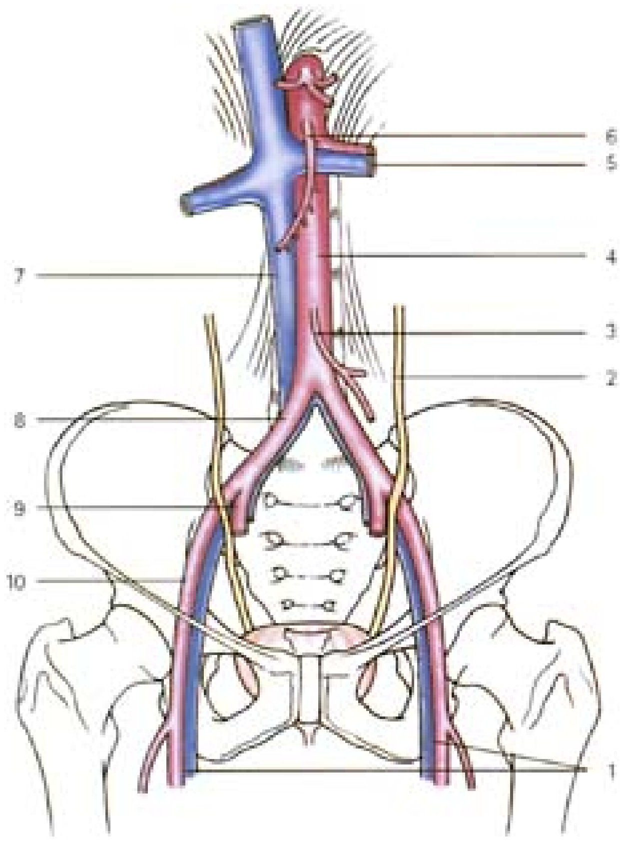

Figure 1

Abdominal and pelvic vasculature
1 Femoral artery and vein
2 Ureter artery
3 Inferior mesenteric artery and vein
4 Aorta
5 Renal artery and vein and vein
6 Superior mesenteric
7 Inferior vena cava
8 Common iliac artery
9 Internal iliac artery
10 External iliac artery and vein

tearing, and easier to repair than veins. Veins, by contrast, are thin-walled, do not hold their shape, and tear easily.
The veins tend to lie behind the arteries (Figure 3). This is critically important at the region of the aortic bifurcation and proximal iliac arteries, where dissection behind the arteries (circled area) or within the aortic bifurcation can easily precipitate massive, life-threatening venous hemorrhage.
In general, trying to control an injury directly is counterproductive. For arterial injuries, proximal and distal control at sites remote from the bleeding are required (Figure 4). Direct clamping can sometimes be problematic, for example in the hypogastric arteries. In these cases control can be accomplished by intraluminal balloon catheter occlusion. For venous

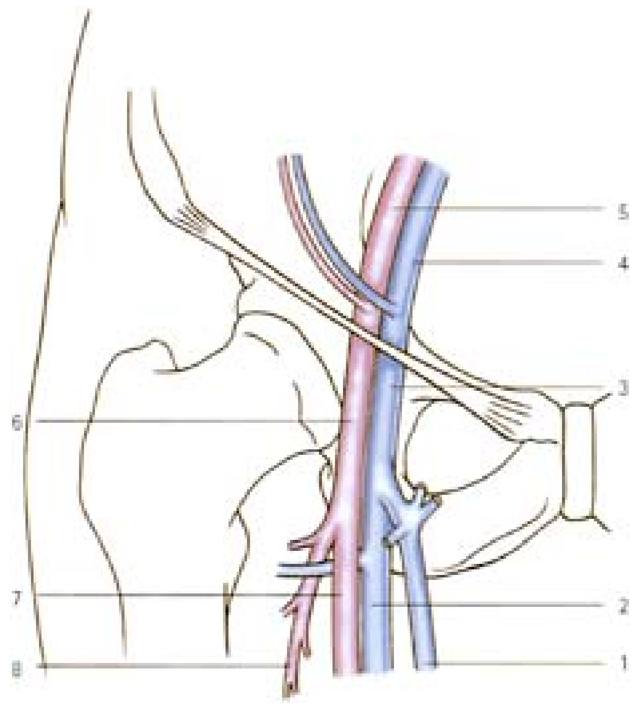

Figure 2

Vasculature of the groin
1 Saphenous vein
2 Superficial femoral vein
3 Common femoral vein
4 External iliac vein
5 External iliac artery
6 Common femoral artery
7 Superficial femoral artery
Deep femoral artery (profunda)

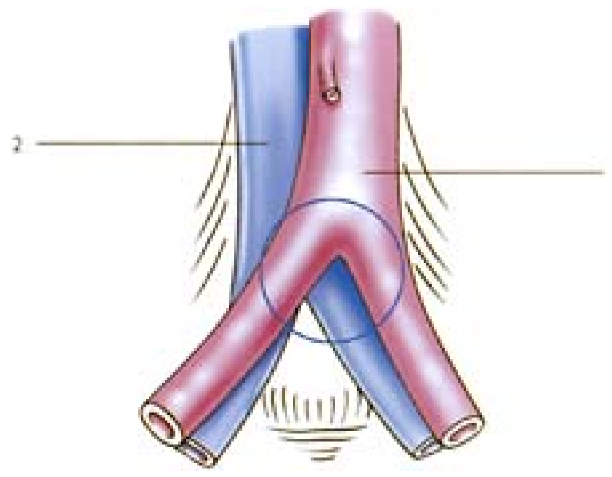

Figure 3

Aortic bifurcation—a danger area (circled)
1 Aorta
2 Vena cava

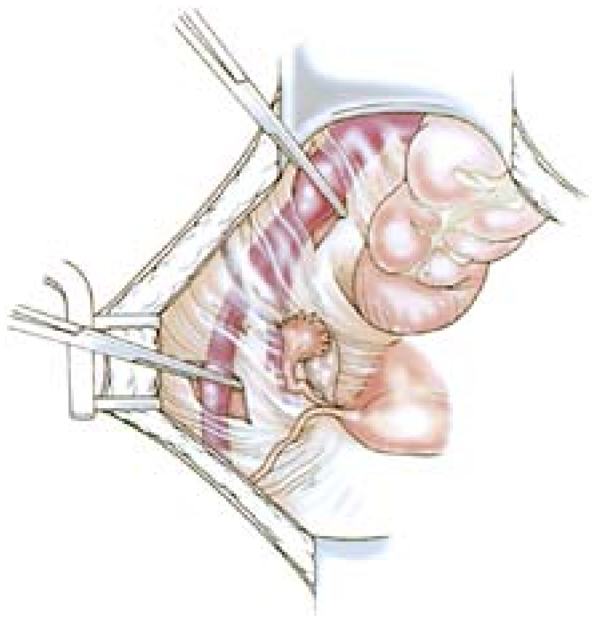

Figure 4

Control at sites remote from the bleeding is essential for arterial injuries

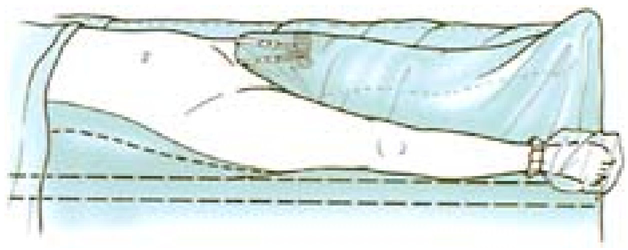

Figure 5

Draping to gain access for saphenous vein harvest

injuries, direct pressure or packing while the situation is sorted out is much more useful than trying to see the injury or control it with a clamp. Direct manipulation with rigid instruments will often extend the tear and worsen the situation.

For vessel repair, autologous tissue is usually preferred (especially in a potentially infected field), although this 'rule' must often be violated. An option in unfavorable situations is to route a graft through an unviolated, 'extra-anatomic' plane. If vessel resection is planned or possible, include a source of autogenous vein (e.g. a leg, circumferentially prepared) in the surgical field (Figure 5).

The best procedure to follow in any unplanned vascular injury is first to control the bleeding with direct pressure; this may be accomplished with a finger or by packing with a sponge. Once the bleeding is controlled, get help (in terms of both additional staff and specialist advice, when needed) and formulate a plan before anything further is done.

Arterial control and repair

When dealing with an arterial injury or planned resection and repair, proximal and distal control are vitally important—this point cannot be overemphasized. In general, circumferential dissection of the aorta and common iliacs is counterproductive because of the risk of venous injury; dissection limited to the sides is usually sufficient. If the aorta is to be clamped, dissection should be carried down to the spine. In all arterial surgery, a dissection plane directly on the arterial adventitia is easiest and safest (Figure 6). Systemic heparin (125 units/kg) should be administered before clamping if bleeding is not diffuse; anticoagulation is reversed

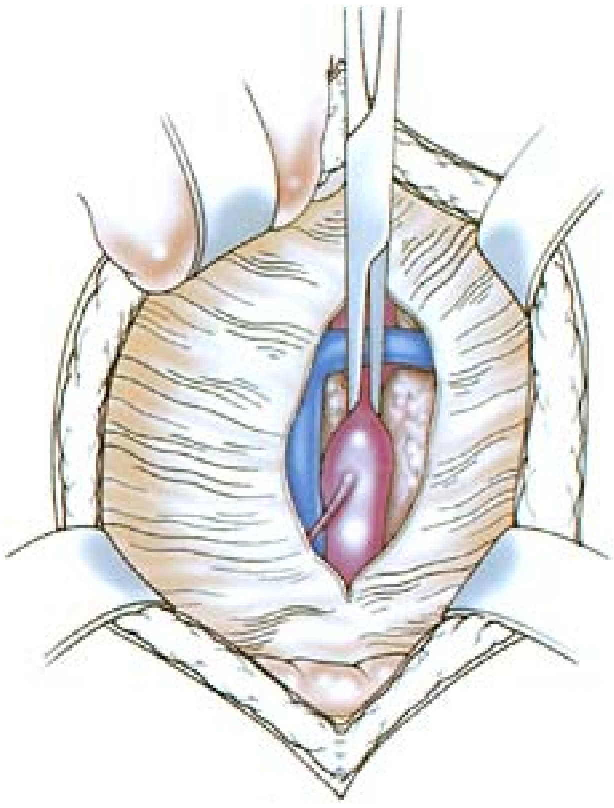

Figure 6

Exposure of the infrarenal aorta (duodenum is retracted laterally and superiorly). Note that the aorta itself is well cleared

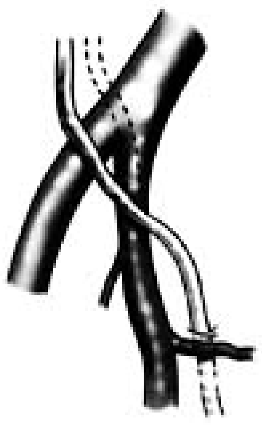

Figure 7

Ureter and the iliac bifurcation

after blood flow is re-established with protamine sulfate (1 mg per 100 units of heparin administered). The ureter passes over the iliac bifurcation (Figure 7), making continuous exposure of the top of the iliac vessels problematic.

Small lacerations of the major vessels, especially if oriented transversely to the vessel axis, can be repaired using monofilament, non-absorbable suture (3–0 or 4–0 for the aorta, 5–0 for the iliac arteries). When the artery is diseased, the needle should be passed from inside to outside to avoid dislodging intraluminal plaque. All knots should be extraluminal (Figure 8). Direct repair of longitudinal injuries in the iliac (or smaller) vessels will usually narrow the lumen, so patch repair is preferred (Figures 9 and 10).

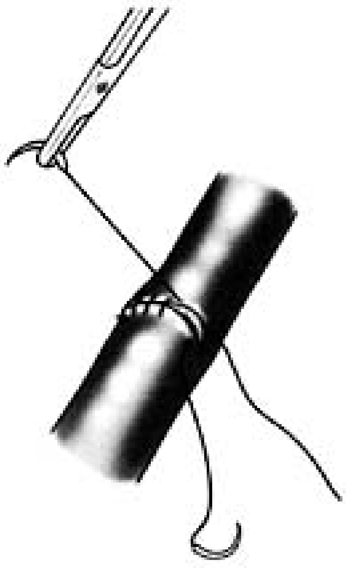

Figure 8

Suture technique for closure of a transverse arteriotomy

Any defect involving actual tissue loss, especially encompassing the entire circumference of a vessel, will usually require an interposition graft and is beyond the scope of this discussion.

Venous control and repair

Major venous injuries, somewhat paradoxically, can be more life-threatening than arterial defects. Veins are thin-walled, do not hold their shape, and are often less accessible. When faced with a major venous injury (dark, non-pulsatile bleeding), the first step is to apply gentle pressure. The temptation to control the injury with forceps or a clamp, even if the tear is apparently visible, should be resisted; doing so will often extend the tear and often convert a remediable situation into

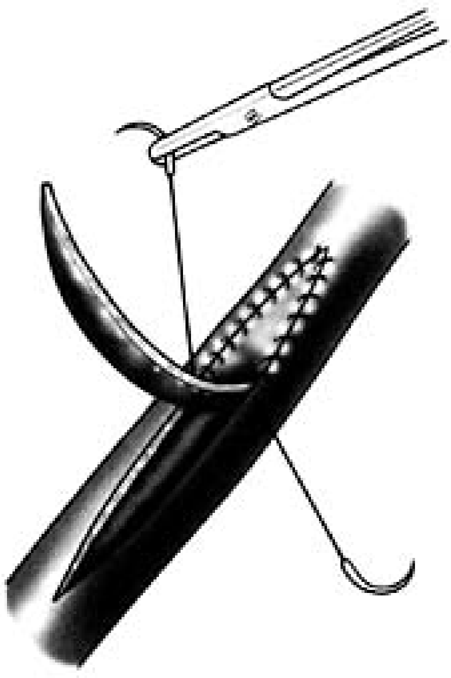

Figure 9

Initial stages of longitudinal arteriotomy: patch closure

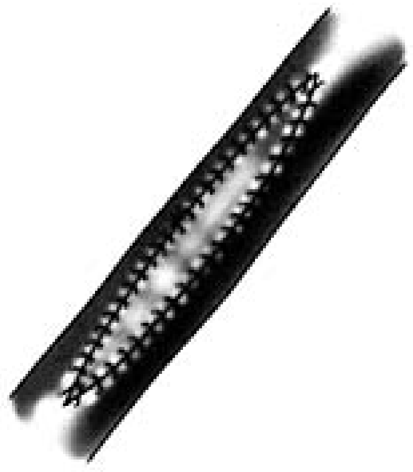

Figure 10

Completed closure

one that is very serious indeed. Several options are available. First, pressure itself will often solve the problem; if you are fortunate, resist the temptation to fiddle any further! Don't look, don't dissect, just accept your good fortune and move on. Second, pressure proximally and distally, without any dissection (e.g. digitally or with sponge-sticks), can control the bleeding enough to make the defect visible. Third, blind suturing is sometimes acceptable if no critical structures (such as the ureter) are near. Finally, ligation is usually safe and well tolerated, especially if the patient's life is at risk.
In these situations, obtaining help, in terms of both experienced assistants to provide exposure and vascular surgical assistance, is of utmost importance, as is gaining control of the hemorrhage without doing further damage so that a plan can be formulated and carried out.

Vascular patches

Most longitudinal defects, even if no tissue is resected, will result in a narrowed lumen if repaired primarily. Thus, patch angioplasty is required for repair of most longitudinal defects in the iliac or smaller vessels.
Autologous tissue is preferred, especially in the presence of a potentially infected field. The greater saphenous vein is an excellent choice, as is the hypogastric artery. It is important that the endothelial surface should be oriented luminally. If, in a clean field, autologous tissue is not available, Dacron or polytetrafluoroethylene (PTFE) can be used. Fine monofilament non-absorbable suture material is used. A continuous suture is perfectly adequate. Exposure is best achieved by starting at one end and placing the first two or three stitches in a 'parachute' fashion before bringing the patch in contact with the vessel (see Figure 9). The first ('heel') suture should be mattressed so that the needle always passes from inside to outside the artery. The suture is then continued around the patch and the knot tied along a long end of the patch (see Figure 10).

Caval interruption

Malignancy has long been known to be associated with hypercoagulability. When combined with pelvic surgery, immobilization and often advanced age, the risk of deep venous thrombosis and pulmonary embolus is frequently high enough to warrant prophylactic caval interruption. Caval interruption can be performed by placement of one of a variety of intraluminal devices percutaneously via the groin or subclavian vein into the infrarenal cava. During laparotomy, however, the cava can be effectively interrupted by means of an external clip.

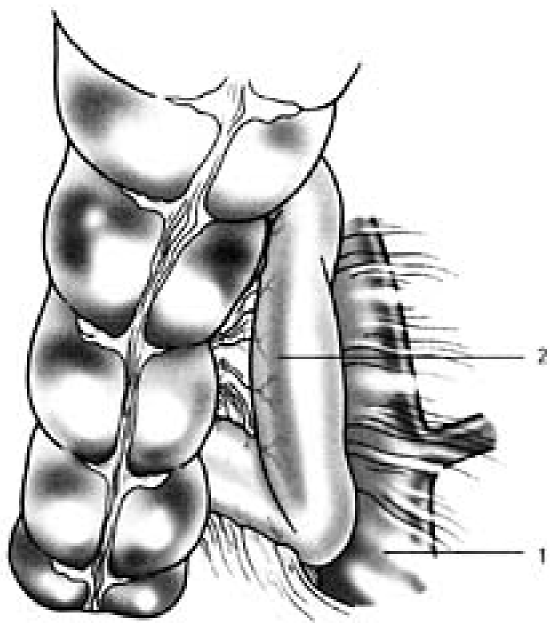

Figure 11

Location for the clip
1 Inferior vena cava
2 Colon and duodenum being mobilized to right

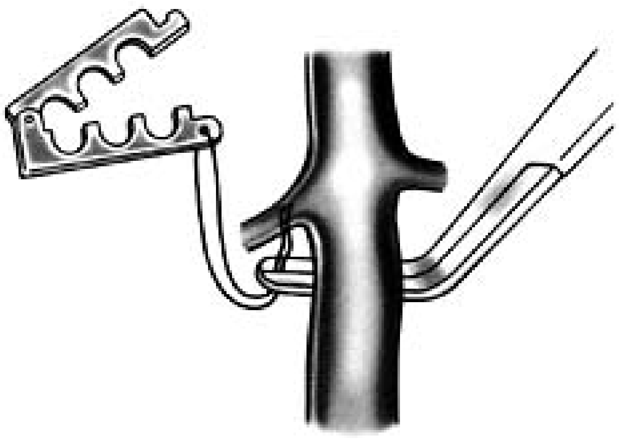

Figure 12

A clamp is used to grasp the string attached to the DeWeese-Adams clip

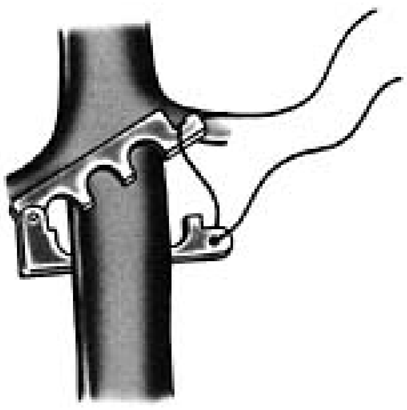

Figure 13

The clip is brought around the inferior vena cava

The clip is applied to the inferior vena cava (IVC) below the level of the renal veins (Figure 11). The cava is exposed by mobilizing the right colon and the duodenum in the avascular plane (Kocher maneuver). Circumferential exposure along a short length of the IVC is required.

Figure 14

The clip in position

A large right-angled clamp is gently passed behind the cava and used to grasp the string attached to the bottom jaw of the clip (Figures 12–14). The bottom jaw is then gently brought behind the cava, and the string tied over the notch on the top, bringing the jaws together over the cava. This creates multiple small channels, each incapable of allowing a significant embolus to pass. Even though pulmonary embolus is prevented with a high degree of certainty, if a deep venous thrombosis of the leg is present, anticoagulation is best continued (if not contraindicated) in an attempt to reduce the risk of extension of clot and post-phlebitic sequelae.

References

Ballew KA, Philbrick JT, Becker DM (1995) Vena caval filter devices. *Clin Chest Med* 16:295–305.
Ouriel K, Rutherford RB (1998) *Atlas of vascular surgery: operative procedures.* Philadelphia: WB Saunders Co.
Rutherford RB (1993) *Atlas of vascular surgery: basic techniques and exposures.* Philadelphia: WB Saunders Co.

24
Plastic reconstructive procedures

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Introduction

Surgical cure demands adequate disease-free margins. Since large debulking procedures are often necessary, reconstructive techniques are required to restore anatomy and promote uncomplicated healing. Regional flaps are the most commonly used and effective of procedures. Flap selection is based on the type of defect and patient characteristics. The pudendal thigh flap is relatively simple and has the distinction of being at least partially sensate. The rectus abdominis muscle flap is a very versatile flap, useful in covering many defects. It is highly reliable, with a consistent vascular supply and muscular development. The gracilis flap has been popular for many years for vaginal reconstruction, but it is somewhat less reliable.

Anatomic considerations

Vascular supply

Skin vascularization may be direct or indirect. Direct vessels travel between muscles and along fascial planes to enter the skin. Indirect vessels arise from named vessels as perforators of the fascia from the underlying muscle. Regional flaps (e.g. gracilis flap) require a well defined vascular pedicle to support the indirect blood supply to the overlying skin. Certain muscles used for flaps have a single dominant vascular pedicle (e.g. epigastric vessels for the rectus abdominis) or one dominant vascular pedicle with several minor ones (e.g. the medial femoral circumflex or femoral artery for the gracilis muscle). The pudendal thigh flap derives its blood supply mostly from the posterior labial vessels and the anastomotic channels involving the medial femoral circumflex and the obturator arteries. Knowledge of the vascular anatomy will allow better planning of the available territories for covering defects.

Nerve supply

No major nerve should be encountered during these reconstructive procedures. Although the gracilis muscle is innervated by a branch of the obturator nerve, it is usually not identified as a distinct structure. As with all surgical procedures, some loss of sensation will be encountered in the operative field. Because reconstructive surgery involves the retention of a large skin island after it is severed from its nerve supply (e.g. the rectus flap), the patient may be more aware of this deficiency than after non-reconstructive surgery. With use of either the pudendal thigh flap or gracilis flap, a partially sensate reconstruction may be achieved.

Muscles involved

The rectus abdominis muscle inserts in the pubic tubercle and arises from the sixth, seventh and eighth ribs. It plays a role in protecting the abdominal contents, breathing and defecating, and stabilizes the pelvis during walking. The gracilis muscle arises from the pubic tubercle and inserts on to the medial tibia pes anserinus. It helps to stabilize the knee and laterally rotates the thigh. Loss of these muscles is usually compensated for by the remaining muscles in their functional group so that no significant motor defect remains.

Bony landmarks

A line drawn from the pubic symphysis to the medial epicondyle should approximate the anterior border of the gracilis muscle.

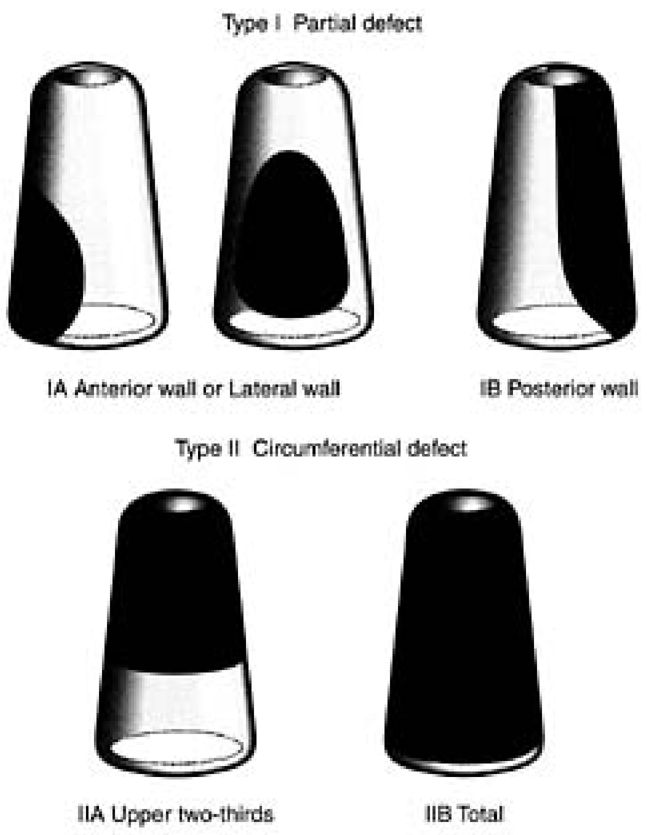

Figure 1

Classification of acquired vaginal defects. Defects are either partial (Type I) or circumferential (Type II)

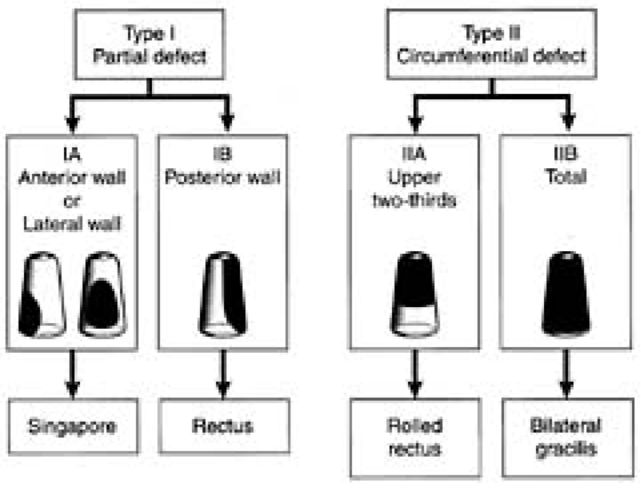

Figure 2

Algorithm for reconstruction of the vagina based on defect type

Indications

Vaginal defects may be classified based on their location and size (Figure 1). The type of defect determines the most appropriate flap choice. Small defects may be amenable to primary or advancement flap closure while more significant defects will require regional flaps. Defects are either partial (Type I) or circumferential (Type II). Type I, or partial, defects can be further classified based on whether they involve the anterolateral or posterior walls of the vagina. Type II, or circumferential, defects involve either the upper two thirds of the vagina or the entire vaginal cylinder (Figure 2).

Partial defects involving the anterior or lateral vaginal walls (Type IA) may be reconstructed with pudendal fasciocutaneous flaps. Unilateral or bilateral flaps can be used. Partial defects involving the posterior wall (Type IB) will benefit from use of the rectus flap. This flap will supply bulk to close dead space in the posterior pelvis. It will also provide sufficient skin to resurface the posterior vaginal wall. Circumferential defects of the upper two thirds of the vagina (Type IIA) are also best reconstructed with the rectus flap. The flap may be ‘tubed’ to create a cap that can be sutured to the remaining vaginal cuff. Circumferential total defects (Type IIB) are generally reconstructed with bilateral gracilis flaps. Such defects commonly result from total pelvic exenteration. The large surface area of the gracilis flaps facilitates restoration of the vaginal cylinder while also providing sufficient volume to fill the pelvis and promote healing.

Surgical procedure

Full-thickness cutaneous advancement flaps

Cutaneous advancement flaps (V-Y procedure, Z-plasty) are useful for closure of small wounds, where mobilization of adjacent skin and subcutaneous tissue can reduce tension and allow adequate skin approximation. Such flaps should not be used for larger defects. Skin islands of varying sizes and shapes can be created adjacent to the defect as long as the patient has a good microvasculature (Figure 3). Advancement flaps should be used with great caution in irradiated tissue. The skin and subcutaneous tissue are mobilized from the underlying fascia of the transverse perineal muscle (Figure 4). The size of the flap is tailored to the size of the defect. The flap is undermined and in a Z-plasty is rotated through 90 degrees to fill the defect (Figure 5). Once the flap is rotated, the remaining skin edges are united (Figure 6). In a V-Y procedure the initial wedge (Figure 7) is advanced to fill the gap and then closed as a Y (Figure 8). Prolene 4–0 sutures should be used for these closures.

The rectus abdominis flap

The flap is dissected with the patient supine or in the lithotomy position. Skin islands may be designed in a wide variety of shapes and orientations as long as a

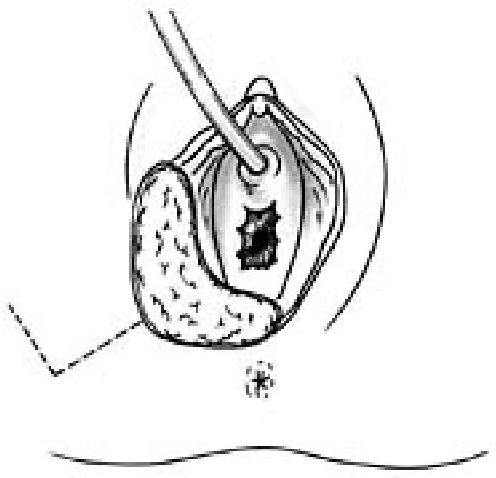

Figure 3

Z-plasty

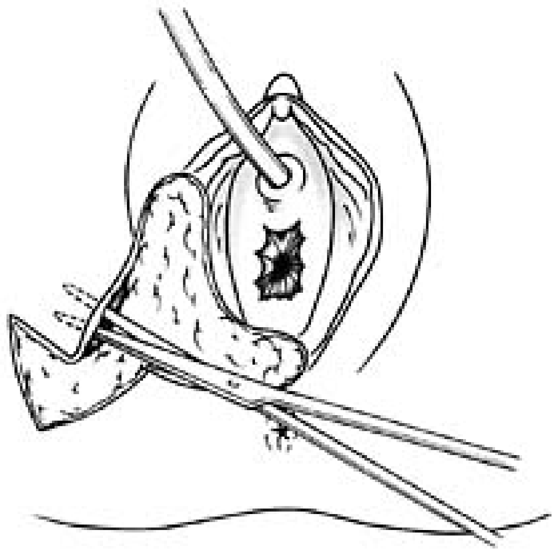

Figure 4

Z-plasty mobilization

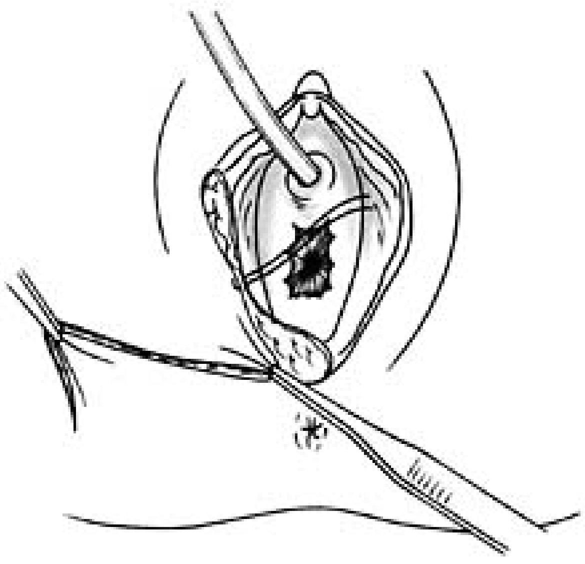

Figure 5

90% rotation of flap

significant portion of the skin and subcutaneous tissues is centered over the muscle. In most cases, an elliptical skin island is oriented vertically over the muscle (Figure 9). For vaginal reconstruction, a more transversely oriented skin island may be designed above or below the level of the umbilicus, depending on the placement of ostomy sites. The skin islands should approximate the dimensions of the defect to be covered.

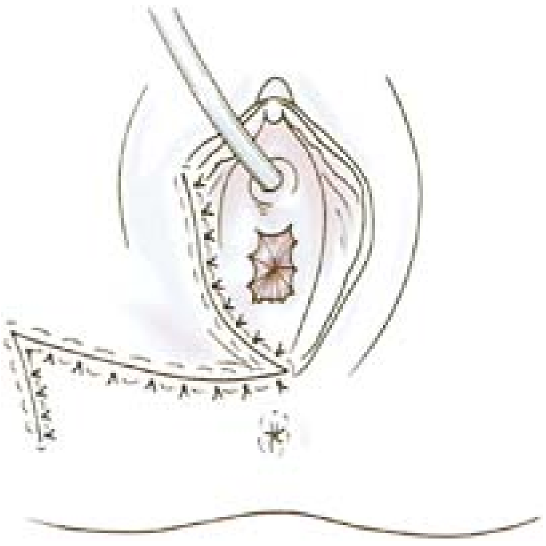

Figure 6

End result

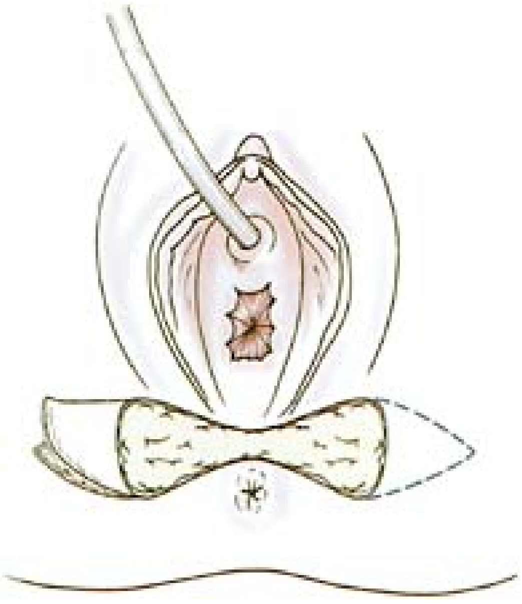

Figure 7

V-Y procedure

The skin incision is carried down to the level of the anterior rectus sheath; subcutaneous tissue and skin are then elevated off the sheath to allow an incision through the fascia to be made 1 cm from the lateral edge of the muscle. The dissection is then carried around the anterior and lateral surfaces of the muscle to the posterior surface. Care is taken to minimize injury to the tendinous intersections while mobilizing

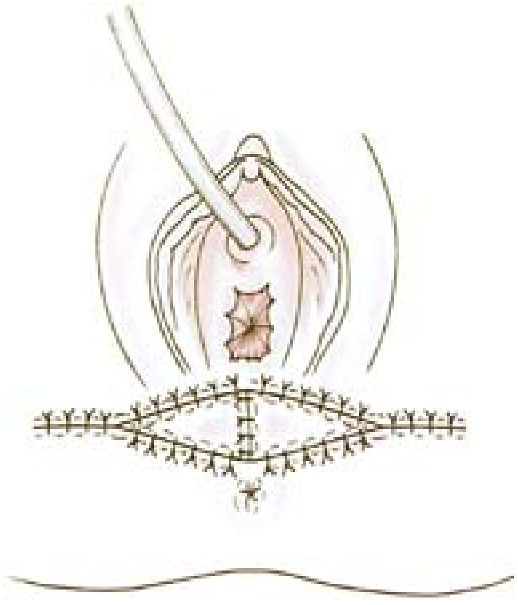

Figure 8 End result

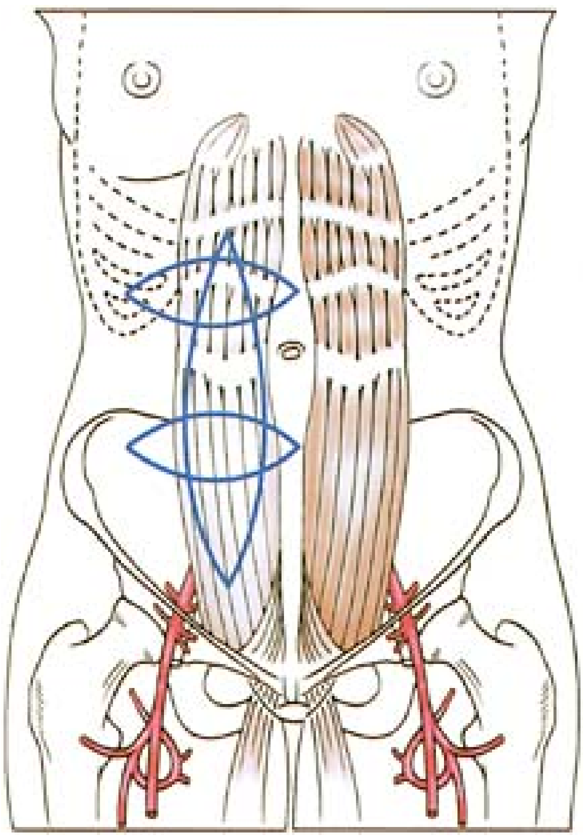

Figure 9 Possible elliptical skin islands

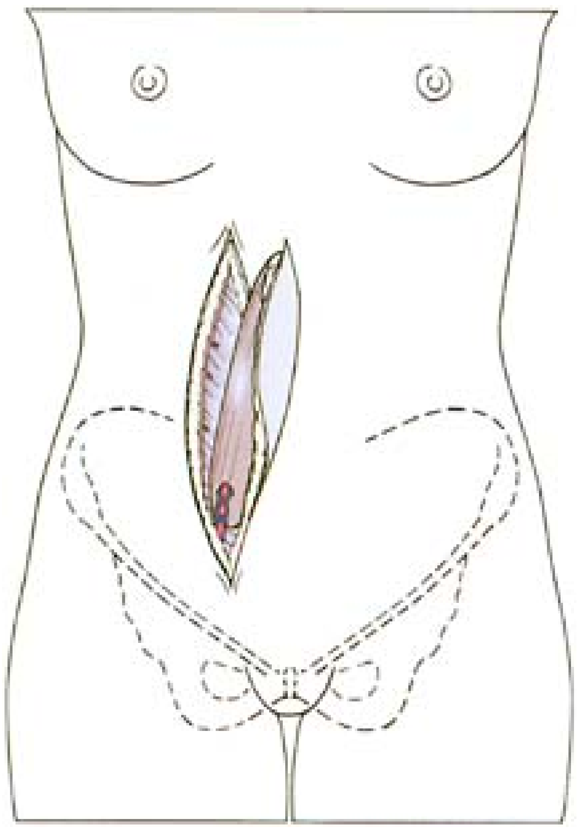

Figure 10

Rectus abdominis myocutaneous flap elevated. Note the inferior epigastric pedicle entering the caudal aspect of the flap

the muscle. The muscle can be divided above the level of the costal margin if needed. The muscle is then dissected away from the abdominal wall in a distal to proximal direction along the posterior rectus sheath towards the inferior epigastric pedicle. Several large intercostal perforators are ligated laterally and the deep inferior epigastric pedicle (artery and two venae comitantes) is then identified and dissected out of its origin from the iliac vessels (Figure 10). The insertion of the muscle into the pubic symphysis can be left intact or detached, depending on the arc of rotation that is required. For vaginal reconstruction, the skin island can be tubed and shaped into a pouch. It is then sutured to the remaining vaginal cuff from above. If perineal coverage is necessary, the flap can be tunnelled in the subcutaneous plane over the inguinal ligament into the perineum or groin as needed (Figure 11). The donor site is closed primarily by approximating the remaining 1 cm cuff of anterior rectus sheath to itself with a large non-absorbable suture. If necessary, skin and subcutaneous tissue flaps can be mobilized to reapproximate the skin flaps in the abdominal donor site.

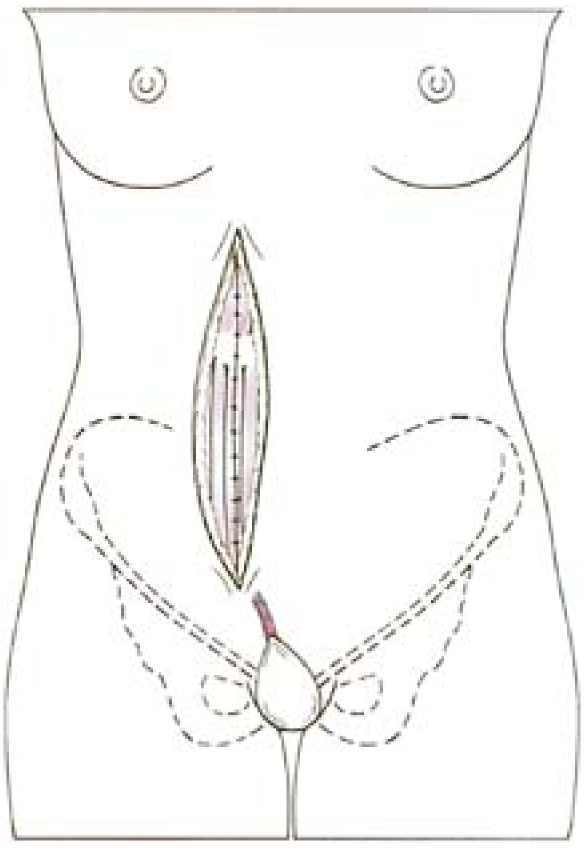

Figure 11

The anterior rectus fascia is approximated

The gracilis flap

The patient is usually placed in the lithotomy position for resections in this area. The hips are flexed and abducted. The medial thigh is prepared circumferentially down to the knee allowing access to the medial group of muscles. Figure 12 shows the underlying anatomy.

An elliptical skin island measuring up to 6 cm× 20 cm is outlined over the proximal two thirds of the muscle (Figure 13). The anterior border of the incision lies on a line drawn between the pubic tubercle and the semitendinosus tendon. A separate, small access incision may be made distally if needed to identify the muscle tendon.

The skin is incised anteriorly down to the medial group of muscles. The sartorius muscle is identified and retracted superiorly The gracilis tendon can now be identified distally, usually through a separate short distal incision, and the tendinous insertion divided (Figure 14). The posterior incision is made down to the muscle, taking care not to undermine perforators

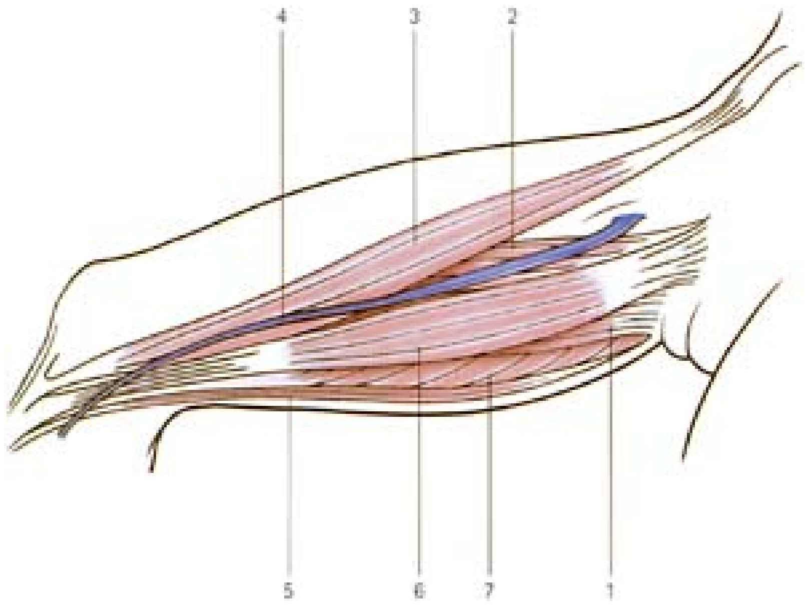

Figure 12

Underlying anatomy of medial thigh
1 Adductor magnus muscle
2 Adductor longus muscle
3 Sartorius muscle
4 Greater saphenous vein
5 Semitendinosus muscle
6 Gracilis muscle
7 Semimembranosus muscle

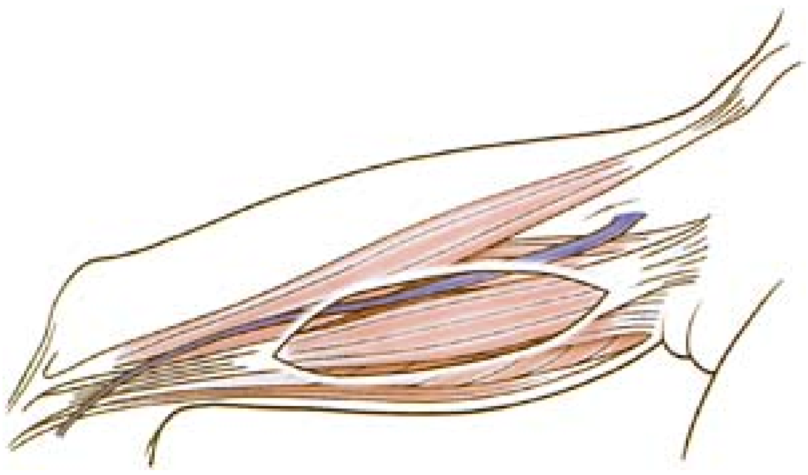

Figure 13

Outline of skin island over proximal two thirds of gracilis muscle

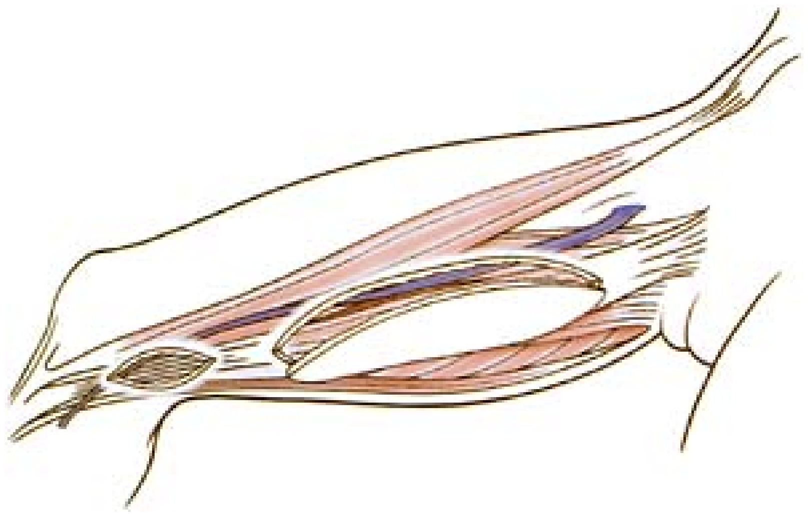

Figure 14

Skin and cutaneous skin island incised and distal gracilis muscle identified near knee

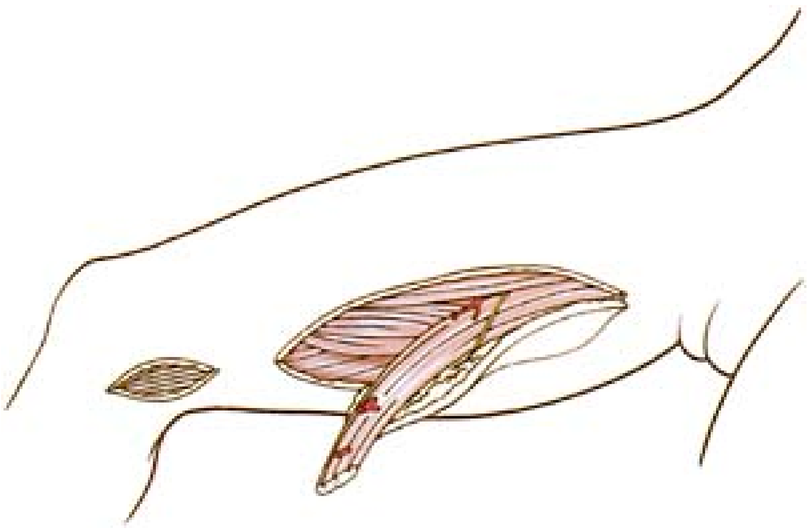

Figure 15

Myocutaneous flap elevated. Note neurovascular pedicle entering into proximal third of muscle

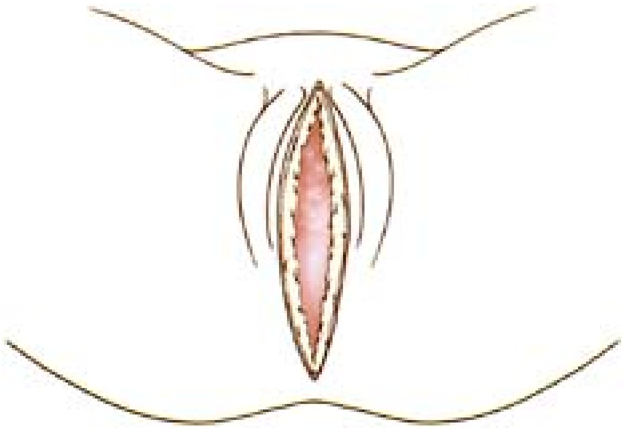

Figure 16

Typical defect in perineum after total pelvic exenteration

from the muscle to the skin or to shear the cutaneous aspect of the flap off the muscle. The flap is then elevated from distal to proximal on the thigh. One or two large perforators to the muscle are ligated distally. The main pedicle is identified entering the proximal third of the gracilis muscle in the space between the adductor longus and adductor magnus muscles (Figure 15), approximately 8–10 cm below the pubic tubercle. Once the pedicle is identified and preserved, the proximal muscle can be dissected and, if necessary, the origin from the pubic symphysis may be divided. The entire myocutaneous flap can then be tunneled through the subcutaneous skin bridge into the vaginal defect (Figure 16) and exteriorized through the introitus (Figure 17). The bilateral flaps are sutured to each other in the midline (Figure 18). The neovagina is

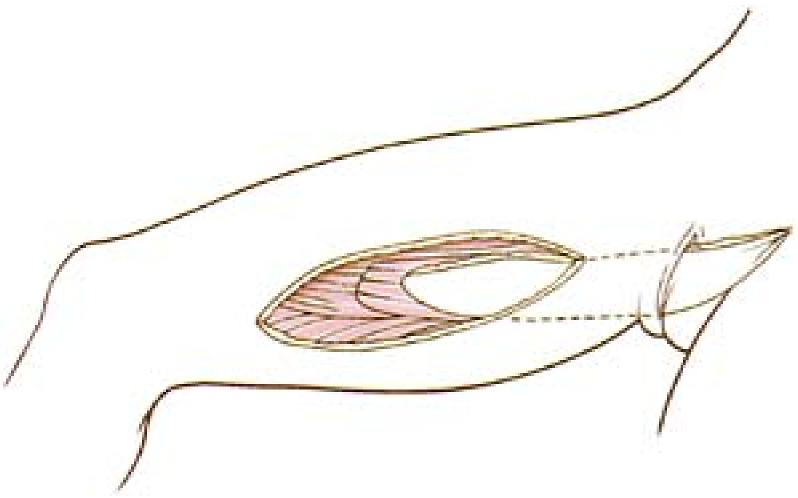

Figure 17

Myocutaneous flap exteriorized through the introitus

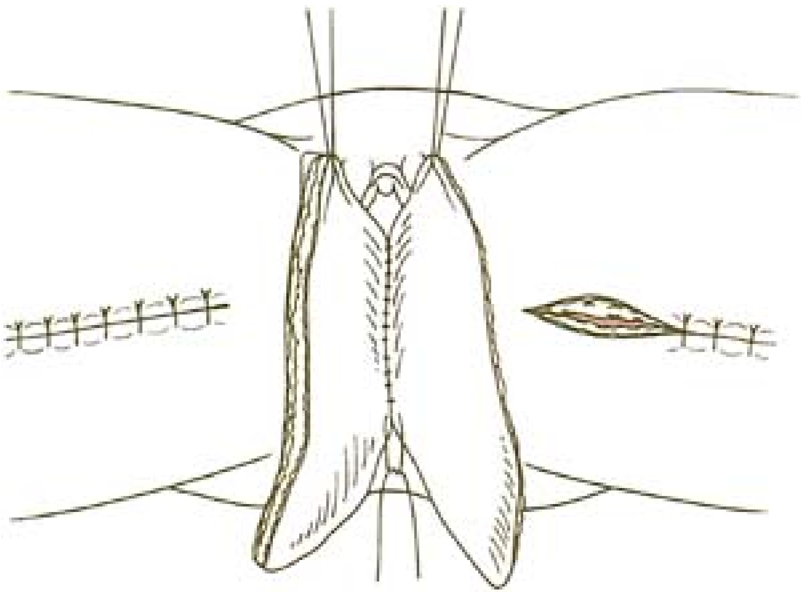

Figure 18

Bilateral gracilis myocutaneous flaps sewn together

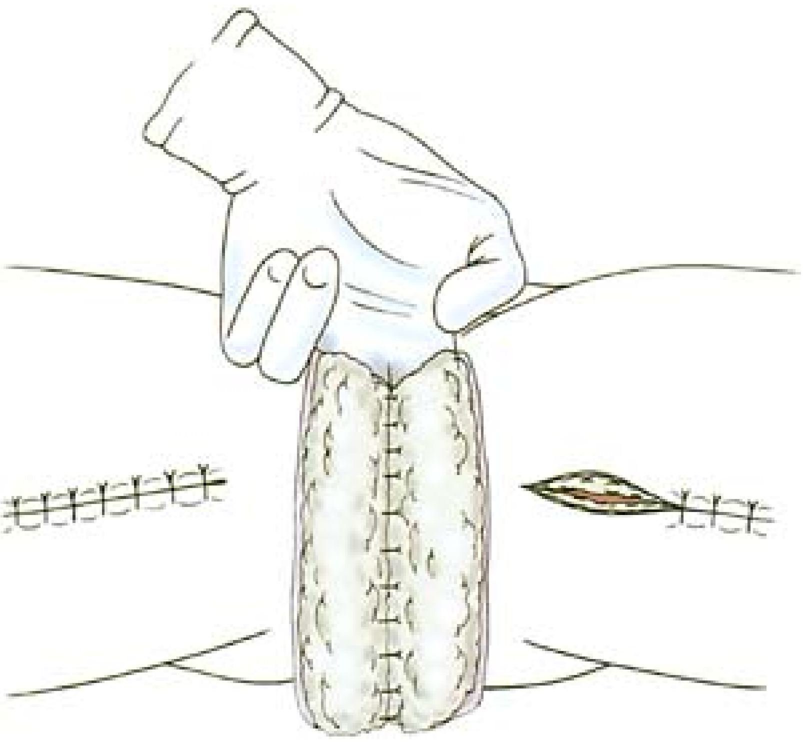

Figure 19

Bilateral flaps shaped into a pouch

shaped into a pouch by approximating the anterior, posterior and distal skin edges of the flaps (Figure 19); this can then be inserted into the pelvic space that is left after the exenteration. The proximal end of the neovagina is sutured to the introitus (Figure 20).

Fasciocutaneous neurovascular pudendal thigh flaps

The fasciocutaneous flap is based on the posterior labial arteries, which are a continuation of the perineal

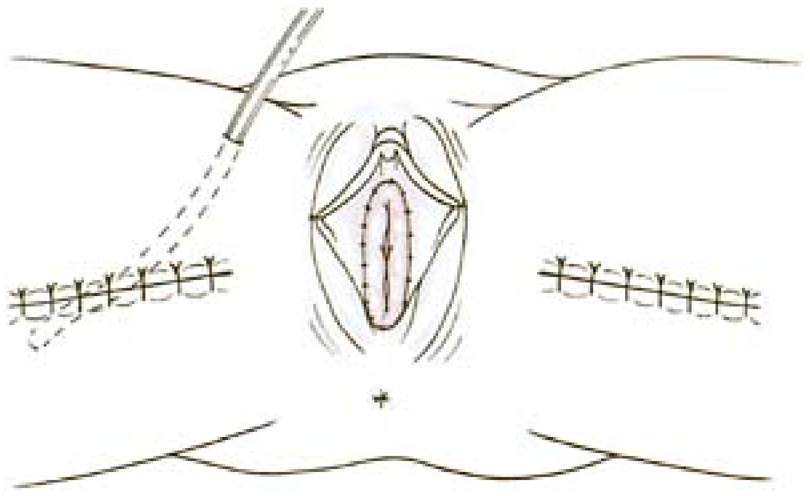

Figure 20

Neovaginal pouch inserted into pelvic space and sutured to the introitus

artery. The posterior aspect of this flap is innervated by the posterior labial branches of the pudendal nerve and the perineal branches of the posterior cutaneous nerve of the thigh.

The patient is placed in the lithotomy position. A flap 3–6 cm wide and 10–15 cm long can be designed within the medial groin crease just lateral to the labia majora and the defect. Bilateral flaps can be designed for large posterior wall defects. The perineal defect is partially closed anteriorly and posteriorly leaving an entrance of suitable size into which the neovagina will be inserted (Figure 21).

The skin and subcutaneous tissues are incised as well as the deep fascia overlying the muscles of the medial thigh compartment as they insert onto the

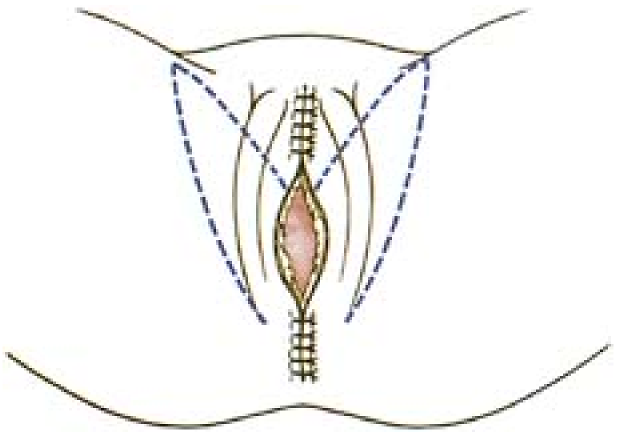

Figure 21

Partial anterior and posterior defect repair

pubis and ischium (Figure 22). The flap is then elevated from distal to proximal in the subfascial plane over the adductor muscles in order to avoid injury to the neurovascular pedicle (Figure 23). The large distal branches of the perineal and pudendal vessels are identified and preserved. Often, the dissection is carried into the fat of the ischiorectal fossa in order to achieve adequate rotation and mobilization of the flap. The flap can then be rotated into the defect. The donor site is closed primarily in layers. A neovaginal pouch can be reconstructed by suturing the lateral margins of bilateral flaps to each other (Figure 24); the neo-vagina is then transposed into the rectovesical space and the proximal ends sutured into the new vaginal introitus.

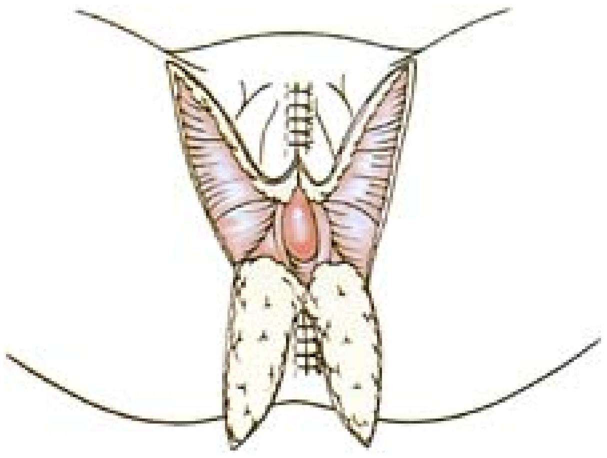

Figure 22

Skin subcutaneous tissue and deep fascial incision

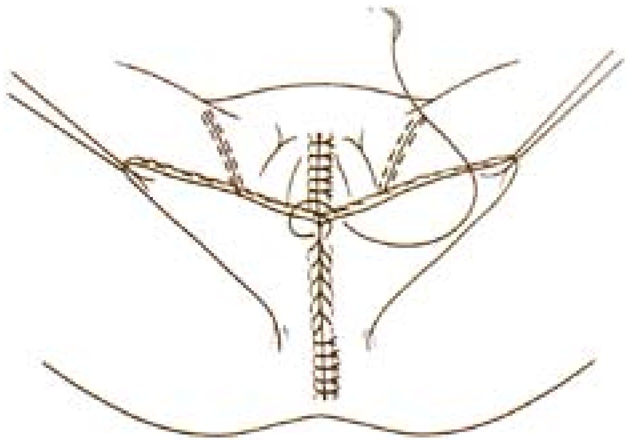

Figure 23

Flap elevation

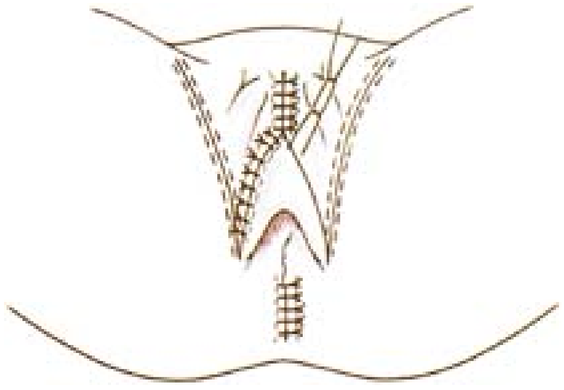

Figure 24

A suture of lateral margins of bilateral flaps to each other

References

Cordeiro PG, Pusic AL, Disa JJ (2002) A classification system and reconstructive algorithm for acquired vaginal defects. *Plast Reconstr Surg* **110**(4):1058–65.
Crowe PJ, Temple WJ, Lopez MJ, Ketcham AS (1999) Pelvic extenteration for advanced pelvic malignancy *Semin Surg Oncol* **17**:152–60 [Review].
Martello JY, Vasconez HC (1995) Vulvar and vaginal reconstruction after surgical treatment for gynecologic cancer. *Clin Plast Surg* **22**:129–40.
McCraw JB, Massey FM, Shanklin KD, et al. (1976) Vaginal reconstruction with gracilis myocutaneous flaps. *Plast Reconstr Surg* **58**:176–83.
Small T, Friedman DJ, Sultan M (2000) Reconstructive surgery of the pelvis after surgery for rectal cancer. *Semin Surg* Oncol **18**:259–65.
Tobin GR, Day TG (1988) Vaginal and pelvic reconstruction with distally based rectus abdominis and myocutaneous flaps. *Plast Reconstr Surg* **83**:62–73.
Tobin GR, Pursell SH, Day TG, Jr (1990) Refinements in vaginal reconstruction using rectus abdominis flaps. *Clin Plast Surg* **17**:705–12.
Wee JT, Joseph VT (1989) A new technique of vaginal reconstruction using neurovascular pudendal thigh flaps. A preliminary report. *Plast Reconstr Surg* **83**:701–9.

25
Objective assessment of technical surgical skill

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Thomas Ind
Jane Bridges

Introduction

In the last few years, there has been growing interest from bodies involved in surgical education, evaluation and certification, and from the public, press and politicians in the assessment of surgical competence. Surgical competence is dependent on many factors, such as core knowledge, decision-making ability, communication skills and technical surgical ability. Whereas most of these qualities are already formally assessed in written, oral and clinical examinations, there is as yet no standardized method for assessing technical surgical skill in an objective manner. The area of technical performance has historically been the most problematic in terms of objective assessment. Technical performance has traditionally been appraised in a subjective manner within the operating room environment. New technologies have been developed in the last decade that seem likely to facilitate objective assessment of technical surgical skill. These have been validated for general surgeons in the main rather than gynecologists. The objective of this chapter is to review available methods for the objective assessment of technical surgical skill and their limitations.

Surgical competence

The objective assessment of technical surgical skill must be seen in the wider context of surgical competence. But what is surgical competence? Darzi and Mackay (2001) propose a simple model of its components (Box 1). In this context we regard technical surgical skill as the dexterity component of technical performance.

Methods of assessment

Although advances in the objective assessment of technical surgical skill have been made in recent years, different investigators have been using different tests, criteria, validation methods and even nomenclature. An international workshop of experts, convened in July 2001, reviewed all available methods of assessment of surgical technical skill, and provided a standardization of definitions, measurements and criteria, and a foundation for communication among educators, researchers, training bodies and certification boards (Satava et al. 2003).

Box 1 Components of surgical competence

Diagnostic ability: Ability to reach a diagnosis or differential diagnoses on the basis of history, physical examination, and investigations (these need to be recommended and explained to the patient, and their results interpreted)
Treatment plan: Ability to establish a plan of treatment (after considering available options, evaluating their pros and cons, and discussing them with the patient), and to change the plan if the clinical situation dictates so
Technical performance: Ability to carry out a surgical or other procedure effectively. This ability is a combination of three components:
Judgment: Decision making that takes place during a surgical procedure and establishment of a plan to carry it out (e.g. deciding whether or not to perform a bowel resection in the course of an operation for ovarian cancer)
Knowledge: Knowledge base required to implement the plan (e.g. knowing how to perform the bowel resection)
Dexterity: Ability required to execute the plan accurately and effectively (e.g. whilst performing the bowel anastomosis tying knots tight enough to prevent fluid leakage but loose enough to prevent tissue damage)
Postoperative care: Ability to deliver routine care, and to diagnose and treat complications at an early stage

Box 2 Essential definitions for objective assessment

Ability: The natural state or condition of being capable, such as psychomotor, visuospatial, perceptual and haptic (tactile) aptitudes
Skill: A developed proficiency or dexterity in some art, craft, or the like, such as instrument handling, bimanual dexterity, navigation, ligation, suturing, knot tying, incision, exploration, palpation, cannulation, tissue handling, cutting and blunt dissection
Task: A piece of work to be done, such as anastomosis, excision, closure, tissue extraction, exploration and camera navigation
Procedure: A series of steps taken to accomplish an end, such as laparoscopic cholecystectomy, tracheostomy, chest tube insertion, diagnostic peritoneal lavage, vein patch and breast biopsy

There are a few essential definitions for objective assessment (Box 2).

There are several validated methods for objective assessment that measure abilities, skills, tasks and/or procedures (Table 1). Some of these methods will be reviewed in detail later in this chapter. Only a few of the existing methods evaluate fundamental abilities or total procedures; the majority assess the same or similar technical skills and complex tasks, and therefore can be expected to provide a basis for comparison of results. There are a few abilities and skills, such as haptic aptitude or tissue handling, that are considered important, for which there are no validated methods of assessment.

There are some parameters that have been suggested as potential outcome data to measure technical surgical skill (Box 3).

The good method of assessment

Reznick (1993) suggests that a good method of assessment should exhibit three basic components: feasibility, validity and reliability (Box 4).

Table 1 Validated methods for objective assessment

Method	*Abilities*	*Skills*	*Tasks*	*Procedures*
ADEPT	X	X		
OSATS		X	X	X
MISTELS		X	X	
MIST VR		X	X	
ICSAD		X	X	X
Rosser Drills		X	X	
PicSOr	X	X		
ESSS		X	X	X
FSM		X	X	
LST 2000		X	X	
LapSim		X	X	
BSSC		X	X	X

ADEPT, Advanced Dundee Endoscopic Psychomotor Tester; OSATS, Objective Structured Assessment of Technical Skill; MISTELS, McGill Inanimate System for Training and Evaluation of Laparoscopic Skills; MIST VR, Minimally Invasive Surgical Trainer, Virtual Reality; ICSAD, Imperial College Surgical Assessment Device; PicSOr, Pictorial Surface Orientation; ESSS, Endoscopic Sinus Surgery Simulator; FSM, Fundamental Surgical Manipulations; LST 2000, Laparoscopic Surgery Trainer, 2000; LapSim, Laparoscopic Simulator; BSSC, Intercollegiate Basic Surgical Skills Course.

Box 3 Suggested outcome data

- Economy of movement
- Purposefulness of movement
- Absence of movement (indecision)
- Path length
- Time to completion
- Sequence of steps
- State analysis (still/moving)
- Force measurements
- Errors
- Recovery from error
- Repose latency (time to recover from error)
- Final product
- Global assessment of performance

Current methods of assessment

There are now several methods available for the objective assessment of technical surgical skill. Whereas some of these methods are well established, others are research tools in the process of being evaluated. Broadly speaking, the majority of these methods involve a standardized set of tasks. Although most assessments are carried out in the laboratory setting, there are some methods that are amenable for use in the operating room environment.

Basic methods

Watts and Feldman (1985) report five basic methods used to assess technical surgical skill with varying degrees of reliability and validity (Table 2).

Procedure lists with logs

A common method of assessment of technical surgical skill is the use of procedure lists with logs. It consists of keeping a record of all the procedures carried out by a surgeon without any description of the quality of the performance.

Procedure lists with logs are not a new concept for many trainees. They have traditionally maintained a log of the procedures that they have performed, including a description of the level of supervision received, and have been asked to submit them at the time of annual assessments, examinations and job interviews. More recently, even accredited surgeons in some countries need to keep such records as part of their revalidation process.

This method of assessment is cheap and easy to evaluate. However, it is a pure numerical account of

Box 4 Components of a good method of assessment

Feasibility: A method of assessment exhibits feasibility if it is practical and straightforward to administer
Validity: A method of assessment exhibits validity if it gives genuine information about what is being measured
Content validity: Refers to the extent to which the trait we are intending to measure is being measured by the method of assessment
Concurrent validity: Refers to the extent to which the results of the method of assessment correlate with the accepted reference gold standard known to measure the same trait
Construct validity: Refers to the extent to which the method of assessment is capable of discriminating between different levels of experience
Face validity: Refers to the extent to which the method of assessment resembles a situation in real life
Predictive validity: Refers to the extent that the method of assessment is able to predict future performance
Reliability: A method of assessment exhibits reliability if it can be repeated with minimal variation in the results
Inter-rater reliability: Refers to the extent of agreement in the results by independent raters
Test—retest reliability: Refers to the extent of agreement in the results achieved by administering the test to the same individual on separate occasions in the absence of any learning

Table 2 Reliability and validity of five basic methods of assessment

Method of assessment	*Reliability*	*Validity*
Procedure lists with logs	NA	Poor
Direct observation without criteria	Poor	Modest
Direct observation with criteria	High	High
Models with criteria	High	Proportional to realism
Videotapes	High	Proportional to realism

NA, not applicable.

operative performance and not a reflection of surgical dexterity; it therefore exhibits poor content validity (Reznick 1993, Cuschieri et al. 2001). Assuming that a surgeon is competent after having performed a designated number of procedures is wrong. Although repetition and practice are very important for the acquisition of technical surgical skill, in the absence of feedback a surgeon may learn to be consistently wrong (Kaufman et al. 1987).

Direct observation without criteria

Another common method of assessment of technical surgical skill is by direct observation without criteria. It consists of assessing surgical dexterity by direct observation of a surgeon performing a procedure on a patient with no explicit criteria.

Direct observation without criteria is again not a new concept for many trainees, as this form of assessment currently takes place on a regular basis in the operating room.

This method of assessment exhibits poor test-retest reliability, as no explicit criteria are used and the process is therefore influenced by the subjectivity of the observer. It also exhibits poor inter-rater reliability, as two senior surgeons assessing a junior surgeon performing a procedure will have a high level of disagreement in their results (Reznick 1993).

Direct observation with criteria

Direct observation with criteria consists of assessing surgical dexterity by direct observation of a surgeon performing a procedure on a patient with explicit criteria against which technical surgical skill can be assessed.

It has been suggested that criteria turn raters into observers, instead of interpreters, of performance and therefore add objectivity to the assessment process (Regehr et al. 1998). This method of assessment satisfies most validity concerns and exhibits high inter-rater reliability (Kopta 1971). The more objective and structured the criteria are, the more reliable is the process. It has been shown that if a group of raters cooperatively identify important items for inclusion in a list of criteria, there is greater reliability than if the list was to be created by one rater alone (Valentino et al. 1998).

Models with criteria

Another method of assessment of technical surgical skill is the use of models with criteria. It consists of assessing surgical dexterity by direct observation of a surgeon performing a procedure on a model. The model can be a live animal (such as an anesthetized pig), animal tissue (such as pigs' trotters or small bowel) or a bench model.

The use of models, when explicit criteria are applied, exhibits high reliability. The validity of this method of assessment is directly proportional to the realism of the process; it is directly proportional to the degree to which it mirrors operations on real patients.

Although anesthetized animal models have been used for education and research, there is growing concern about the moral and ethical issues involved in the use of live animals for this purpose. The legislation in some countries even prohibits the use of live animals for surgical training, although there may be no restriction to the use of animal parts. It is therefore increasingly difficult to justify the use of animals if alternative methods, such as bench models, are available. It has been shown that the use of live anesthetized animals is equivalent to the use of bench models for evaluating technical surgical skill (Martin et al. 1997). Using bench models instead of patients or animals has the advantage that the former are cheaper, easier to transport, reusable, readily available, and do not create ethical dilemmas.

Videotapes

Another method of assessment of technical surgical skill consists of videotaping a surgeon performing a procedure on patients or models, and then having the tape analyzed by raters using explicit criteria. Setting up the camera in such a way that the surgeon's face is not visible and eliminating any sound, will preserve anonymity and therefore add objectivity to the assessment process. The use of videotapes exhibits high reliability. Its validity is again proportional to the realism of the process.

This method of assessment is invaluable for providing feedback to a surgeon. However, it is expensive, and reviewing the videotapes can be very time-consuming.

Other methods

Time taken for a procedure

The time taken to complete a surgical procedure does not assess the quality of the operative performance. These types of data are an unreliable measure when used during real procedures, due to the influence of other variable factors.

Morbidity and mortality data

Morbidity and mortality data are commonly used as a method of assessment of operative performance. These forms of data often attribute the outcome of a patient solely to the operation and skill of the surgeon performing it, without taking into account other factors, such as patients' characteristics, case selection, preoperative morbidity, postoperative care and local facilities. It is therefore believed that they do not truly reflect surgical competence (Poloniecki et al. 1998, Bridgewater et al. 2003).

Recent developments in assessment

Task-specific checklists and global rating scales

Research aimed at developing objective methods of assessment of technical surgical skill, such as checklists and rating scales, is promising. Winckel et al. (1994) demonstrate that task-specific checklists and global rating scales exhibit high construct validity and high inter-rater reliability when used to assess surgical dexterity in the operating room. However, consistently valid and reliable assessment in this environment may be difficult to achieve mainly due to lack of standardization.

Objective Structured Assessment of Technical Skill (OSATS)

The Objective Structured Assessment of Technical Skill (OSATS) is an objective method of assessment of technical surgical skill developed at the University of Toronto (Canada).
It consists of assessing surgical dexterity by direct observation of a surgeon performing a variety of standardized laboratory-based tasks within a time-limited multistation setting with explicit criteria against which technical surgical skill can be assessed. Both live anesthetized animals and bench models have been used in this setting.
Two types of scoring systems are used in the OSATS, a task-specific checklist and a global rating scale. The task-specific checklist (Table 3) is different for each task. It identifies the steps that are necessary to perform a task effectively. These range between 22 and 32 steps, depending on the particular task that is being assessed. The observer indicates which of these steps are correctly or incorrectly performed. If a new task is included in the assessment, a new task-specific checklist must be developed and validated. By contrast, the global rating scale (Table 4) is identical for each task. It identifies seven general operative competencies that are necessary to perform a task effectively. The observer rates the level of performance of each competency on a 5-point scale that is anchored at the middle and extreme points by behavioral descriptors. The global rating scale assesses surgical skill in a less concrete way than the task-specific checklist, but has broad applicability.
The OSATS evaluates skills (such as cannulation and clamping), tasks (such as sutured and stapled bowel anastomosis, skin lesion excision, abdominal wall closure and major hemorrhage control), and procedures (such as chest tube insertion, and more recently tracheostomy and pyloroplasty).
There are now several studies that demonstrate that the OSATS is a valid and reliable objective method of assessment of technical surgical skill. Faulkner et al. (1996) show that both task-specific checklists and global rating scales correlate well with the independent opinion of senior surgeons regarding the surgical dexterity of more junior surgeons, suggesting that this method of assessment exhibits concurrent validity. Martin et al. (1997) demonstrate that the use of bench models is equivalent to the use of live anesthetized animals in this setting. Also, both task-specific checklists and global rating scales exhibit moderate to high interstation reliabilities, and their correlations are high, both within the live anesthetized animal format and the bench model format, suggesting that both scoring systems are measuring the same quality. Further, the inter-rater reliabilities found indicate that the use of one rater per station is adequate. Reznick et al. (1997) show that the OSATS exhibits high construct validity and high interstation reliability for both scoring systems. Regehr et al. (1998) demonstrate that global rating scales exhibit higher concurrent validity, higher construct validity and higher interstation reliability than task-specific checklists. Further, the use of task-specific checklists in conjunction with global rating scales does not improve the validity or reliability of the global rating scale over that of the global rating scale used in isolation. Also, global rating scales are more useful the more senior the surgeons and the more difficult the tasks are.

Motion analysis systems

Motion analysis consists of using markers placed on a surgeon's hands to track their movements during the performance of a standardized surgical task, and then to analyze the data obtained as an alternative method of assessment of technical surgical skill. Motion tracking can be based on electromagnetic, mechanical or optical systems.

Imperial College Surgical Assessment Device (ICSAD)

The Imperial College Surgical Assessment Device (ICSAD) is an objective method of assessment of technical surgical skill developed at Imperial College of Science Technology and Medicine in London (UK).
The ICSAD (Figure 1) consists of a commercially available electromagnetic tracking system and bespoke software to assess surgical dexterity by analyzing the hand movements of a surgeon performing a standardized surgical task. The tracking system (Isotrak II, Polhemus, USA) uses electromagnetic fields to determine the position of a remote object, in this case a surgeon's hands. The technology is based on generating magnetic field vectors from a transmitter, and detecting the field vectors with a receiver. The sensed signals are input to a mathematical algorithm that computes the receiver's position relative to the transmitter. A single electromagnetic tracker or receiver is attached

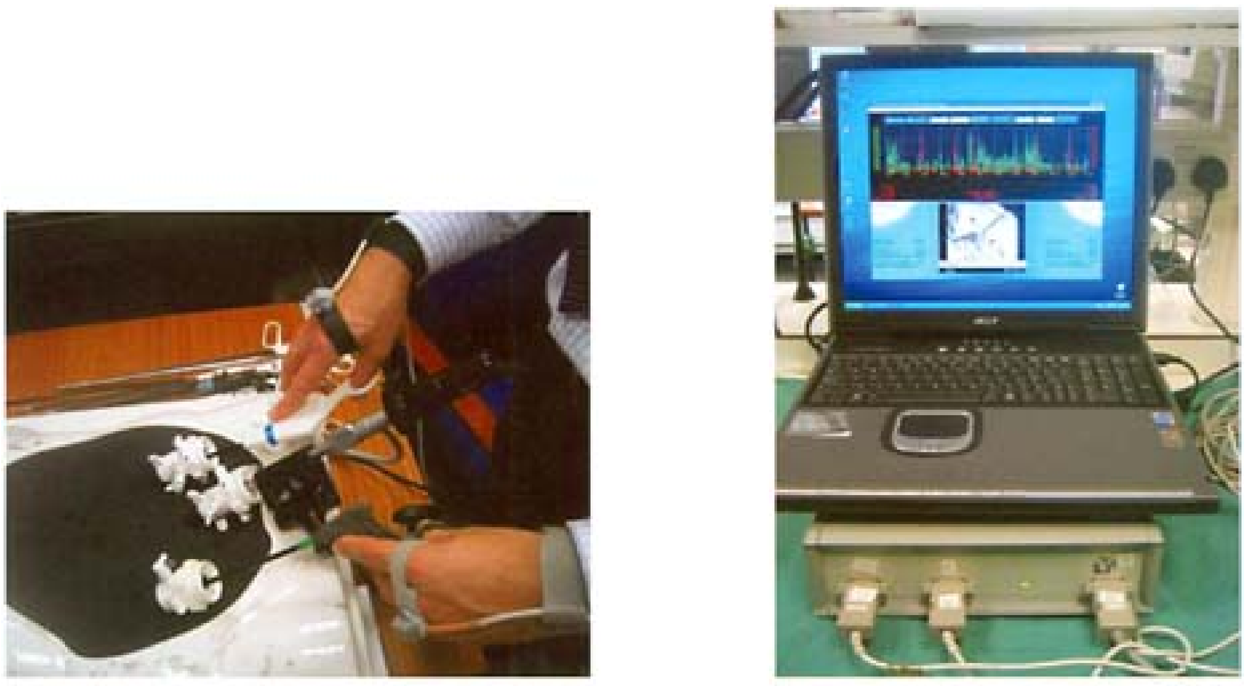
Table 3 Task-specific checklist for sutured bowel anastomosis used in the OSATS

Steps	*Correctly performed*	*Incorrectly performed*
Bowel orientated mesenteric border to mesenteric border, no twisting		
Stay sutures held with artery forceps		
Selects appropriate instruments		
Selects appropriate suture		
Needle loaded 1/2 to 2/3 from tip		
Use of index finger to stabilize needleholder		
Needle enters bowel at right angles on 80% of bites		
Single attempt at needle passage through bowel on 90% of bites		
Follow-through on curve of needle on entrance on 80% of bites		
Follow-through on curve of needle on exit on 80% of bites		
Use of forceps on seromuscular layer of bowel only, majority of time		
Minimal damage with forceps		
Use of forceps to handle needle		
Inverting sutures		
Suture spacing 3–5 mm		
Equal bites on each side on 80% of bites		
Individual bites on each side on 90% of bites		
Square knots		
Minimal three throws on knots		
Suture cut to appropriate length		
No mucosal pouting		
Apposition of bowel without excessive tension on sutures		

Table 4 Global rating scale used in the OS ATS

Competencies	*Level of performance*				
Respect for tissue	1	2	3	4	5
	Frequently uses unnecessary force on tissue or causes damage by inappropriate use of instruments		Careful handling of tissue but occasionally causes inadvertent damage		Consistently handles tissue appropriately with minimal damage
Time and motion	1	2	3	4	5
	Many unnecessary moves		Efficient time and motion but some unnecessary moves		Clear economy of movement and maximal efficiency
Instrument handling	1	2	3	4	5
	Repeatedly makes tentative or awkward moves with instruments by their inappropriate use		Competent use of instruments but occasionally appears stiff or awkward		Fluid moves with instruments and no awkwardness
Knowledge of instruments	1	2	3	4	5
	Frequently asks for wrong instrument or uses inappropriate instrument		Knows names of most instruments and uses appropriate instrument		Obviously familiar with the instruments and their names
Flow of operation and forward planning	1	2	3	4	5
	Frequently stops operating and seems unsure of next move		Demonstrates some forward planning with reasonable progression of procedure		Obviously planned course of operation with effortless flow from one move to the next
Use of assistants	1	2	3	4	5
	Consistently places assistants poorly or fails to use assistants		Appropriate use of assistants most of the time		Strategically uses assistants to the best advantage at all times
Knowledge of specific procedure	1	2	3	4	5
	Deficient knowledge needing specific instruction at most operative steps		Knows all important steps of operation		Demonstrates familiarity with all aspects of operation

by velcro straps to the back of each hand at standardized positions. Three-dimensional information from each tracker is obtained with an update rate of 20 per second. These raw three-dimensional positional data from the tracking system are transferred to a computer and extrapolated by the software into scores of technical surgical skill, such as path length, number and speed of hand movements, and time to task completion. The software includes a filter to eliminate background noise from sources, such as hand tremor and experimental error in the tracking device, ensuring that only purposeful actions are recorded.



A B

Figure 1

Imperial College Surgical Assessment Device (ICSAD). Raw three-dimensional positional data obtained from the electromagnetic trackers (A) are transferred to a computer (B) and extrapolated into scores of technical surgical skill. Courtesy of Department of Surgical Oncology and Technology, Imperial College, London, UK.

ICSAD evaluates skills, tasks and procedures. There are now several studies that demonstrate that the ICSAD is a valid and reliable objective method of assessment of technical surgical skill. These have shown that outcome data, such as path length, number and speed of hand movements, and time to completion, are valid indicators of technical surgical skill using standardized surgical tasks. This method of assessment has been validated for minimal access (Taffinder et al. 1999a) and open (Datta et al. 2001) surgical tasks. In laparoscopic surgery, outcome data, such as path length of instrument tips, number of hand movements, and time to completion, are capable of discriminating between different levels of experience, and therefore exhibit construct validity. This is true for simple tasks in a training box (Taffinder et al. 1999b) as well as for complex tasks, such as laparoscopic cholecystectomy on a cadaveric porcine liver model (Smith et al. 1999, 2002). Experienced surgeons tend to use a fewer number of movements (economy of movement) and shorter paths (accuracy in target localization). In open surgery, however, although outcome data, such as number of hand movements and time to completion, are capable of discriminating between different levels of experience, and therefore exhibit construct validity, path length is not.

Virtual reality systems

Virtual reality has been described as a collection of technologies that allow people to interact efficiently with three-dimensional computerized databases in real time using their natural senses and skills (McCloy and Stone 2001). Its strength lies in its ability to allow a surgeon to practice surgical tasks repeatedly, in a short period of time, without the need for a particular clinical situation to arise, and without the pressures of a real-live scenario. It is also preferable for patients that new surgical maneuvers have been practiced outside the operating room before attempts are made during real surgical procedures. The main advantage of virtual reality systems, when compared to motion analysis systems, is that they provide real-time feedback about skill-based errors. Although virtual reality systems are extensively used for training purposes, few have been validated for the assessment of technical surgical skill.

Minimally Invasive Surgical Trainer (MIST)

The Minimally Invasive Surgical Trainer (MIST) is an objective method of assessment of technical surgical skill originally developed in the UK. It is now commercially available from Mentice AB (Sweden).
The MIST is an example of a low-fidelity virtual reality system, as it attempts to replicate the skills of laparoscopic operating but not the appearance.
The MIST (Figure 2) consists of a frame holding two standard laparoscopic instruments electronically linked to a computer. The movements of the surgical instruments are viewed in real time on a screen with three-dimensional graphics. Two modules are available: one for core skills and another for suturing. In the core skills module, the user is guided through 12 exer-

Figure 2

Minimally Invasive Surgical Trainer (MIST) Courtesy of Mentice AB, Sweden.

cises of progressive complexity that enables the development of essential laparoscopic skills. Each task is based on a key surgical technique employed in laparoscopic cholecystectomy, using simple geometrical shapes rather than tissue, to allow the user to concentrate on the development of key psychomotor skills. In the suturing module, the user is guided through 12 suturing tasks of progressive complexity, from basic stitching to knot-tying. Right and left repetitions are employed to encourage ambidextrous working. Performance is measured by time, number of errors and the efficiency with which the exercise is performed.
The MIST evaluates skills (such as transfer/traversal, peg-board, and clamping) and tasks (such as energy use).
There are now several studies that demonstrate that the MIST is a valid and reliable objective method of assessment of technical surgical skill. It is the only virtual reality system that has been extensively validated as a method of assessment of technical skill in minimal access surgery (Taffinder et al. 1998a; Chaudhry et al. 1999). Taffinder et al. (1998a, b) show that the system can distinguish between senior and junior surgeons using outcome data, such as number of movements made, time taken, number of errors made and economy of movement; it therefore exhibits construct validity. Factors that affect surgical performance, such as sleep deprivation, have also been evaluated with the MIST (Taffinder et al. 1998c).
Many improvements may be possible in the future using virtual reality systems. There is much interest in the development of high-fidelity systems, where the appearance, as well as the skills of laparoscopic operating, is replicated.

Other systems

Advanced Dundee Endoscopic Psychomotor Tester (ADEPT)

The Advanced Dundee Endoscopic Psychomotor Tester (ADEPT) is an objective method of assessment of technical surgical skill developed at the University of Dundee (UK).
The ADEPT was originally designed as a tool for the selection of surgeons for laparoscopic surgery, based on the ability of psychomotor tests to predict innate abilities to perform relevant tasks. The ADEPT is a system that uses standardized laboratory-based tasks but real laparoscopic instruments and imaging for the objective assessment of laparoscopic technical surgical skill (Hanna et al. 1997).

The ADEPT consists of an opaque dome that encloses a workspace. The dome has three apertures to reach the workspace: one for a laparoscope, and two for laparoscopic graspers. The apertures for the graspers incorporate hinge mechanisms that have the same degree of freedom as laparoscopic instruments through access ports. A target is situated in the center of the workspace and can be viewed on a standard monitor. The target consists of a rectangular plate mounted on four pins at each corner. If excessive manipulation resulting in contact with the pins occurs, this constitutes a plate error. The target plate has structured tasks involving the manipulation of switches and dials. Between the dome and the target plate there is a transparent spring-mounted sheet with apertures of varying shapes that allow the passage of the manipulating instrument while the sheet is retracted by the assisting instrument. If the assisting instrument establishes contact with the aperture in the sheet, this constitutes a probe error. The system is controlled by a computer. It gives instructions to the user by randomly picking tasks with instructions on the task details. The computer software generates outcome data on performance, such as instrument errors, execution time and task completion score (involves completing the task within the allocated time and tolerance limit).

The ADEPT evaluates psychomotor abilities (such as tracking, pick and place, translation, aiming and precision), and skills (such as bimanual dexterity).

There are now several studies that demonstrate that the ADEPT is a valid and reliable objective method of assessment of technical surgical skill. The extent to which the system resembles a situation in real life, and therefore exhibits face validity, includes the use of a real laparoscopic imaging system, and real laparoscopic instruments with the same degree of freedom as real laparoscopic instruments through real access ports. As the performance on the ADEPT is scored by computer software, this eliminates any inter-rater variability. Macmillan and Cuschieri (1999) show that performance on the system correlates well with the independent opinion of senior surgeons regarding the surgical dexterity of more junior surgeons, suggesting that this method of assessment exhibits concurrent validity. The ADEPT evaluates aspects of surgical dexterity that do not improve with practice (innate abilities). Because of this, it could be used to predict future performance, and therefore exhibit predictive validity. Francis et al. (2002) demonstrate that the system can distinguish between senior and junior surgeons, and therefore exhibits construct validity. Senior surgeons tend to incur less instrument errors, with shorter execution times, and higher task completion scores than junior surgeons; the former complete the tasks more accurately without sacrificing execution time.

Conclusion

The assessment of surgical competence is certainly a fascinating as well as an important area in our profession that in the last few years has been under the scrutiny of the public, press and politicians. The development of objective methods of assessment of technical surgical skill was initially seen as the most difficult aspect of assessing surgical competence. Considerable progress has been made in the last decade, and there has been a shift towards using objective rather than subjective systems. The surgical community can now choose from a variety of objective methods of assessment of surgical dexterity. However, as promising as the methods described in this chapter may appear, the objective assessment of technical surgical skill is still in its early stages of development, and some issues are yet to be addressed. These include the further validation of these systems, and the incorporation of these methods for training, evaluation and potentially for certification and revalidation purposes, proving that once introduced, they do make a difference in outcome. Future research should probably be focused in these directions.

References

Bridgewater B, Grayson AD, Jackson M, et al. (2003) Surgeon specific mortality in adult cardiac surgery: comparison between crude and risk stratified data. *BMJ* **327**:13–17.

Chaudhry A, Sutton C, Wood J, et al. (1999) Learning rate for laparoscopic surgical skills on MIST VR, a virtual reality simulator: quality of human—computer interface. *Ann R Coll Surg Engl* **81**:281–6.

Cuschieri A, Francis N, Crosby J, Hanna GB (2001) What do master surgeons think of surgical competence and revalidation? *Am J Surg* **182**:110–16.

Darzi A, Mackay S (2001) Assessment of surgical competence. *Qual Health Care* **10**(suppl 2):ii64–ii69.

Datta V, Mackay S, Mandalia M, Darzi A (2001) The use of electromagnetic motion tracking analysis to objectively measure open surgical skill in the laboratory-based model. *J Am Coll Surg* **193**:479–85.

Faulkner H, Regehr G, Martin J, Reznick R (1996) Validation of an objective structured assessment of technical skill for surgical residents. *Acad Med* **71**:1363–5.
Francis NK, Hanna GB, Cuschieri A (2002) The performance of master surgeons on the Advanced Dundee Endoscopic Psychomotor Tester: contrast validity study. *Arch Surg* **137**:841–4.
Hanna GB, Drew T, Cuschieri A (1997) Technology for psychomotor skills testing in endoscopic surgery. *Semin Laparosc Surg* **4**:120–4.
Kaufman HH, Wiegand RL, Tunick RH (1987) Teaching surgeons to operate—principles of psychomotor skills training. *Acta Neurochir (Wien)* **87**:1–7.
Kopta JA (1971) An approach to the evaluation of operative skills. *Surgery* **70**:297–303.
Macmillan AI, Cuschieri A (1999) Assessment of innate ability and skills for endoscopic manipulations by the Advanced Dundee Endoscopic Psychomotor Tester: predictive and concurrent validity. *Am J Surg* **177**:274–7.
Martin JA, Regehr G, Reznick R, et al. (1997) Objective structured assessment of technical skill (OSATS) for surgical residents. *Br J Surg* **84**:273–8.
McCloy R, Stone R (2001) Science, medicine, and the future. Virtual reality in surgery. *BMJ* **323**:912–15.
Poloniecki J, Valencia O, Littlejohns P (1998) Cumulative risk adjusted mortality chart for detecting changes in death rate: observational study of heart surgery. *BMJ* **316**:1697–700.
Regehr G, MacRae H, Reznick RK, Szalay D (1998) Comparing the psychometric properties of checklists and global rating scales for assessing performance on an OSCE-format examination. *Acad Med* **73**:993–7.
Reznick RK (1993) Teaching and testing technical skills. *Am J Surg* **165**:358–61.
Reznick R, Regehr G, MacRae H, et al. (1997) Testing technical skill via an innovative 'bench station' examination. *Am J Surg* **173**:226–30.
Satava RM, Cuschieri A, Hamdorf J (2003) Metrics for objective assessment. *Surg Endosc* **17**:220–6.
Smith SG, Torkington J, Darzi AW (1999) A computerized assessment of surgical dexterity during perfused cadaveric porcine laparoscopic cholecystectomy. *Br J Surg* **86**(suppl 1):95.
Smith SG, Torkington J, Brown TJ, et al. (2002) Motion analysis. *Surg Endosc* **16**:640–5.
Taffinder N, Sutton C, Fishwick RJ, et al. (1998a) Validation of virtual reality to teach and assess psychomotor skills in laparoscopic surgery: results from randomised controlled studies using the MIST VR laparoscopic simulator. *Stud Health Technol Inform* **50**:124–30.
Taffinder NJ, Russell RC, McManus IC, et al. (1998b) An objective assessment of surgeons' psychomotor skills: validation of the MIST-VR laparoscopic simulator. *Br J Surg* **85**(suppl 1):75.
Taffinder NJ, McManus IC, Gul Y, et al. (1998c) Effect of sleep deprivation on surgeons' dexterity on laparoscopy simulator. *Lancet* **352**:1191.
Taffinder N, Smith SG, Huber J, et al. (1999a) The effect of a second-generation 3D endoscope on the laparoscopic precision of novices and experienced surgeons. *Surg Endosc* **13**:1087–92.
Taffinder NJ, Smith SG, Mair J, et al. (1999b) Can a computer measure surgical precision? Reliability, validity and feasibility of the ICSAD. *Surg Endosc* **13**(suppl 1):81.
Valentino J, Donnelly MB, Sloan DA, et al. (1998) The reliability of six faculty members in identifying important OSCE items. Acad Med **73**:204–5.
Watts J, Feldman WB (1985) Assessment of technical skills. In: Neufeld VR, Norman GR, eds. *Assessing clinical competence.* New York: Springer: 259–74.
Winckel CP, Reznick RK, Cohen R, Taylor B (1994) Reliability and construct validity of a structured technical skills assessment form. *Am J Surg* **167**:423–7.

26
Pain management

Andrew Lawson

Introduction

This chapter deals with the management of pain in gynecological malignancy. It does not deal with the management of pain arising from surgical intervention but with pain resulting from the effects of the tumor and its treatment (Figure 1).

Pain in patients with malignancy may be caused by the erosive effects of the tumor itself or by treatment, for example radiation plexopathy following deep X-ray therapy, or constipation secondary to opioid drug administration. Patients may complain of pain resulting from muscle spasm or musculoskeletal problems which may be secondary to the illness, such as occurs in prolonged immobilization. Patients may therefore complain of various different types of pain. Tumor erosion, muscle spasm and bony secondaries will tend to produce nociceptive pain—pain secondary to actual or potential tissue damage. This may be sharp and stabbing, cramping or throbbing. Neuropathic pain—pain resulting from a lesion in or damage to the nervous system—is characteristically shooting, lancinating or burning. It is often associated with paraesthesias and dysesthesias. The severity of pain may increase in proportion to either tumor mass or the occurrence of new metastases. A tumor enlarging within a fibrous capsule causes continuous pain, which is gradual in onset, tending to start with an ache. Those involving a hollow viscus, however, such as the small intestine, cause cramp-like or colicky abdominal pains. Tumors may become inflamed or infected, which will also produce pain. Tumor necrosis may produce sudden increases in pain. Tumors may invade bone, either by direct growth into it or by metastatic spread, though most gynecological tumors rarely metastasize to bone. Vulval and cervical carcinomas may invade bone directly.

The female pelvic organs are in close proximation to a wide variety of structures within the pelvis, both neurological and vascular. Thus, local infiltration by a cervical, endometrial and/or ovarian tumor may cause pain due to pressure on any of the structures within the pelvis. The pelvis also acts as conduit for the neurovascular supply to the lower limb and consequently nerve involvement may occur at the sites of entry and exit from the pelvis as well as within. For example, the sciatic nerve may be affected by malignant infiltration, not only proximal to the sciatic foramen but also in its nerve roots, where it is formed as part of the sacral plexus. The femoral nerve on the pelvic side-wall may be damaged due to either hematoma or malignant infiltration, as may the obturator nerve. Pressure on or obliteration of lymphatic drainage may produce lymphedema of the lower limb. Compression of the venous supply to the lower limb may produce venous edema, leading to pronounced swelling which may be unilateral and may be exquisitely painful.

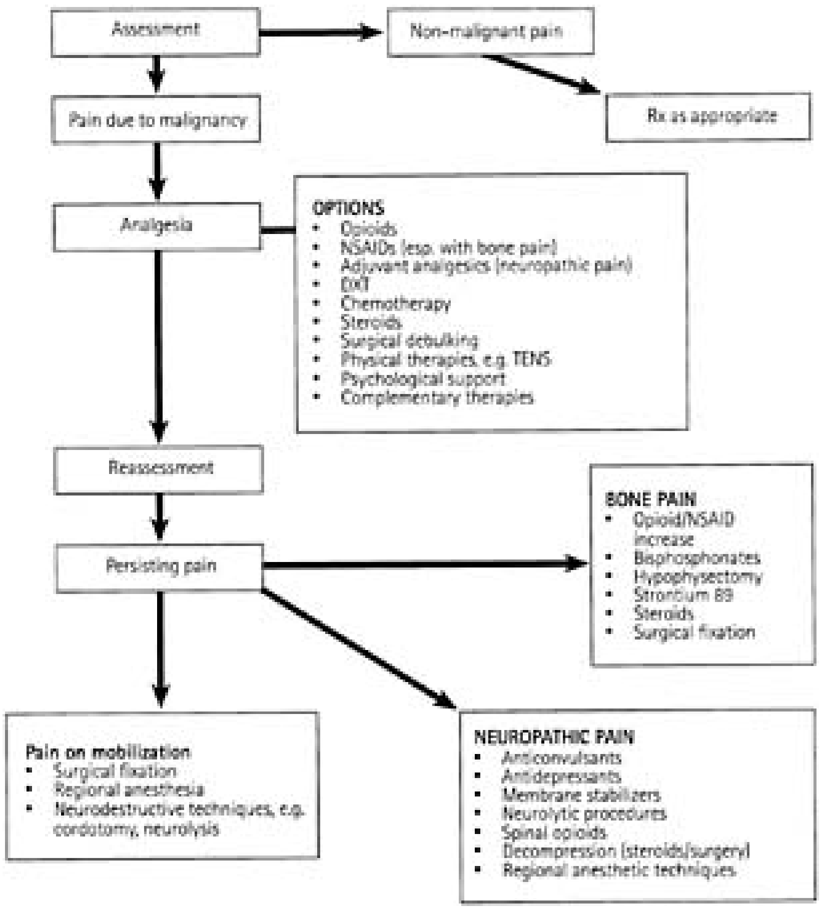


Figure 1

Algorithm for the management of continuing pain in patients with gynecological malignancy. DXT, deep X-ray therapy; NSAID, non-steroidal anti-inflammatory drug; TENS, transcutaneous electrical nerve stimulation

Initial management of pain

In patients with gynecological malignancy who have not had a curative surgical procedure, it is unlikely that simple analgesics alone will provide satisfactory pain relief. In the author's opinion, patients such as these who have pain should be treated with opioid analgesics from the start. Slow-release morphine preparations and/or regular oral morphine preparations remain the 'gold standard' of pain relief in patients with malignant disease. There is no convincing evidence that any of the newer analgesics have significant advantages over morphine. In the UK and in other parts of the world, diamorphine (diacetylmorphine, heroin) is commonly used as an analgesic agent. Table 1 lists opioid drugs and dosage regimens.

Opioids may also be given by the subcutaneous route either intermittently or using a syringe driver. Fortunately, effective management of pain is achievable for the majority of patients with gynecological malignancy who are using opioid-based analgesic drugs in combination with drugs for the treatment of neuropathic pain. For those with pain resistant to standard treatments, perseverance and referral to a specialist at a chronic pain center is likely to result in an improved quality of life.

To optimize analgesia, patients should at the same time be prescribed non-opioid analgesics. Paracetamol (acetaminophen) is widely prescribed in the UK and overseas and has the advantages of being available without prescription. Patients with bone infiltration may also respond to non-steroidal anti-inflammatory drugs such as indomethacin, diclofenac and ketorolac. Care should be taken in patients with impaired renal, hepatic or cardiovascular function and in those who have reversible airways obstruction. Steroids may be beneficial in reducing the compressive effects of tumors.

Neuropathic pain

Patients who have nerve involvement may well respond to the usage of antidepressant, anticonvulsant and membrane-stabilizing agents, all of which have been demonstrated to be efficacious in the treatment

Table 1 Opioid drugs in severe pain equianalgesic dose for 70 kg adults

Drug	*IM (mg)*	*PO (mg)*	*Interval (hours)*
Dextromoramide	7.5	10	1.5–3
Diamorphine	5	N/A	2–3
Hydromorphone	1.5	7.5	2–3
Methadone	10	10–15	8–48
Morphine	10	40–60	2–4
Oxycodone	N/A	30	4–6

1. Pethidine is not recommended for prolonged use due to metabolite toxicity.
2. The dose used should be titrated to patient response.
3. Subcutaneous and intravenous infusions are recommended where oral intake is limited and dose requirements are high.
4. The maximum dosage is limited only by side-effects.

Table 2 Drug treatment of neuropathic pain

Class	*Drug*	*Daily dose (mg)*	*Route*
Tricyclicantidepressants	Amitriptyline	10–150	PO/IM
	Clomipramine	10–150	PO
	Desipramine	10–150	PO
	Doxepin	12.5–150	PO/IM
	Imipramine	12.5–150	PO
Selective serotonin re-uptake inhibitors (SSRIs)	Fluoxetine	20–60	PO
	Parozetine	10–40	PO
Anticonvulsants	Carbamazepine	100–1200	PO
	Clonazepam	2–10	PO
	Gabapentin	300–1200	PO
Membrane stabilizers	Mexiletine	150–1500	PO

of neuropathic pain. Pain due to radiation damage to the sacral plexus is likely to be resistant to standard analgesic techniques and in such circumstances anti-depressants and membrane-stabilizing agents may be the first-line drugs of choice (Table 2).

Interventional techniques in gynecological malignancy

Epidural and spinal opiates

Where standard routes of analgesic administration have failed, the epidural route using a percutaneous epidural catheter can provide optimal analgesia. The benefits of opioid administration by the spinal route have been acknowledged for some time and there is clear evidence that some patients find epidural analgesia of a higher quality with a diminished incidence of unwanted side effects such as nausea, drowsiness and constipation. Epidural catheters can be inserted percutaneously and brought out through the skin or attached to a number of subcutaneous administration devices (Figure 2). Subcutaneous pumps have been

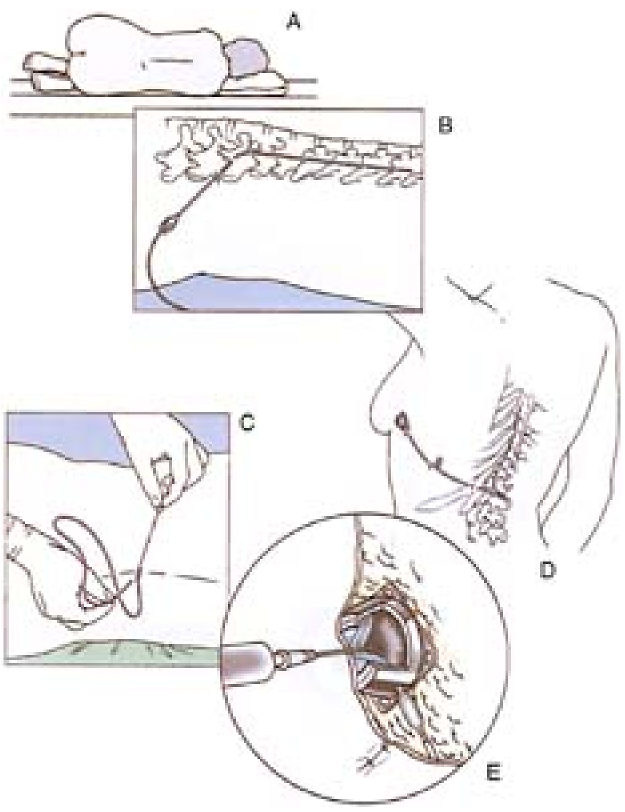


Figure 2

Insertion of tunnelled epidural catheter. (A) Position of patient: insertion marked at L2. (B) Insertion of 16-gauge epidural catheter via a Tuohy needle. (C) Second incision over 11th rib allows the catheter to be moved over the anterior chest wall. (D) Portal attached to catheter after tensioning loop and second tunnel. (E) Injection technique.

used to facilitate epidural and spinal analgesia, as have subcutaneous ports through which opiates can be given on a daily or more frequent basis.
All opiates currently on the market have been used in the epidural space. The most commonly used are morphine and (in the UK) diamorphine. Opiates have been given also in combination with local anesthetic drugs to improve the quality of analgesia. This may be particularly helpful in terminal cases where there is extreme and intractable pelvic and neuropathic pain. Drugs such as clonidine, midazolam and baclofen have also been given epidurally in such circumstances.

Superior hypogastric plexus block

The superior hypogastric plexus is formed by the union of the lumbar sympathetic chains in branches of the aortic plexus in combination with the parasympathetic fibers originating in the ventral routes of S2–S4, which form the pelvic splanchnic nerve, some fibers of which ascend from the inferior hypogastric plexus to join the superior hypogastric plexus. The superior hypogastric plexus is situated anterior to the lower part of the body of the fifth lumbar vertebra and the upper part of the sacral promontory. It is retroperitoneal and is often called the presacral nerve. The superior hypogastric plexus gives off branches to the ovarian plexuses.

Technique

The patient is placed prone and two 20 or 22 gauge needles are advanced from a point roughly 5–7 cm lateral to the L4/L5 interspace to a point just anterior to the L5/S1 interspace. These needles are inserted under fluoroscopic or CT guidance, and injected contrast material demonstrates that the needles are anterior to the vertebral body and not in any of the vascular structures. Following aspiration, neurolytic solution of aqueous phenol 8–10 mL is injected, or for local anesthetic blockade, 10–20 mL 0.5% bupivacaine (Figure 3).

Blockade of ganglion impar

Ganglion impar block has been described for the treatment of intractable perineal and pelvic pain where the sympathetic nerve seems to predominate. The gan-

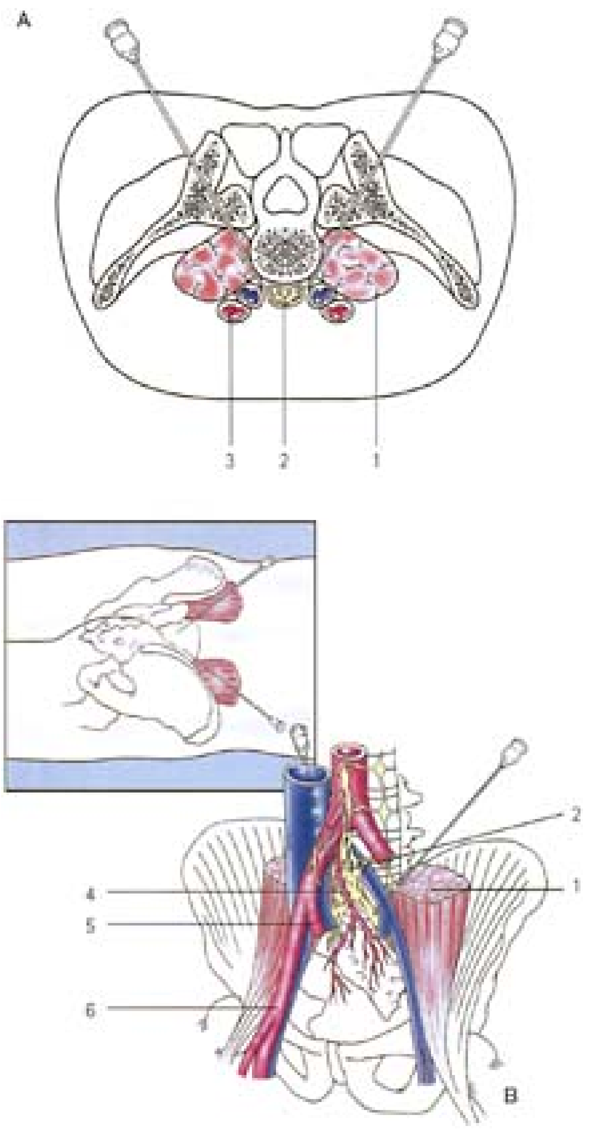


Figure 3

Superior hypogastric plexus block. (A) Sagittal section at L5; (B) pelvic anatomy
1 Psoas major muscle
2 Superior hypogastric plexus
3 Bifurcation of iliac vessels
4 Superior rectal artery
5 Internal iliac artery and vein
6 External iliac artery and vein

glion impar is a retroperitoneal structure located at the level of the sacrococcygeal junction. The technique involves placement of a needle through the skin under X-ray control to lie anterior to the coccyx

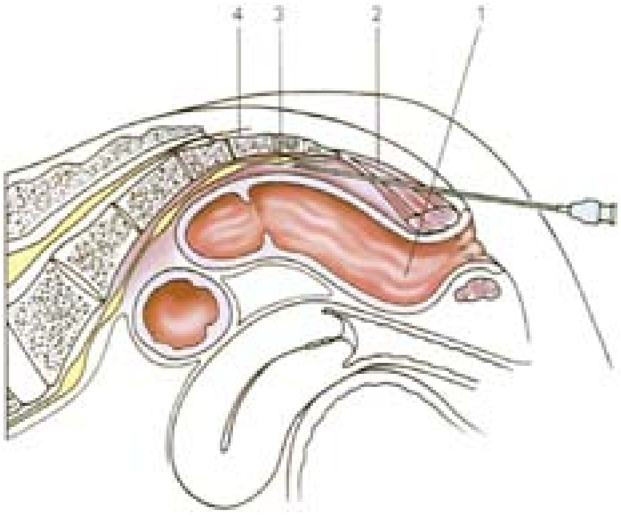


Figure 4

Blockade of ganglion impar
1 Rectum
2 Anococcygeal ligament
3 Ganglion impar
4 Sacrococcygeal junction

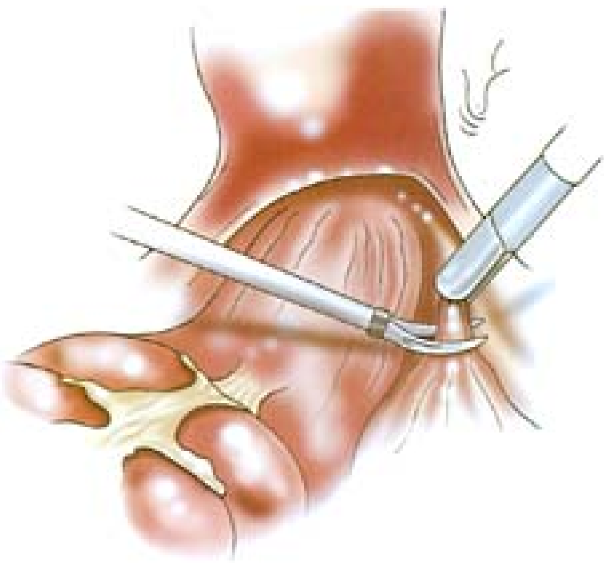


Figure 5

Presacral neurectomy: opening the presacral space

close to the sacrococcygeal junction. Retroperitoneal location of the needle is demonstrated by the injection of contrast medium. Local anesthetic and/or neurolytic solutions can then be injected. Care must be taken to ensure that puncture of the rectum and accidental

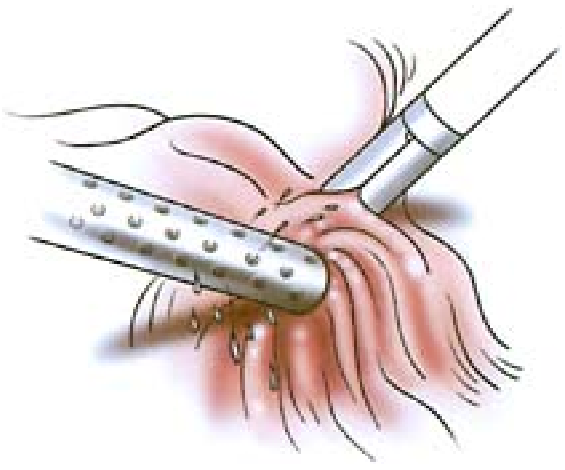


Figure 6

Presacral neurectomy: opened spaces

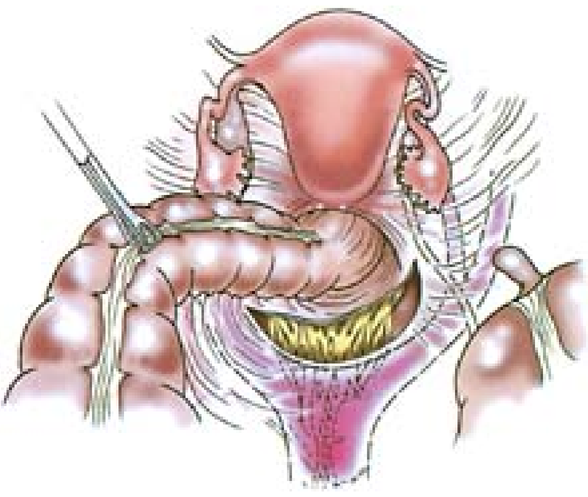


Figure 7

Sacral plexus exposed

trans-bone injection into the epidural space are avoided (Figure 4).

Presacral neurectomy

Presacral neurectomy has been used for the control of intractable pelvic pain, whether due to malignancy or chronic pelvic pain syndromes. The technique involves the division of the superior hypogastric plexus at the L5/S1 region as described above. The presacral nerves can be divided as an open procedure or via the laparoscope. Laparoscopic presacral neurectomy is probably the technique of choice (Figures 5 and 6). Bowel preparation is indicated preoperatively to decompress the bowel. Under direct vision an incision is made in the peritoneum over the lateral sacral promontory and dissecting forceps are used to dissect out the hypogastric plexus. It may then be ligated, cut or cauterized (Figure 7).

References

Bonica JJ (1990) *The management of pain*, second edition. Malvern: Lea & Febiger.

Cousins MJ, Bridenbaugh PO, eds. (1996) *Neural blockade in clinical anaesthesia and the management of pain*, third edition. Philadelphia: Lippincott/Williams & Wilkins.

Doyle D, Hanks GW, MacDonald N, eds. (1997) *The Oxford textbook of palliative medicine*, second edition. Oxford: OUP

27
Palliative care

Sarah Cox
Catherine Gillespie

What is palliative care?

In 1990, the World Health Organization defined palliative care as:

…the active total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of psychological, social and spiritual problems, is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families.

Modern palliative care has evolved from terminal care to a more dynamic multidisciplinary approach which tries to address priorities from an individual patient's perspective. It recognizes that some patients will need palliative care input from diagnosis or soon after. It places emphasis on the need to support the family and carers and to continue that support into bereavement. Above all, is the concept of enabling people to 'live well' despite having a fatal diagnosis.

Specialist palliative care requires a team approach to identify and address the issues that are having a negative impact on the patient's quality of life. Specialist palliative care teams are now available as a resource to most hospitals, primary care teams and specialist inpatient units or hospices.

The clinical nurse specialist in gynecologic oncology complements the palliative care team in the cancer unit or cancer center. They will often have met the patient in the early stages of her disease and will be key in providing continuity of care as they tend to be the most consistent health professional involved in the patient's management. They will liaise between health professionals and be an important source of information and emotional support to patients throughout their treatment.

Hospices collect together a wide range of disciplines with specialist expertise to provide emotional, practical and financial help as well as medical and nursing care. Social workers are essential to help with such complex problems as psychosocial counseling, financial and housing issues, immigration, preparing young families for loss, and bereavement support. Occupational therapists help patients cope with sometimes rapidly increasing disability and may enable patients to remain in their own homes for longer. Physiotherapists are essential to maximize mobility, to teach relaxation techniques and non-pharmacologic management of breathlessness. Specialized care may also be available from psychologists, spiritual advisers, art and music therapists, dieticians, pharmacists and complementary therapists, with volunteers to support them all.

Hospices usually have a small number of inpatient beds with a high staff-to-patient ratio. Admissions may be for terminal care but around 40% of patients are discharged back home after a few weeks of symptom control or psychological support. This is an important statistic to emphasize to patients who may feel referral to a hospice is the 'first nail in the coffin'. Women affected by gynecologic malignancy may benefit from the outpatient services available at many hospices which might include a day center, complementary therapy, such as massage, appointments with dieticians or physiotherapy or medical outpatients. Hospices may be a useful alternative to consider for

Figure 1

Trinity Hospice, London, UK

women with advanced disease who require medical interventions, such as ascitic drainage or blood transfusion (Figure 1).

Specialist palliative care is also available to patients at home and works alongside primary care. Community palliative care teams work across the UK in a network of interlocking catchment areas. Teams are often based in a hospice and will consist of nurse specialists (‘Macmillan nurses’ when funded by that charity) with medical, paramedical and social work input. Nurse specialists complement the input of primary care and social services with specialist advice on symptom control, information and support. They will communicate closely with other health professionals such as the general practitioner and the hospital gynecologic oncology team about the patient’s condition. They are also in a position to reflect, with the patient, on their illness and possible treatment options.

When should palliative care begin?

Palliative care is usually considered appropriate when curative treatment is no longer possible. However, there is evidence to suggest that women experience distressing physical and psychological effects during and after successful treatment for gynecologic cancer. Persistent difficulties with pain, fatigue, bladder dysfunction and sexual problems were reported in a group of disease-free patients. Half were depressed and 39% reported persistent psychosocial difficulties (Steginga and Dunn 1997). Palliative care should therefore be available on the basis of need at all points along the patient’s pathway. In particular, emotional or symptomatic difficulties may be experienced around the time of diagnosis, during active chemotherapy or radiotherapy, at relapse and in advanced disease.

Sexual dysfunction or psychosexual problems can arise either as a direct result of gynecologic cancer or as a result of its treatment. Surgery, radiotherapy and chemotherapy may influence the physical ability to have and gain pleasure from sexual intercourse, whilst altered body image may impact upon a women’s ability to enjoy the emotional side of sexual activity. Despite this, the need to feel close to people both physically and emotionally will remain and women will need support in order to come to terms with their altered sexual function.

Ovarian cancer is often diagnosed at an advanced stage with about 60% of women presenting with stage III disease and around 20% with stage IV Other gynecologic malignancies usually present earlier but may progress despite treatment. Clinical problems arising commonly in advanced ovarian cancer include malignant bowel obstruction, recurrent ascites and fistulas. Ureteric obstruction and renal failure are not unusual in end-stage cervical cancer. Decisions around appropriate treatment in these situations will often involve input from the palliative care team. Prognosis depends on patient characteristics and staging of the particular cancer but ovarian cancer represents the fourth most common cause of cancer death in women. End-of-life issues may include ethical dilemmas, consideration of place of care and support for the family into bereavement. Support should be available for staff around the loss of a patient.

General principles of palliative care

A palliative care interview will involve taking a medical history with particular attention to symptoms, insight and understanding, family and social history and medications both current and previous. Assessment should also identify psychological and spiritual concerns and anxieties about the present or future. It may be possible to discuss wishes around future care including advanced refusal of treatment, and preferred place of death. The concerns of the family and carers also need to be heard and discussed.

Symptom management and treatment

It is important to determine the likely cause of any symptoms, and to assess their relative significance to the patient in order to plan management. It is common for individuals to have multiple symptoms or problems and a full history should be taken for each. Not all symptoms may be due to the main disease. Symptoms may be caused because of secondary effects of the illness (e.g. weakness or debility), because of side effects of treatment, or because of unrelated, concurrent illness. Symptoms also interact with emotional, social and spiritual problems, so that pain can be exacerbated by worry, lack of information, fears, anxiety or any unresolved matters.

Investigations should be considered to aid diagnosis and guide treatment. However, if an individual is too frail to receive treatment for a specific problem, invasive tests to diagnose that problem are usually not warranted.

There are many reports of symptom prevalence in mixed populations of cancer patients, but very little published on symptoms associated with advanced gynecologic malignancies (Table 1). Symptom surveys vary depending on the stage of disease, but even in cancer center outpatient populations treatable symptoms are very common (Lidstone et al. 2003).

Symptomatic or palliative management embraces an enormous range of interventions from teaching breathing techniques to disease-modifying management, such as surgery. The common intention with such treatment is not to cure the patient but to make them better, if only for a while. This principle can be

Table 1 Prevalence of symptoms in advanced cancer and ovarian cancer

Symptom	*Population with advanced cancer*[a]	*Advanced ovarian cancer*[b]
Pain	57%	69%
Anorexia	30%	44%
Weakness	51%	28%
Breathlessness	19%	–
Confusion	8%	–
Nausea	21%	47%
Vomiting	–	50%
Constipation	23%	13%
Dry mouth	–	13%
Depression	–	16%

[a] Vainio and Auvinen (1996). b Cox S, not published.

applied to every management decision and used to weigh risks against the potential benefit. Treatment decisions need to be individualized and reviewed frequently. It is sensible to minimize the number of medications in order to aid compliance.

Disease-modifying treatment

In the treatment of cancer, surgery, radiotherapy and chemotherapy are amongst the most commonly used forms of disease-modifying treatment. They may be offered even when cure is not possible to improve quality of life, or because they offer the chance of prolonged life. In a patient with advanced ovarian cancer causing recurrent ascites, chemotherapy may offer the most effective symptomatic relief.

Non-pharmacologic treatment

Examples of non-pharmacologic treatment approaches include:

- Breathing control techniques for breathlessness
- Relaxation techniques for anxiety
- Dietary modifications for anorexia
- Provision of a pressure-relieving mattress for debilitated patients
- Acupuncture or TENS for the relief of pain
- Provision of a quiet and supportive environment for agitated or distressed patients.

Prescribing for symptom control

The aim when prescribing for persistent symptoms is to render the patient symptom-free. Appropriate drugs must therefore be taken regularly rather than on an ad hoc basis. Each new drug should be perceived to have benefits which outweigh potential side effects in the context of the patient's condition. It is good practice to avoid polypharmacy; regular review will allow drugs to be stopped that are no longer necessary or helpful. Both patients and carers need clear concise guidelines to ensure maximal cooperation. Drug regimens should ideally be written out in full for patients and families and patient's self-medication charts are a useful adjunct to this. Where patients and families are easily confused by treatment regimens, this should be reviewed to reduce the number of drugs/tablets. Compliance may be further aided by the use of a dossette box, which can be filled by a relative, district nurse or pharmacist. Patients and carers also benefit from a clear plan of action should a current management plan not be working and know who to contact and how to contact them.

Breathlessness

Breathlessness may become more severe in the last weeks of life, and is often difficult to control. It has many potential causes including pleural effusion, pulmonary embolism, muscle weakness, anemia, pneumonia, chronic heart failure, chronic obstructive pulmonary disease and/or psychological distress. Consideration should be given to treating reversible causes if the benefit of doing so outweighs the burden to the patient. The goal of symptomatic treatment is to improve the subjective sensation as experienced by the patient, rather than to improve abnormalities in blood gas or pulmonary function. Difficulty in breathing is often associated with a high level of anxiety which exacerbates the problem. Patients may need to reduce their expectations and adapt their home environment to make daily activities more manageable. General measures include ensuring that the patient is comfortable, and providing information and reassurance. Teaching breathing exercises can give some feeling of control. Oxygen can be helpful, especially where there is hypoxia, but similar effects can be achieved by a stream of air which produces less practical difficulties. If there is some reversible airway obstruction bronchodilators may be useful. Opioids can improve exercise tolerance in advanced airway limitation and reduce the sensation of breathlessness. Benzodiazepines are central sedatives and can also relieve the unpleasant feeling of dyspnea. Cortico-steroids may be helpful where dyspnea results from a large tumor mass.

Anorexia

Anorexia is very common in advanced malignancy. It may be associated with considerable weight loss which may be a source of distress to affected women and their relatives. Loss of appetite also results in loss of the social activity of eating with friends and family. Limited evidence exists for aggressive nutritional support in far advanced cancer. Women should be advised to try small portions and dietary supplements. Corticosteroids and progestrogens can be used to stimulate appetite where appropriate.

Nausea and vomiting

Management of nausea and vomiting will be most effective if a cause can be identified and treatment targeted appropriately. Symptoms may result from gastric irritation or poor gastric emptying because of massive ascites or significant hepatomegaly. Bowel obstruction will often result in vomiting. Raised intracranial pressure should be suspected if there is early morning nausea and vomiting associated with headache and drowsiness or confusion. Since each of these causes has a different mechanism and is mediated by different receptors, specific antiemetics should be chosen. Oral administration may not be effective and parenteral routes (e.g. continuous subcutaneous infusion) should be considered at an early stage.

Constipation

Constipation is a common cause of discomfort in advanced cancer. Causes include inactivity, weakness, dehydration, diminished food intake, low-fiber diet and drugs. In addition, there may be direct or indirect effects of the cancer, such as hypercalcemia or bowel obstruction. Patients who are able to should be encouraged to drink plenty of fluids, eat appropriately and move about. However, in advanced malignancy these measures are usually inadequate by themselves and a laxative such as polyethylene glycol (movicol) will need to be taken daily. With fecal impaction, rectal intervention will also be required to initiate bowel movement.

Anxiety and depression

Anxiety and depression are common in advanced cancer and may be underdiagnosed. Risk factors for the development of depression include previous depressive episodes and uncontrolled pain. Biological symptoms, such as loss of appetite and weight, poor sleep and lethargy, are unhelpful in making the diagnosis as they occur with advanced cancer itself. Loss of interest or pleasure and hopelessness may be more discriminating symptoms in this population. Treatment with antidepressants may allow the patient to achieve a better quality for the remainder of her life.

Clinical challenges for palliative care

Advanced gynecologic cancer presents a range of clinical challenges for the multiprofessional team. Women with advanced cervical cancer may go into renal failure as a result of bilateral ureteric obstruction. It may be possible to decompress one kidney with a nephrostomy tube and than attempt placement of a J-J stent into the ureter. However, in some cases, extrinsic compression makes stenting unsuccessful or of shortlived benefit. Overaggressive treatment may result in a woman spending much of her limited time in hospital. The multiprofessional team needs to work closely with the patient and carers and health professionals in the community to make the best decision.

Malignant bowel obstruction

Malignant bowel obstruction is a common feature of advanced gynecologic malignancy. Retrospective and postmortem surveys give prevalence rates of 5–51% (Ripamonti and Bruera 2002). Malignant bowel obstruction is the most frequent cause of death in ovarian cancer. In these patients, obstruction may be of the small or large bowel, or, most commonly, at multiple sites. The pathophysiology of obstruction is usually by extrinsic compression from mesenteric, omental, and pelvic masses with intra-abdominal adhesions. Contributing factors may include inflammatory edema, fecal impaction, fatigue of intestinal muscles and the constipating effect of drugs.

Clinical presentation may vary depending on the level of the obstruction, but is usually subacute with a relapsing and remitting course (Figure 2).

Surgery should be considered in all patients with malignant bowel obstruction. In advanced malignancy, surgery will be palliative and symptom control may be possible using less-invasive means. Most studies of surgery in malignant bowel obstruction have been retrospective and conclusions are difficult to draw. Postoperative morbidity and mortality figures vary widely with reobstruction rates from 10% to 50%. Symptomatic relief is said to be achieved in 42% to over 80% (Feuer et al. 1999). Advanced age, medical frailty and poor nutritional status may mitigate against operative treatment. The presence of ascites or palpable abdominal masses are poor prognostic signs. Previous abdominal radiotherapy or chemotherapy are associated with poorer outcomes from surgery. Treatment options must be honestly discussed with

Figure 2

Plain abdominal X-ray showing malignant bowel obstruction in a women with advanced ovarian cancer

the patient and their carers in order to come to an appropriate decision.
Symptomatic relief of symptoms can be achieved pharmacologically in a majority of patients. Symptoms are usually a combination of nausea and vomiting, continuous abdominal pain and/or abdominal colic. Stimulant laxatives should be stopped and prokinetic drugs, such as metoclopromide, used with caution. Appropriate antiemetics are given parenterally, usually subcutaneously by continuous infusion. To this infusion can be added diamorphine for constant pain and hyoscine butylbromide for intestinal colic. Patients should be allowed to eat and drink as they choose. Thirst is rarely a problem, but subcutaneous or intravenous fluids can be given if needed. Symptoms can be controlled this way in about 75% of patients with malignant obstruction. In the remainder, other measures will be needed which may include the addition of the somatostatin analog, octreotide, corticosteroids or nasogastric intubation (Magili et al. 1946). Conservative management with nasogastric intubation and intravenous hydration is appropriate prior to surgery but is not otherwise recommended. This type of regime can be managed in the patient's home by the primary care team with specialist palliative care support. Being at home at the end of life is an important goal for many women with cancer.

Recurrent malignant ascites

Ovarian cancer is the commonest cause of malignant ascites, occurring in about 30% of patients with ovarian cancer at diagnosis and around 60% at the time of death. In ovarian cancer, the ascites is usually associated with peritoneal metastases. Less commonly, the fluid may be chylous or can accumulate as a result of portal hypertension in the presence of massive liver metastases. Malignant ascites is not such a poor prognostic sign in a woman with ovarian cancer as in other tumor types because of the potential for response to chemotherapy (Mackey and Venner 1996).
Malignant ascites causes symptoms including anorexia, nausea, abdominal distension and pain, dyspnea and fatigue. It can have a negative impact on a woman's body image—she may be treated as if she were pregnant and repeatedly asked 'when is the baby due?'. Knowing her diagnosis, this type of comment can be devastating (Figure 3).
Symptoms may be treated empirically as suggested above, but often the best way to gain relief is to drain some of the ascites. Much debate exists over how to make paracentesis most effective. There is an evidence

Figure 3

Tense abdominal ascities as a presenting feature of ovarian cancer

base to guide our practice but it relates largely to cirrhotic ascites. In undiagnosed cases, a full history and examination will precede imaging and diagnostic tap of the ascitic fluid (Figure 4).
In cases of malignant ascites where active treatment is not able to prevent recurrence, the mainstay of treatment is repeated drainage. Symptomatic paracentesis gives good relief of symptoms in 90% of patients. Potential complications include ascitic leaking, infection and hypovolemia if large volumes are withdrawn. When draining cirrhotic ascites it is usual to provide intravenous fluid replacement with colloids to prevent symptomatic hypovolemia. Symptomatic relief may be achieved by draining 3–5 liters of fluid over a day. The drain can then be removed limiting the chance of

Figure 4

Ascitic drain for symptom relief in a woman with advanced ovarian cancer infection and reducing the time spent as an inpatient. Draining to dryness is sometimes advocated, although ascitic fluid is likely to recur and the burden of this treatment is greater.

The use of diuretics is also associated with controversy. Small studies have supported the use of a combination of loop diuretics and spironolactone to delay re-accumulation of ascitic fluid. Diuretics appear to be most effective when liver metastases are present. Peritoneovenous shunts may be inserted as an alternative to repeated paracentesis. Originally developed for use in patients with cirrhotic ascites, both Leveen and Denver shunts have been studied in small open trials of recurrent malignant ascites. There is a significant shunt-related operative mortality and morbidity up to 60% in some reports, although others reveal 60–80% success rates. Complications include shunt occlusion, coagulopathy, gastrointestinal bleeding, sepsis and pulmonary edema. Peritoneovenous shunting may be considered for patients where other symptomatic treatments for ascites have failed and who have a prognosis of some months. Tunneled catheters may represent safer alternative to peritoneovenous shunts, but are not in widespread usage.

Intraperitoneal treatments, including chemotherapy and radiocolloids, have reported some success with the main complication being small bowel adhesions. Early studies suggest a possible place for intraperitoneal immunotherapy or matrix metalloproteinase inhibitors (Parsons et al. 1996).

Communicating with the family and with other professionals

In palliative care, the patient and their family or those important to them are regarded as the unit of care. However, this does not mean that carers should be given information before patients; and professionals need to follow the patient’s wishes. The fears, anxieties and concerns of the carer can be explored and their more intimate knowledge of the person drawn out. It may also be helpful to discuss with the family the strain that the situation is placing on them and ways in which services and the professionals may help.

One of the common concerns of patients in hospitals and in the community is that of receiving mixed messages from different professionals. It is important that all of the team involved in the care of the patient and family are kept fully informed of the important decisions and wishes of the patient and her family or carer. If people are at home and different services are visiting, the carer or patient can sometimes feel that they have a full-time job coordinating which services arrive when. It is important in these instances to identify a key worker for that patient and family who helps to take on some of the role of coordination and advocacy—so that the patient and the carer receive the services and benefits to which they are entitled. Similarly, in hospital the patient and carer may ask for information from different nurses and doctors—depending on who is with the patient at the time. There may also be different teams involved. This may be particularly likely with the palliative care patient, who may be seeing members of the hospital palliative care team as well as their own doctor. When the circumstances and condition of the patient change rapidly it is especially important that all the team is kept rapidly informed of relevant changes in the treatment plans or in the person’s condition or wishes.

The dying patient

Most deaths from gynecologic cancer can be predicted in advance and therefore planned for and actively managed. However, sudden death from associated causes, such as pulmonary embolism or sepsis, can occur and then the focus is on supporting the relatives.

It can be difficult to recognize that a patient is dying when they have been very slowly deteriorating. It is especially difficult to acknowledge approaching death amongst the team when a relationship has been built up with the woman over a period of time. It may feel like an admission of failure to suggest discussions about preparing for death but there may be important issues that need to be addressed. Integrated care pathways for the care of the dying are increasingly being used in all sites of care to improve recognition and care of the dying patient (Ellershaw and Ward 2003).

Women with advanced disease may ask if they are dying and sensitive honesty is required in answering them. It may be that the medical and nursing team recognize a deterioration and can reflect this to the patient and her family She can then choose whether to take up an offer of further information. Some women will understand that bad news is available and choose not to pursue it or suggest that their family is told instead.

Information allows patients to plan for their limited future including where they would prefer to die and to deal with ‘unfinished business’. This may include financial plans, such as making a will, practical issues, such as formalizing a power of attorney, and making a living will or spending precious time with loved ones. Where there are children involved there are particular issues to consider including how to tell them what is happening, how to leave a living written, or video memory, and sometimes who will be their guardian.

Recognition that a woman is entering the terminal phase of her illness is also important for the health care team. Investigations and treatments that had been appropriate may no longer be in the best interests of the patient. A multitude of decisions will need to be made including about continuing chemotherapy, treating new infections, tube feeding and cardiopulmonary resuscitation. Different patients will want different levels of involvement in such decision making.

As death approaches, patients will become weaker, sleepier and lose their appetite. They will spend longer periods of time in bed and then longer asleep. They need good nursing care to avoid skin breakdown, and good oral care to prevent mouth discomfort. Blood tests, X-rays and routine recordings, such as blood pressure measurement, become unhelpful and should be discontinued. Oral medication becomes more difficult to tolerate and can be cut down and then stopped. Symptomatic drugs must be continued, and may be given by continuous subcutaneous infusion, which is more comfortable than the intravenous route and can be managed by the nursing staff. Pain, nausea, agitation and 'bubbly' breathing can occur towards the end of life and drugs should be prescribed to be given subcutaneously for each of these symptoms. Fluids are not routinely given at the end of life although this needs to be assessed on an individual basis together with the family.

The health care team should be available regularly to talk with family and friends who often find the bedside vigil emotionally and physically exhausting. They may receive important support from a few minutes conversation a day with one of the team. They will need an explanation for changes as they happen and in advance if they can be predicted. Enquiries should be made about the patient's spiritual beliefs to allow them and their families to benefit from this support. Support for the family in their bereavement may be available from the palliative care team or locally through the general practitioner or national bereavement agency.

References

Ellershaw J, Ward C (2003) Care of the dying patient: the last hours or days of life. *BMJ* **326**:30–4.

Feuer D, Broadley K, Shepherd J, Barton D (1999) Systematic review of surgery in malignant bowel obstruction in advanced gynecological and gastrointestinal cancer. The Systematic Review Steering Committee. *Gynecol Oncol* **75**(3):313–22.

Lidstone V, Butters E, Seed P, et al. (2003) Symptoms and concerns amongst cancer outpatients: identifying the need for specialist palliative care. *Palliat Med* **17**(7):588–95.

Mackey J, Venner P (1996) Malignant ascites: demographics, therapeutic efficacy and predictors of survival. *Can J Oncol* **6**(2):474–80.

Mangili G, Franchi M, Mariani A, et al. (1996) Octreotide in the management of bowel obstruction in terminal ovarian cancer. *Gynecol Oncol* **61**(3):345–8.

Parsons S, Watson S, Steele J (1996) Malignant ascites. *Br J Surg* **83**:6–14.

Ripamionti C, Bruera E (2002) Palliative management of malignant bowel obstruction. *Int J Gynecol Cancer* **12** (2):135–43.

Steginga S, Dunn J (1997) Women's experiences following treatment for gynaecological cancer. *Oncol Nurs Forum* **24**:1403–8.

Vainio A, Auvinen A (1996) Prevalence of symptoms among patients with advanced cancer: an international collaborative study. *J Pain Symptom Manage* **12**:3–10.

28
Doctor-patient communication

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Unlike the rest of this book, this final chapter does not concern itself with practical surgical techniques; instead it looks at the problems of communication between the patient and her gynecologic oncologist. Entire books have been devoted to this subject and it may seem presumptuous even to attempt to address this in a brief chapter. However, we feel that the bare bones of good communication are extremely simple and may be summed up as imparting the truth and nothing but the truth in a compassionate manner.

In gynecologic oncology patients face a frightening diagnosis and an uncertain future. It is increasingly recognized that patients wish to know their diagnosis and to be kept informed of the progress of treatment. This has resulted in a revolution in the approach to patient-doctor communication. The era of professional paternalism, protecting patients from the diagnosis and remaining unrealistically optimistic to the dying patient, is over. With this change in approach has come a realization that effective communication skills are not innate, but can be taught, learnt, retained and used to improve patient care. More and more health care professionals, including gynecologic oncologists, are receiving training in communication with patients, the families and other professionals.

This increased communication with cancer patients has costs to health care professionals that need to be appreciated and addressed. The improved communication brings health care professionals closer to the patient and may increase feelings of inadequacy when faced with insoluble issues and of failure when patients die. Gynecological oncologists dealing with dying patients and their families risk 'burn-out'; although the medical profession is notoriously resistant to external help, a team spirit, adequate training through communication workshops, and peer support are important elements in tackling this problem.

Many junior doctors identify breaking bad news as their greatest fear and their top problem in communicating with patients. In many cases, doctors continue to carry this anxiety with them through years of clinical practice. Why do doctors fear breaking bad news? Obviously, the information causes pain and distress to our patients and their relatives, making us feel uncomfortable. We fear being blamed and provoking an emotional reaction. Breaking bad news reminds us of our own mortality and fears of our own death. Finally, we often worry about being unable to answer a patient's difficult questions since we never know what the future holds for either our patients or ourselves. Breaking bad news to patients should not involve protecting them from the truth but rather imparting the information in a sensitive manner at the patient's own pace. The setting for this conversation should be considered carefully. A confidential, quiet and comfortable location should be used rather than a busy gynecology ward with neighboring patients eavesdropping. An interruption-free period of 20–30 minutes should be allocated and the patient should be asked if she wishes anyone else to be present. Many patients will already be aware of how serious their condition is and will have guessed the diagnosis. Thus, an initial screening question asking what the patient believes to be the matter may change the interview from breaking to confirming bad news. Subsequently, the conversation may be viewed as a series of cycles repeated for each piece of information imparted. An initial warning shot from the doctor ('I'm afraid that the biopsy result was not normal') should be followed by a pause to enable the patient to respond or curtail the conversation. Further information can then be given and the patient again asked if she wishes to know any more. In this way it is the patient, not the doctor, who determines the quantity of information delivered and who controls the conversation without realizing it.

In general, prognostication with respect to 'duration of remaining life' and the quoting of 5-year mortality statistics is rarely helpful. Few of us are able to explain the implications of skewed distributions, medians and confidence intervals in a way that is easily understood by patients. Moreover, many of us have enough optimism to believe that we will fall on the lucky side of whatever statistic is quoted, however fallacious this belief. The last thing that we should do is to destroy all hope. Many patients will ask for predictions as to length of or guarantees of survival, often hoping for reassurance. In these circumstances, it is always easier to give the false reassurance but the temptation must be avoided as you will not be doing your patient a favor in the long run. Despite these restrictions, all consultations ideally should end on a positive note, the motto being 'never say never'. Even in the bleakest of situations, setting short-term achievable goals leaves patients with aims for the future and hope. This maxim applies to both the patient and—where the patient agrees—the next of kin.

It is desirable to communicate at each stage in a private setting and preferably to the patient and her next of kin at the same time. Failing this, a discussion should take place with the patient and be followed at a future date by a joint consultation between doctor, patient and her next of kin. It is rarely appropriate to allow relatives to 'protect' the patient by withholding information or over-optimistically lying. These issues can become particularly difficult when dealing with cultural differences. This act of collusion needs to be explored with relatives, on the basis that the patient needs to understand what is happening to her. With careful negotiation including an acknowledgment of the views of the relatives, access to the patient can usually be secured to determine the patient's own understanding of her illness. It is then common to discover that the patient is well aware of the diagnosis and is herself colluding to spare the relatives. In such circumstances honest discussion may reduce anxiety and resolve the relationship difficulties within the family.

In addition to keeping the patient abreast of developments, it is vital to involve the whole multidisciplinary team so that the patient and her relatives hear the same message from all the health care professionals. The roles of individuals within the team and their boundaries of care may lead to friction within teams. Philosophical differences in treatment approaches need to be explored. Frequent team meetings and open discussion that avoids a hierarchical structure will enhance team spirit and reduce tensions. Occasionally, an external facilitator may be helpful to coordinate such meetings.

The following pages set out what could be described as a four-cusp approach which may be useful in discussions on treatment strategies and prognosis (Table 1). We have been surprised at how often patients have taken away the scraps of paper used to demonstrate this four-cusp approach. In addition, we have noticed that our junior staff who frequently lack experience in talking through those difficult issues with patients find this a helpful framework. The cusps are illustrated by case examples. We used to refer to cusps 1, 2, 3 and 4, but a couple of our patients were upset because they confused cusps with 'staging' and since then we have referred to four cusps: A, B, C and D.

The 'four-cusp' approach

Cusp A: potentially curable

The first cusp applies to most patients from the time of the first visit to the clinic when the surgeon imparts the probable diagnosis and discusses with the patient the plan of action to achieve staging and hopefully removal of the tumor. It is rare to feel totally confident that a tumor is incurable before surgery; one may suspect it, but rarely can one know until the histology is confirmed and the staging completed. An honest appraisal of the possibilities is required, coupled with a plan of action. This should include date of surgery, length of time in hospital, and when final and definitive histological and cytological reports will become available. It is almost always possible to achieve these results within 2 weeks of the first visit to the clinic. The patients thus know they will have a good idea where they stand by a specific date. The concept of cancer staging should be explained and that the stage and type of tumor will influence the necessity for further treatment with radiotherapy or

Table 1 The four-cusp approach to patient communication

	Cusp A	*Cusp B*	*Cusp C*	*Cusp D*
Status	Potentially curable	Living with cancer	Pre-terminal	Terminal
Duration	Weeks to years	Months to years	Weeks to months	Days
Treatment	Radical surgery Adjuvant therapy	Palliative chemotherapy or radiotherapy	Supportive care	Terminal care
Aims	Cure Prolong survival	Prolong survival Improve QoL	Improve QoL	Improve QoL End-of-life issues

chemotherapy. We usually explain that, if we achieve treatment by surgery alone there is a presumption of cure. This, however, can only be confirmed by the passage of time, and the longer all remains well the higher is the likelihood that cure has been achieved. A high level of positivity and a buoyant approach are usually applicable both before and after surgery for those with complete resection of tumor, although the need for careful follow-up and the possibility of relapse should be discussed.

Case 1

A woman is referred to the gynecological oncology clinic with postcoital bleeding and a suspected cervical cancer. On examination, a small cervical tumor is found which is approximately 2–3 cm in diameter. The uterus and cervix are mobile and there are no other detectable abnormalities. A colposcopy and biopsy are performed.

Following the examination, the consultation should continue, usually by asking the patient if she has any idea what she thinks the diagnosis might be. Many patients will state their worst fear, namely cancer; others will say they have no idea. This is generally the point at which to communicate that you also believe the diagnosis to be one of cancer and that the biopsy will confirm or exclude this within the next few days. It is then possible to say that the initial examination suggests that this is an eminently curable cancer, and to outline the plan of action: first, the patient will be admitted on a specific date within the next week for staging of the tumor and on a subsequent date, probably within the next 2 weeks, for definitive surgery. Explain that there are four stages of cervical cancer, that stage I is the best and stage IV the worst. Tell the patient that the first admission will take one day and will deliver an answer which she will probably know later that same day. Explain that you believe the tumor to be stage I and therefore highly curable, probably by surgery alone, but possibly requiring further treatment with chemoradiotherapy Ask the patient to have her next of kin present at the poststaging ward round if they are not there at the clinic. The patient should be invited to ask any questions and encouraged to write down any questions she thinks of when she is home and to ask them when she is admitted.

It is our practice to copy the letter written to the referring doctor to the patients themselves. We undertook a survey of patient acceptability of this practice, and over one hundred patients surveyed all believed it was helpful and none chose not to receive further copies of future letters. Carefully organized and coordinated staging protocols allow women rapid access to results, reducing delays, and hence minimizing the anxiety caused by waiting for results. The patient will have the usual prestaging investigations, such as radiographic scans, and will then be admitted for a staging examination under anesthesia. These findings along with the histology are communicated to the patient that day. The date for radical hysterectomy is then set and an explanation of this given, including the prognostic significance of nodal status and its impact on likely adjuvant therapy. The discussion may be supplemented with patient information leaflets (either written in-house or available from patient support groups). However, this information should never replace the discussion between the patient and her gynecologist but rather complement it. It should be explained that, although we will have a good idea where the patient stands immediately following surgery, definitive answers require histological confirmation and that this usually takes 7 days. It is usually better to predict a longer wait for histologic results than one expects, since patients' anxieties naturally rise when they believe their results to be imminent,

and if for any reason results are delayed this only further increases anxiety.
The operation is then performed, and either the same day or the following day an explanation is given. A few days later the full histological picture is given.
Scenario 1: the histology report shows complete resection of a 2 cm well-differentiated squamous carcinoma with adequate resection margins and negative nodes.
This patient can be told that you believe cure has been achieved, and while long-term follow-up is warranted you expect to see her in the clinic for the next 5–10 years (depending on individual protocol) and to discharge her from care at this time ‘fit and well’.
Scenario 2: the histology report shows complete resection of a moderately differentiated squamous cervical carcinoma with 3 positive metastatic nodes out of 40 removed.
This information is imparted and the patient is told that although there is complete removal of tumor further treatment is required with combination chemoradiotherapy Such patients can be told that you believe cure is likely and that this is a ‘belt and braces (suspenders)’ approach, but that there is no denying they do have a higher chance of relapse than if their nodes had been negative. The concept of adjuvant therapy following radical surgery may be explained as an ‘insurance policy’ to mop up any tumor cells that could have escaped the surgery.

Case 2

A 55-year-old woman is referred by her general practitioner with abdominal swelling which she has noted in the last few weeks. She has no other symptoms. Abdominal examination reveals fluid in the abdomen on percussion. Vaginal examination is suggestive of a mass arising from the right adnexa, probably ovarian in origin, and nodules are felt in the pouch of Douglas.
The patient is informed that there are findings suggestive of an ovarian mass and that these require urgent investigation. The patient should be told that you suspect cancer and that the investigations you are about to request will go some way to eliciting a diagnosis.
Hematological and biochemical tests are ordered, as are tumor markers, an ultrasound scan with color flow Doppler, and a computed tomography (CT) scan of abdomen and pelvis to detect lymphadenopathy. The patient is reviewed shortly thereafter and the risk of malignancy index is used. The findings are highly suggestive of a stage IC ovarian cancer.
Staging of ovarian cancer is explained to the patient, together with the fact that there are three possible outcomes from the operation which will be communicated to her immediately postoperatively:

- complete macroscopic resection of tumor
- resection of tumor down to nodules less than 1–2 cm in diameter
- inadequate debulking.

The last two possibilities seem unlikely, bearing in mind the optimistic findings of the investigations. Full staging will be arrived at a few days after surgery when all the cytologic and histologic results will be available. Patient consent is obtained for a total abdominal hysterectomy, bilateral salpingo-oophorectomy omentectomy and debulking as required.
Scenario 1: at surgery a smooth-walled cyst is found with some free fluid in the pelvis. There is no evidence of any tumor elsewhere in the abdomen on macroscopic examination.
Postoperatively, the patient can be told that she falls into the first category (fully macroscopically resected tumor) and a few days later the histological report confirms a well-differentiated ovarian epithelial carcinoma, with negative cytology from washings and peritoneum. The patient is informed that she has a stage IA tumor and should have no further problems. She remains at cusp A.
Scenario 2: at surgery the abdomen is opened and 500 mL of straw-colored fluid is aspirated and sent for cytology. Abdominal exploration reveals small studs of tumor on the diaphragm and a small omental deposit. A total hysterectomy, bilateral salpingo-oophorectomy and omentectomy are performed with minimal residual tumor left at the end of the operation.
The patient is informed postoperatively that she falls into the second category, namely tumor debulked to less than 1 cm, and that she probably has a stage III tumor depending on results and almost certainly will require further treatment. A few days later the histologic and cytologic reports confirm that this clinical impression was correct. The patient is informed and chemotherapy planned. She should be informed that she has now entered the cusp B, ‘living with cancer’, that she may regain cusp A following chemotherapy, but that only time will tell.

Cusp B: living with cancer

Cusp B is for treated patients who are in remission but are unlikely to be cured (i.e.‘living with cancer’) but not terminal. Again a positive approach is appropriate, but the long-term goals are less optimistic. The patient should be informed that it is impossible to determine how long she will remain in remission, that we certainly have many patients who are alive many years after chemotherapy and a few who have returned to cusp A (i.e. presumed cured). Sadly, we also have some who have not survived as long. The golden rule is that the longer one is in complete remission, the better the prospects become. The biggest difficulty is that neither the patient nor the doctor knows which category she is in until time elapses, but it is important that both can see that it is well worth following through with treatment.

The patient described in scenario 2 above then undergoes chemotherapy.

Scenario 1: the patient goes into complete remission for 5 years.

This patient is one of the lucky ones and has returned to cusp A—presumed cured.

Scenario 2: the patient goes into complete remission which lasts for 3 years and then at the follow-up joint oncology clinic is found to have a raised serum level of CA125 and a palpable nodule in the pouch of Douglas. Staging investigations reveal radiologic evidence of a solitary nodule. She therefore has a second laparotomy: complete excision of the tumor is achieved, followed by a further course of chemotherapy. Again, the patient enters complete remission.

She can be told that she appears to have a relatively non-aggressive tumor and can expect to remain in the second cusp for a good time longer.

Scenario 3: following first-line chemotherapy the patient achieves a partial remission which lasts for 5 months when she re-presents at follow-up to the joint oncology clinic with a rising serum CA125 level and abdominal swelling. Radiologic investigation suggests that there are widespread metastatic peritoneal nodules.

This patient may be given the choice of whether to be observed until she develops symptoms or to have second-line chemotherapy. The role of chemotherapy is to palliate symptoms rather than prolong survival in this context and the balance between the possible benefits and toxicities of the chemotherapy should be explored with the patient. The patient declines further chemotherapy and then deteriorates over the next few weeks. She needs to be informed that she has moved to cusp C.

Cusp C: pre-terminal phase

The third cusp applies to patients with virtually no chance of cure, who have entered the ‘pre-terminal phase’. It is important that the patient is informed and made aware that she has a limited time left to her, and that she is given the opportunity to ‘put her house in order’, see relatives and friends, make a will, etc. No patient should ever be told that there is nothing more than can be done for her. She should be informed that while she has virtually no chance of cure, and aggressive treatments to obtain cure are not appropriate, there are plenty of measures available to ameliorate symptoms, such as pain, nausea or upset bowels. The therapies that are appropriate at this phase of the disease are supportive measures to improve the quality of her life without causing toxicity.

Scenario: a patient with carcinoma of the cervix presents 3 years after radical radiotherapy for a stage 3 tumor. She is passing urine permanently per vaginam. On investigation and examination under anesthesia she is found to have extensive recurrence of tumor both in the para-aortic region and on the pelvic side-wall. In addition, she has a large irreparable cystovaginal fistula. She also has deteriorating renal function.

The patient is informed that she has recurrent cancer and there are no curative treatments available. She says she had guessed that anyway and is clearly very angry. She is then asked the vital question for cusp C ,what in addition to the fact that she is dying is most bothering her? To this she replies that she accepts death as inevitable and this does not make her angry—what makes her angry is her permanent incontinence which is preventing her from going out and seeing family and friends. She is referred to the interventional radiologist and bilateral nephrostomy tubes are inserted, which render her dry. The patient goes home and returns 4 weeks later, in a terminal condition. She has entered cusp D. She does, however, inform us that she has had a great four weeks, been to the pub every day and seen all her friends. She dies 24 hours later.

Cusp D: terminal phase

The terminal phase of life lasts from hours to days and all interventions are only designed to ‘ease the passing’. Patients, in general, need no telling that this is where they have arrived, although the relatives may need help in understanding it. Care is focused on emotional support rather than medical intervention, and frequently most of the patient’s medication can be stopped apart from analgesia. The death of a patient whose physical symptoms are well controlled and who is spiritually calm is an achievable goal to which we should all strive.

References

Fallowfield LJ (1993) Giving sad and bad news. *Lancet* **341**:476–8.
Maguire P, Faulkner A (1988a) Communication with cancer patients: 1. Handling bad news and difficult questions. *Br Med J* **297**:907–9.
Maguire P, Faulkner A (1988b) Communication with cancer patients: 2. Handling uncertainty, collusion and denial. *Br Med J* **297**:972–3.
Nordin A, ed. (1999) *Gynaecological cancer. Patient pictures.* Oxford: Health Press.
Slevin ML (1987) Talking about cancer. How much is too much? *Br J Hosp Med* July: 56–9.

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