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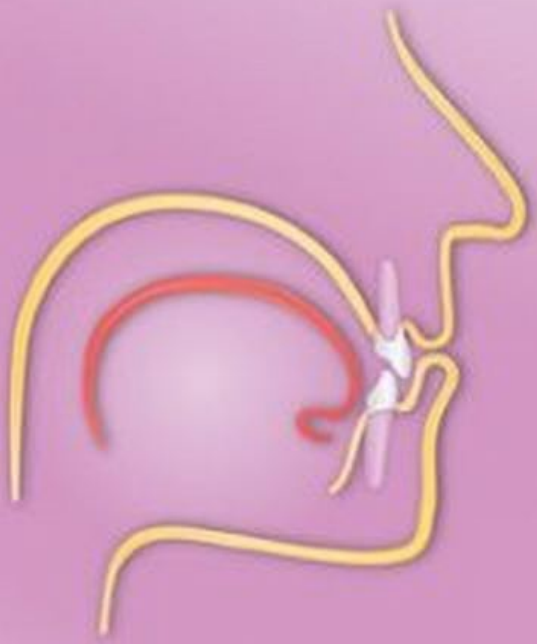
Pocket Atlas of Oral Diseases

G. Laskaris

Second Edition

clinical sciences



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Pocket Atlas of Oral Diseases

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Dedication

To my wife, **Vivi**,
for her love and her continuous
support of my efforts

Preface to the Second Edition

Seven years have passed since publication of the first edition of the *Pocket Atlas of Oral Diseases*, and its enthusiastic acceptance by dentists, physicians, and medical and dental students has exceeded an expectations. For the second edition the clinical orientation of the book remains unchanged. However the book now contains 31 new topics and over 100 additional color plates. A number of existing illustrations have been replaced by more representative high-quality color plates. The original text has been revised and updated to keep pace with the latest concepts in oral medicine.

For more clinical information, readers may refer to my major book *Color Atlas of Oral Diseases*, third edition, 2003, and for treatment details to my recent book Treatment of Oral Diseases, 2005, both published by Georg Thieme Publishers.

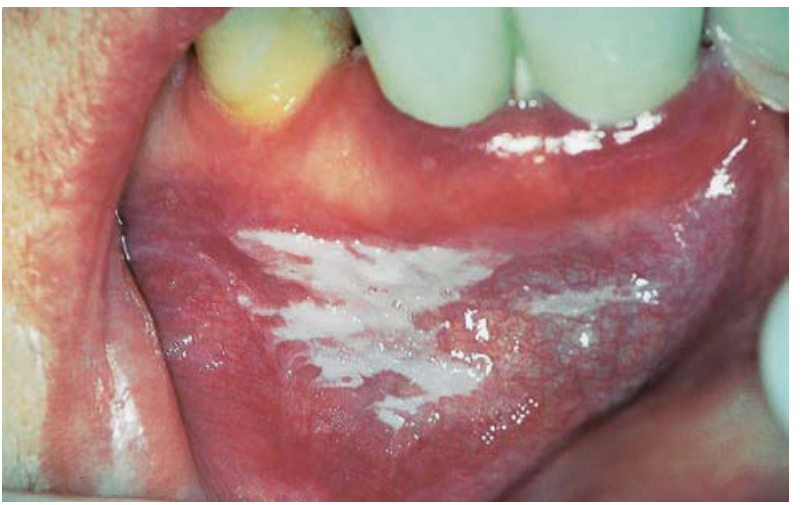
Athens *George Laskaris, M.D., D.D.S., Ph.D.*

Contents

1 White Lesions

White lesions of the oral mucosa are a multifactorial group of disorders, the color of which is produced by the scattering of the light through an altered epithelial surface. The diagnosis and differential diagnosis of oral white lesions should be made on the basis of the medical history, clinical features, and laboratory tests.

- Leukoplakia
- Hairy leukoplakia
- Lichen planus
- Lichenoid reactions
- Linea alba
- Nicotinic stomatitis
- Uremic stomatitis
- Cinnamon contact stomatitis
- Chemical burn
- Candidiasis
- Chronic biting
- Geographic tongue
- Hairy tongue
- Furred tongue
- Materia alba of the gingiva
- Fordyce's granules
- Leukoedema
- White sponge nevus
- Dyskeratosis congenita
- Pachyonychia congenita
- Focal palmoplantar and oral mucosa hyperkeratosis syndrome
- Papilloma
- Verrucous carcinoma
- Squamous-cell carcinoma
- Skin and mucosal grafts
- Epithelial peeling



Leukoplakia

Definition Leukoplakia is a clinical term, and the lesion is defined as a white patch or plaque, firmly attached to the oral mucosa, that cannot be classified as any other disease entity. It is a precancerous lesion.

Etiology The exact etiology remains unknown. Tobacco, alcohol, chronic local friction, and *Candida albicans* are important predisposing factors. Human papilloma virus (HPV) may also be involved in the pathogenesis of oral leukoplakia.

Clinical features Three clinical varieties (Figs. **1** and **2**) are recognized: *homogeneous* (common), *speckled* (less common), and *verrucous* (rare). Speckled and verrucous leukoplakia have a greater risk for malignant transformation than the homogeneous form. The average percentage of malignant transformation for leukoplakia varies between 4% and 6%. The buccal mucosa, tongue, floor of the mouth, gingiva, and lower lip are the most commonly affected sites.

Laboratory tests Histopathological examination.

Differential diagnosis Lichen planus, cinnamon contact stomatitis, candidiasis, hairy leukoplakia, lichen planus reactions, chronic biting, tobacco pouch keratosis, leukoedema, chemical burn, uremic stomatitis, skin graft, some genodermatoses and discoid lupus erythematosus.

Treatment Elimination or discontinuation of predisposing factors, systemic retinoid compounds. Surgical excision is the treatment of choice.

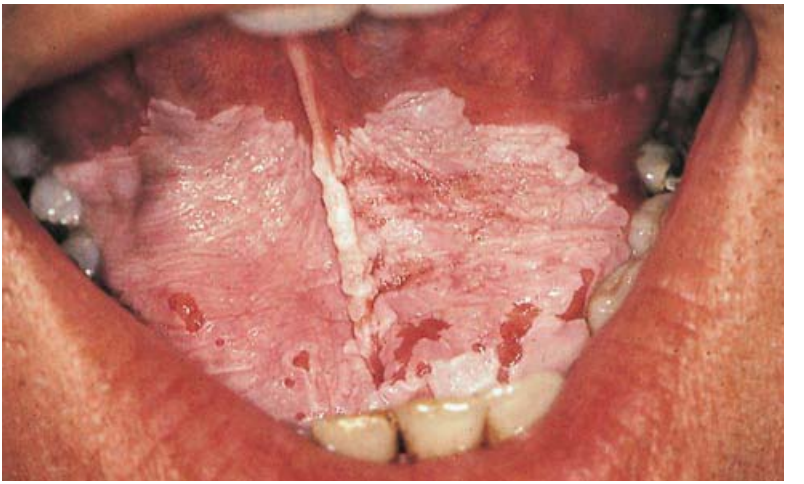


Fig. 1 Homogeneous leukoplakia.

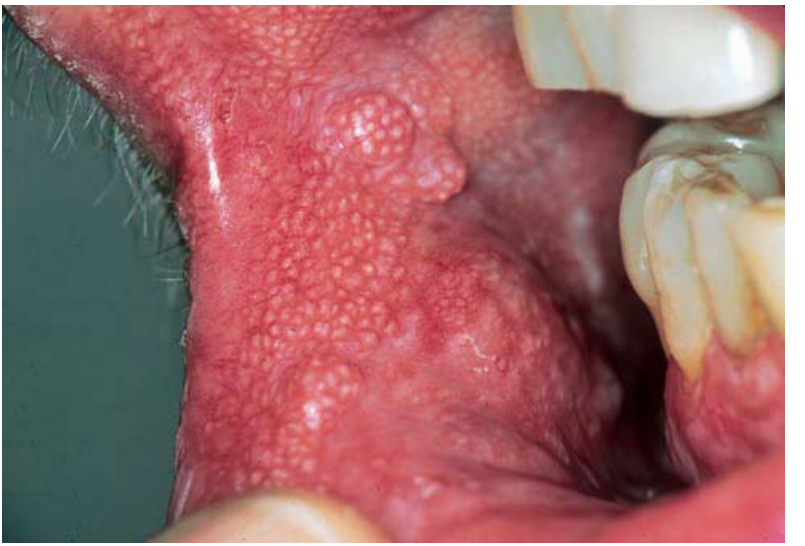


Fig. 2 Speckled leukoplakia.

Hairy Leukoplakia

Definition Hairy leukoplakia is one of the most common and characteristic lesions of human immunodeficiency virus (HIV) infection. Rarely, it can also appear in immunosuppressed patients after organ transplantation.

Etiology Epstein–Barr virus seems to play an important role in the pathogenesis.

Clinical features Hairy leukoplakia presents as a white asymptomatic, often elevated and unremovable patch. The lesion is almost always found bilaterally on the lateral margins of the tongue, and may spread to the dorsum and the ventral surface (Fig. **3**). Characteristically, the surface of the lesion is corrugated with a vertical orientation. However, smooth and flat lesions may also be seen. The lesion is not precancerous.

Laboratory tests Histological examination, in situ hybridization, polymerase chain reaction (PCR) and electron microscopy.

Differential diagnosis Chronic biting, lichen planus, frictional keratosis, cinnamon contact stomatitis, uremic stomatitis, candidiasis.

Treatment Not required; however, in some cases aciclovir or valaciclovir can be used with success.

Lichen Planus

Definition Lichen planus is a relatively common chronic inflammatory disease of the oral mucosa and skin.

Etiology Although the cause is not well known, T cell-mediated autoimmune phenomena are involved in the pathogenesis of lichen planus.

Clinical features White papules that usually coalesce, forming a network of lines (Wickman's striae), are the characteristic oral lesions of the disease. Six forms of the disease are recognized in the oral mucosa, classified according to frequency: the common (reticular, erosive, Figs. **4**, **5**); the less common (atrophic, hypertrophic, Fig. **6**); and the rare (bullous, pigmented, Fig. **7**). Middle-aged individuals are more com-

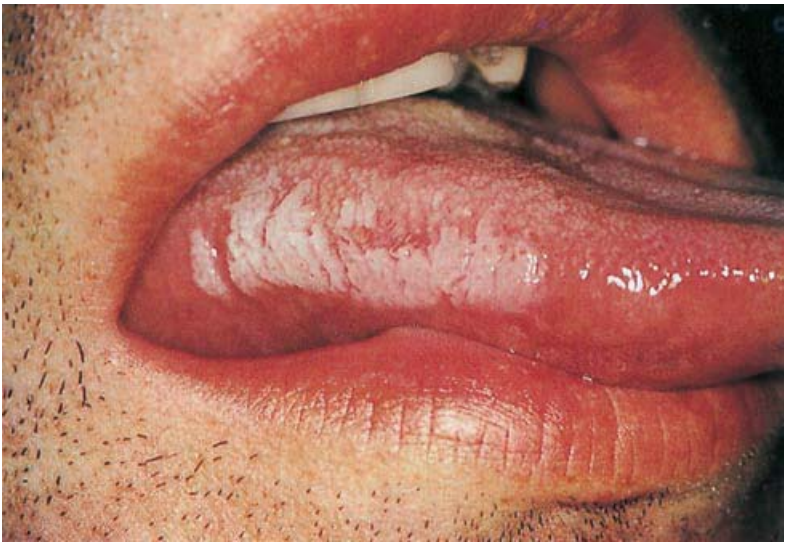


Fig. 3 Hairy leukoplakia.

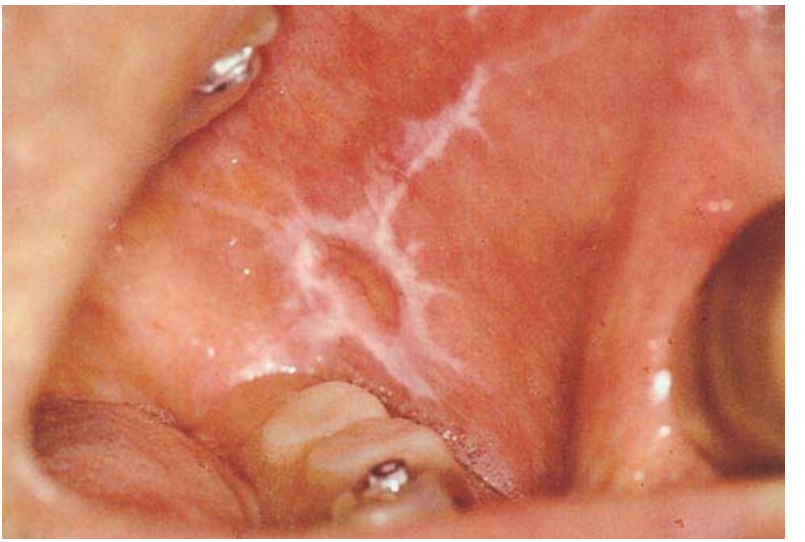


Fig. 4 Lichen planus of the buccal mucosa: reticular form.

monly affected (the ratio of women to men ratio is 3 : 2). The buccal mucosa, tongue, and gingiva are the sites of predilection. The skin lesions characteristically appear as polygonal purple, pruritic papules, usually affecting the flexor surfaces of the extremities. The glans penis and nails may also be affected. The disease can usually be diagnosed on clinical grounds alone. The prognosis of lichen planus is usually good, and malignant transformation (particularly of the erosive form) remains controversial.

Laboratory tests Histopathological examination is very helpful. Direct immunofluorescence can also be used, although the features are not specific.

Differential diagnosis Discoid lupus erythematosus, candidiasis, graft-versus-host disease, geographic tongue, leukoplakia, erythroplakia, cicatricial pemphigoid, pemphigus, bullous pemphigoid.

Treatment No treatment is needed in asymptomatic lesions. Topical steroids (ointment in Orabase, intralesional injection), may be helpful. Systemic steroids in low doses can be used in severe and extensive cases. The topical use of antiseptic mouthwashes should be avoided.

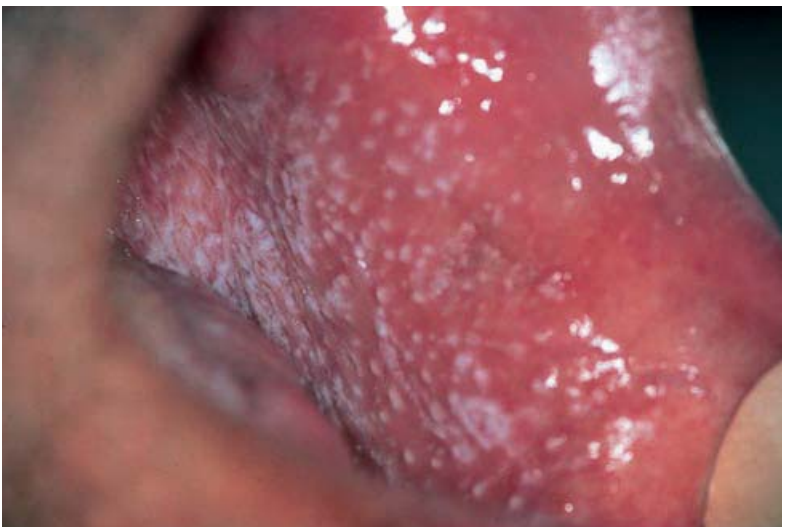


Fig. 5 Lichen planus, papular and reticular forms, of the buccal mucosa.

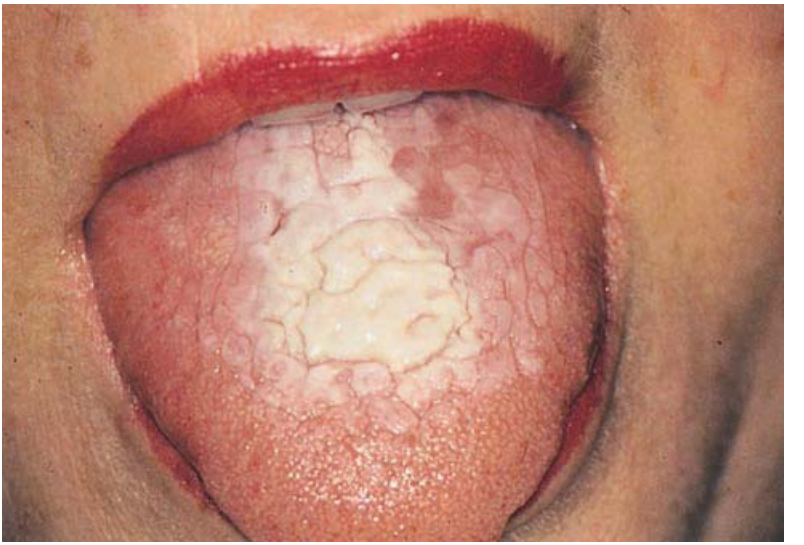


Fig. 6 Lichen planus of the dorsum of the tongue: hypertrophic form.

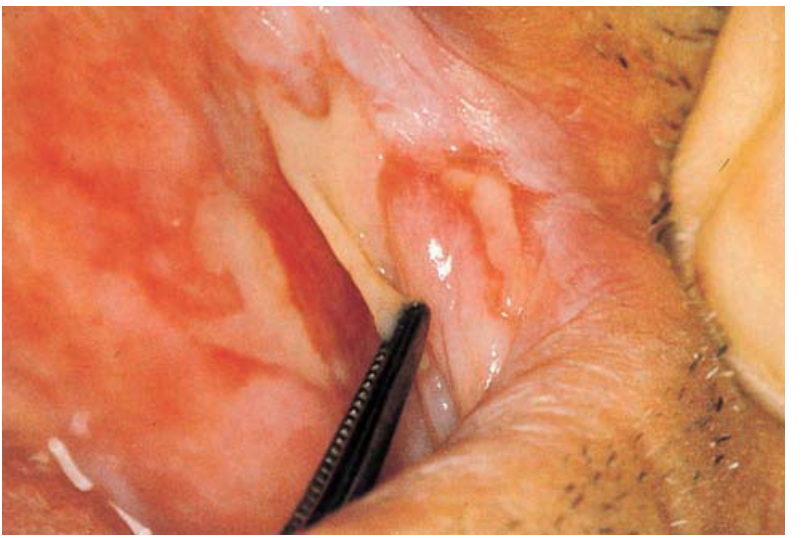


Fig. 7 Lichen planus, pigmented form, of the buccal mucosa.

Lichenoid Reactions

Definition Lichenoid or lichen planus reactions are a heterogeneous group of lesions of the oral mucosa that show clinical and histopathological similarities to lichen planus, but have a different course.

Etiology Hypersensitivity to dental restorative materials, amalgam, composite resins and dental plaque accumulation are the most common causative factors. Rarely, a reaction to drugs may be responsible.

Clinical features Clinically, they appear as white and/or erythematous lesions, usually associated with peripheral delicate white striae (Fig. **8**). Erosions are also common (Fig. **9**). The lesions mimic erosive lichen planus. Characteristically, the lesions are strictly confined to the mucosa directly in contact with the restorative materials, and do not migrate to other sites. The lesions disappear after removal of the adjacent material. The diagnosis is usually made clinically.

Laboratory tests A skin punch test may be helpful in some cases.

Differential diagnosis Lichen planus, fixed drug eruption, discoid lupus erythematosus, cicatricial pemphigoid, cinnamon contact stomatitis.

Treatment Replacement of the restorative material, polishing and smoothing, and good oral hygiene are recommended. Topical steroid treatment for a short time is also helpful.

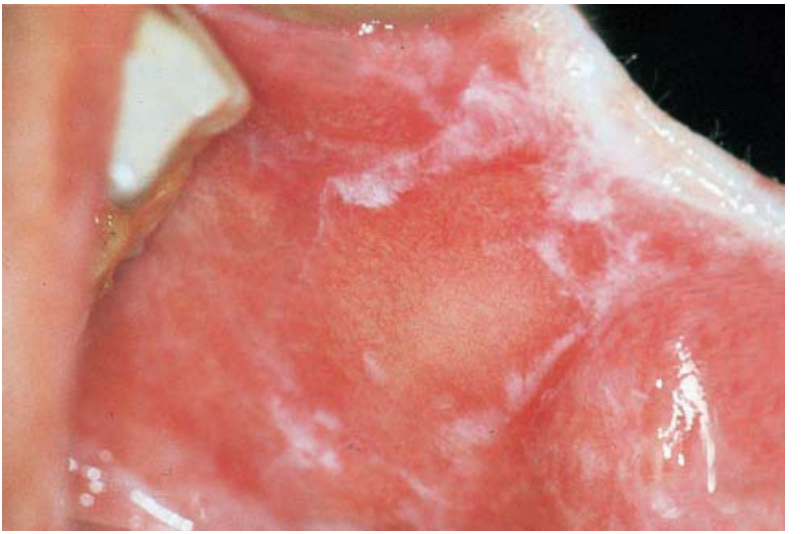


Fig. 8 Lichenoid reaction to dental amalgam and cold: white and erythematous lesions on the buccal mucosa.

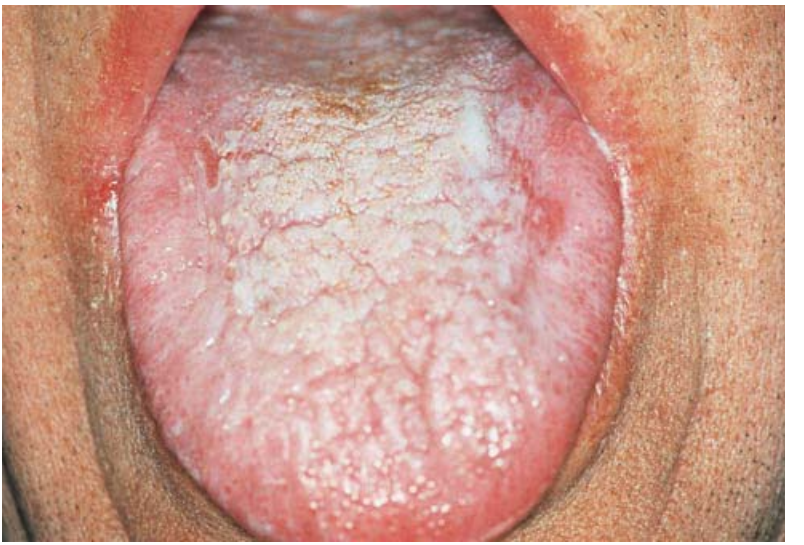


Fig. 9 Lichenoid drug reaction to allopurinol: white hyperkeratotic lesions and superficial erosions on the sides of the tongue.

Linea Alba

Definition Linea alba is a relatively common alteration of the buccal mucosa.

Etiology Pressure, sucking from the buccal surface of the teeth.

Clinical features It presents as an asymptomatic, bilateral, linear elevation with a slightly whitish color at the level of the occlusal line of the teeth (Fig. **10**). It has a normal consistency on palpation. The diagnosis is based on clinical grounds alone.

Treatment No treatment is required.

Nicotinic Stomatitis

Definition Nicotinic stomatitis, or smoker's palate, is a common tobacco-related type of keratosis that occurs exclusively on the hard palate, and is classically associated with heavy pipe and cigar smoking.

Etiology The elevated temperature, rather than the tobacco chemicals, is responsible for this lesion.

Clinical features Clinically, the palatal mucosa initially responds to the high temperature with redness. Later, it becomes wrinkled and takes on a diffusely grayish-white color, with numerous micronodules with characteristic punctate red centers, which represent the inflamed and dilated orifices of the minor salivary gland ducts (Fig. **11**). The lesions are not premalignant, in contrast to the "reverse smoker's palate" lesion, which is associated with reverse smoking.

Laboratory tests Usually not required. However, a histopathological examination is useful.

Differential diagnosis Reverse smoker's palate, leukoplakia, discoid lupus erythematosus, candidiasis, lichen planus.

Treatment Cessation of smoking.

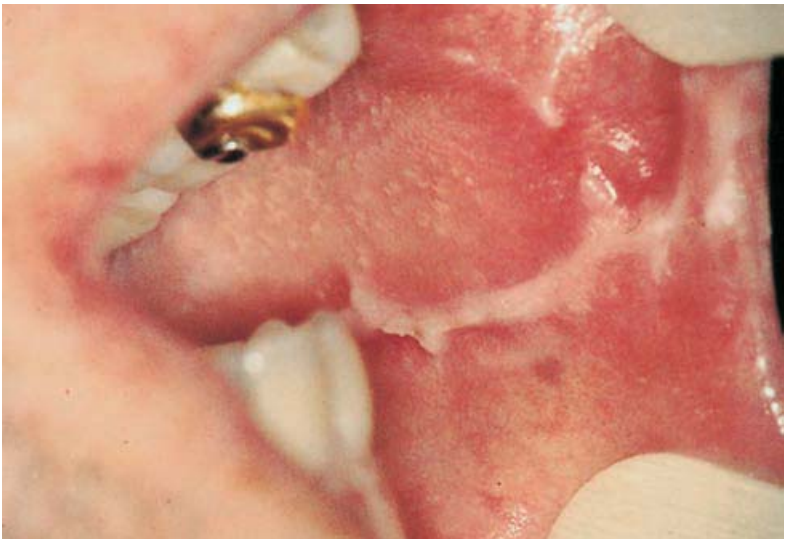


Fig. 10 Linea alba.

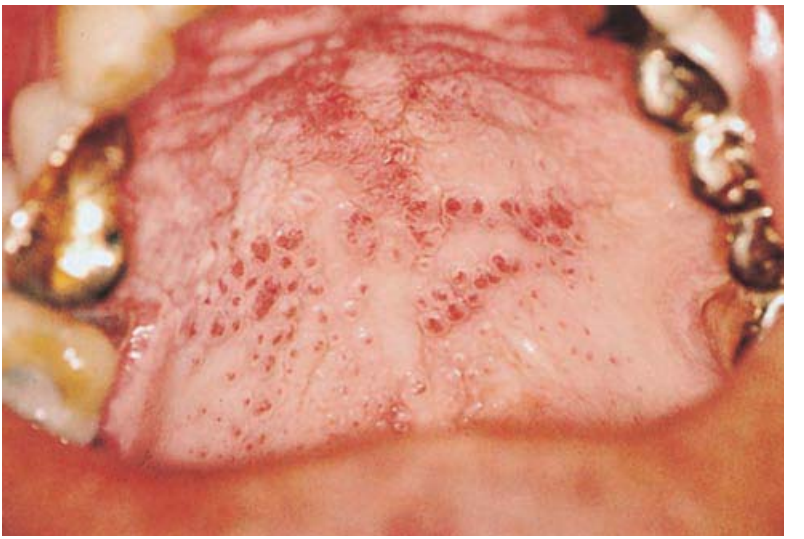


Fig. 11 Nicotinic stomatitis.

Uremic Stomatitis

Definition Uremic stomatitis is a rare disorder that may occur in patients with acute or chronic renal failure.

Etiology Increased concentration of urea and its products in the blood and saliva. The pathogenesis of oral lesions is not clear. It usually appears when blood concentration of urea exceeds 30 mmol/1. The degradation of oral urea by the enzyme urease forms free ammonia, which may damage the oral mucosa.

Clinical features Four forms of uremic stomatitis are recognized: (a) *the ulcerative form*, (b) *the hemorrhagic form*, (c) *the nonulcerative, pseudomembranous form*, and (d) *the hyperkeratotic form*. The last two forms appear as white lesions. The nonulcerative, pseudomembranous form presents as painful diffuse erythema covered by a thick whitish-gray pseudomembrane (Fig. **12**). The hyperkeratotic form presents as multiple painful white hyperkeratotic lesions with thin projections (Fig. **13**). The tongue, and the floor of the mouth are more frequently affected. Xerostomia, uriniferous breath odor, unpleasant taste, and a burning sensation are common symptoms. Candidiasis and viral and bacterial infections are common oral complications. The diagnosis is based on the history, the clinical features, urinalysis and blood urea level determination.

Differential diagnosis Candidiasis, cinnamon contact stomatitis, hairy leukoplakia, white sponge nevus, drug reactions.

Treatment The oral lesions usually improve after hemodialysis. A high level of oral hygiene, mouthwashes with oxygen release agents, and artificial saliva are suggested. Antimycotic, antiviral, and antimicrobial agents if necessary.

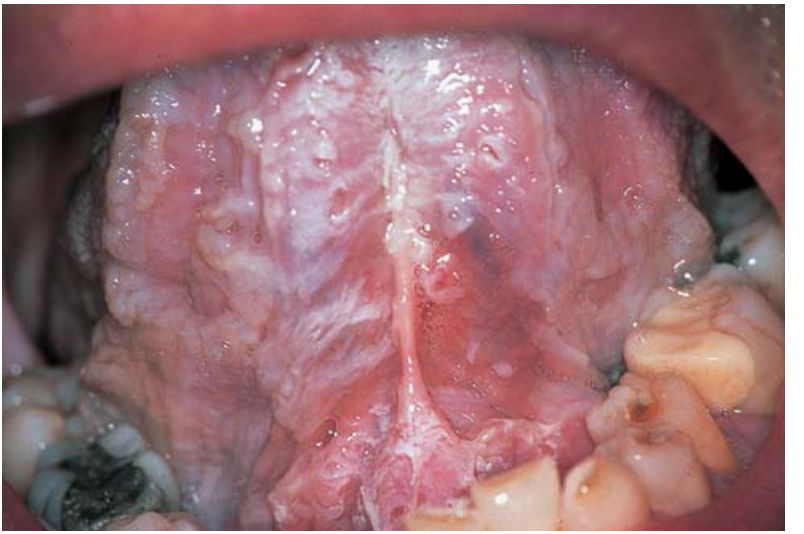


Fig. 12 Uremic stomatitis, whitish-gray pseudomembranes on the tongue and floor of the mouth.

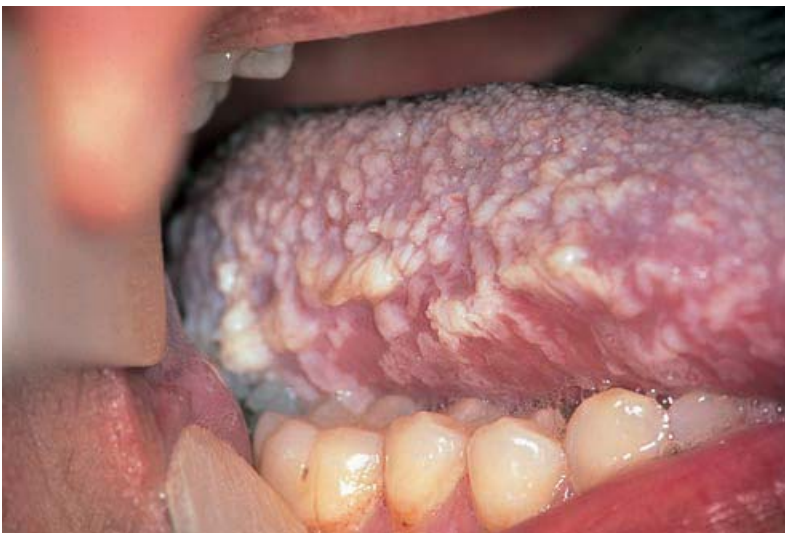


Fig. 13 Uremic stomatitis, white hyperkeratotic lesions mimic hairy leukoplakia on the lateral border of the tongue.

Cinnamon Contact Stomatitis

Definition Cinnamon contact stomatitis is a relatively common oral mucosal reaction to continuous contact of substances with cinnamon.

Etiology Artificial cinnamon flavoring especially in the form of chewing gum, candies, toothpaste, drops, etc.

Clinical features The condition is characterized by erythema of the oral mucosa, usually in association with desquamation and erosions. White hyperkeratotic plaques are very common (Figs. **14**, **15**). A burning sensation and pain are common symptoms. The lateral borders of the tongue, the buccal mucosa, and the gingiva are more frequently affected. Exfoliative cheilitis and perioral dermatitis may occur. The diagnosis is based on the history and the clinical features.

Differential diagnosis Amalgam contact stomatitis, chronic biting, leukoedema, epithelial peeling, hairy leukoplakia, leukoplakia, candidiasis, uremic stomatitis, lichen planus, discoid lupus erythematosus.

Treatment Discontinuation of any cinnamon product improves the signs and symptoms in approximately two weeks. In severe and extended lesions with erosions, low doses of steroids (e.g., 10 mg/day prednisolone) for one week help the lesions to heal.

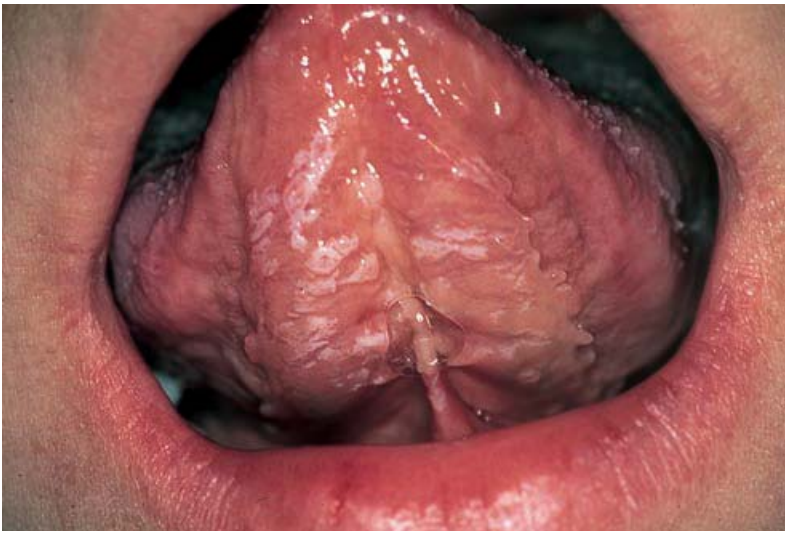


Fig. 14 Cinnamon contact stomatitis, white lesion on the ventral surface of the tongue.

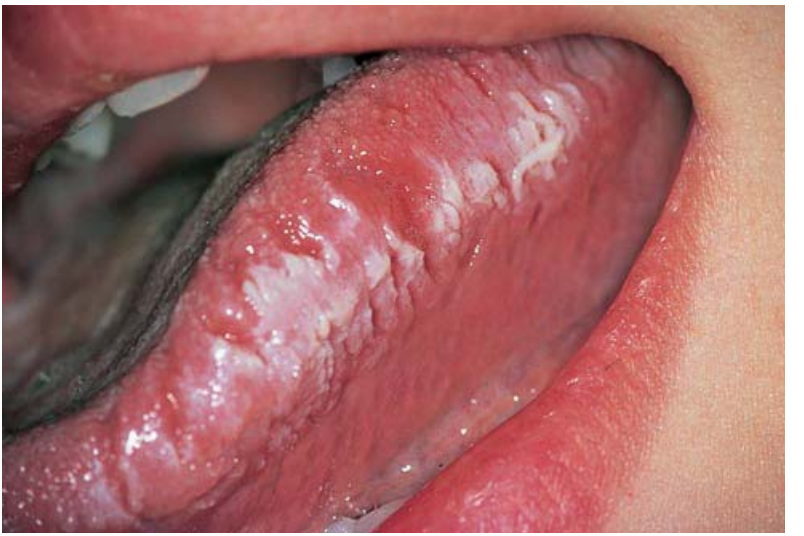


Fig. 15 Cinnamon contact stomatitis, severe white lesions on the lateral border of the tongue.

Chemical Burn

Definition This is an injury to the oral mucosa caused by topical application of caustic agents.

Etiology Causative agents include aspirin, hydrogen peroxide, phenol, alcohol, sodium perborate, silver nitrate, trichloroacetic acid, acid etching liquid, and varnishes of tooth cavities.

Clinical features Clinically, the affected mucosa is covered with a white membrane due to necrosis (Figs. **16**, **17**, **18**). The necrotic epithelium can easily be scraped off, leaving a red, bleeding surface. The lesions are painful. The diagnosis should be made on the basis of the clinical features and history.

Differential diagnosis Necrotizing ulcerative gingivitis and stomatitis, materia alba, candidiasis, mechanical trauma, bullous diseases.

Treatment Treatment is symptomatic.

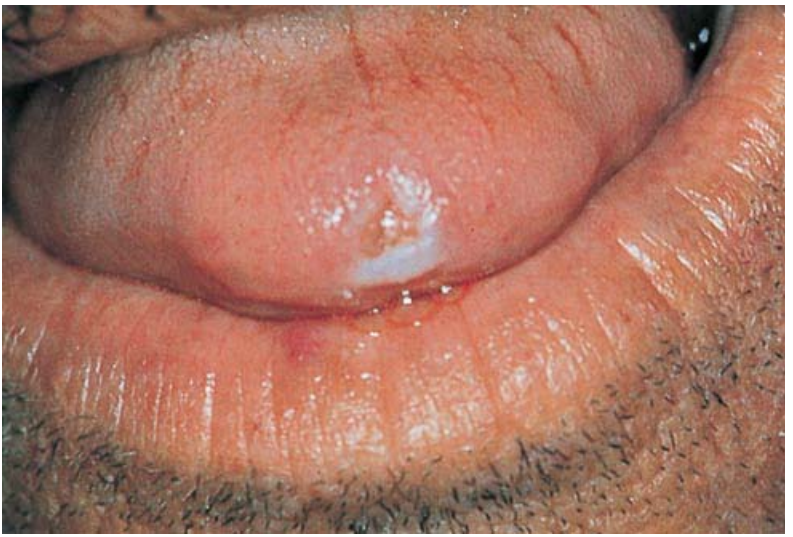


Fig. 16 Phenol burn.

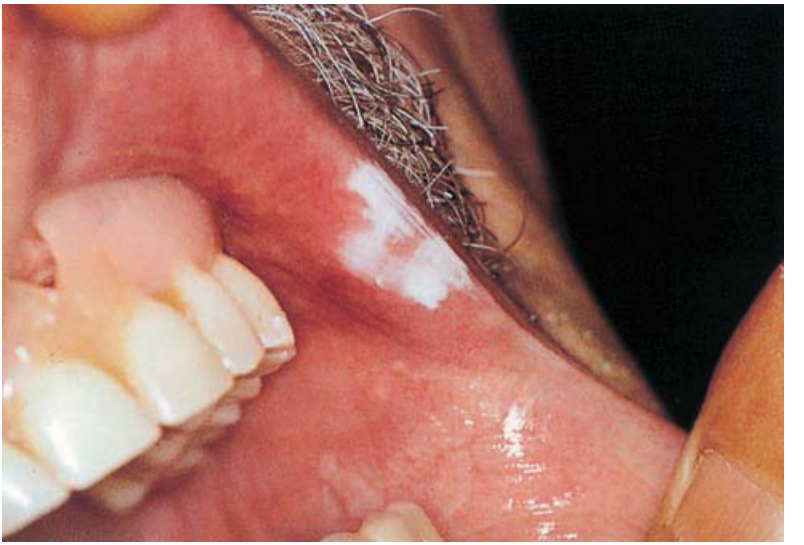


Fig. 17 Trichloroacetic acid burn.

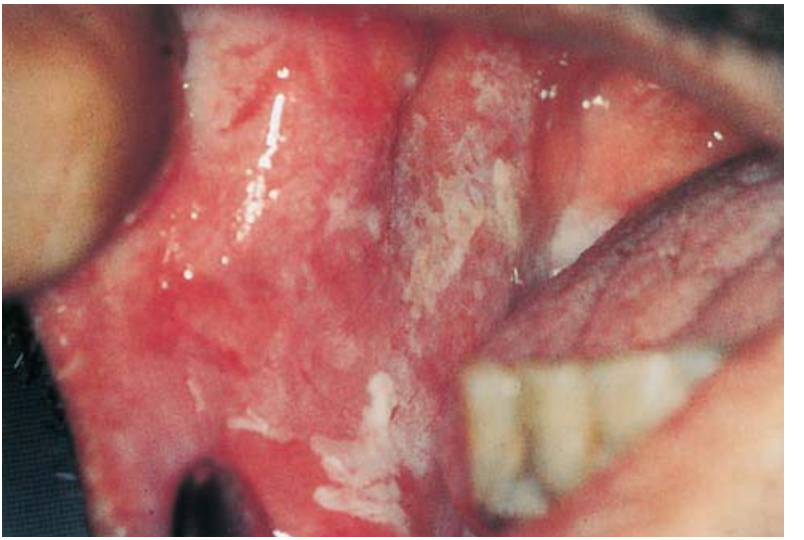


Fig. 18 Aspirin burn.

Candidiasis

Definition Candidiasis is the most common oral fungal infection. Over the last two decades, the disease has taken on major importance.

Etiology It is usually caused by *Candida albicans*, and less frequently by other fungal species (*C. glabrata*, *C. krusei*, *C. tropicalis*, *C. parapsilosis*). Predisposing factors are *local* (poor oral hygiene, xerostomia, mucosal damage, dentures, antibiotic mouthwashes) and *systemic* (broad-spectrum antibiotics, steroids, immunosuppressive drugs, radiation, HIV infection, hematological malignancies, neutropenia, iron-deficiency anemia, cellular immunodeficiency, endocrine disorders).

Clinical features Oral candidiasis is classified as *primary*, consisting of lesions exclusively on the oral and perioral area, and *secondary*, consisting of oral lesions of mucocutaneous disease. Primary candidiasis includes five clinical varieties: pseudomembranous, erythematous, nodular, papillary hyperplasia of the palate, and *Candida*-associated lesions (angular cheilitis, median rhomboid glossitis, denture stomatitis). The main forms of candidiasis that produce white lesions are the following.

Pseudomembranous candidiasis is the most common form of the disease, and is clinically characterized by creamy-white, slightly elevated, removable spots or plaques (Fig. **19**). The lesions may be localized or generalized, and appear more frequently on the buccal mucosa, soft palate, tongue, and lips. Xerostomia, a burning sensation, and an unpleasant taste are the most common symptoms.

Nodular candidiasis is a chronic form of the disease; it appears clinically as a white, firm, and raised plaque that usually does not detach (Fig. **20**).

Mucocutaneous candidiasis is a heterogeneous and rare group of clinical syndromes, characterized by chronic lesions of the skin, nails, and mucosae, and usually associated with immunological defects. Clinically, the oral lesions appear as white and usually multiple plaques, which cannot be removed (Fig. **21**).

Laboratory tests Cytology and tissue culture examination; biopsy only in chronic cases.

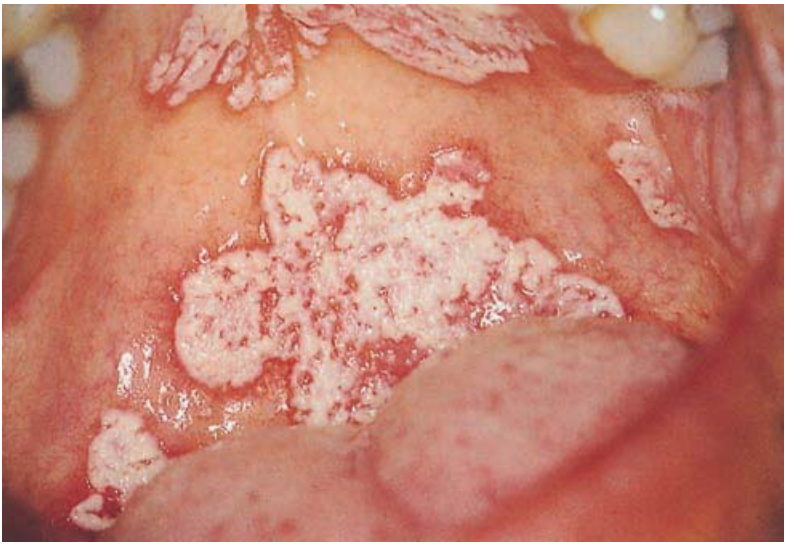


Fig. 19 Pseudomembranous candidiasis on the palate.

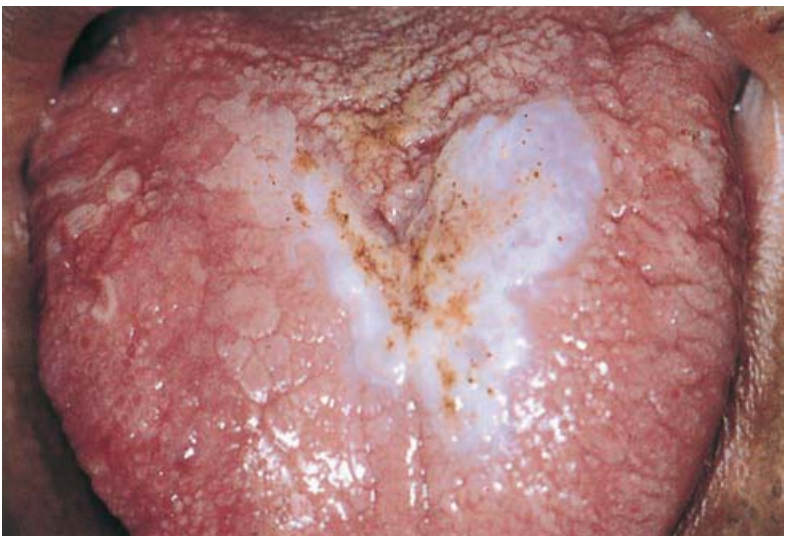


Fig. 20 Nodular candidiasis.

Differential diagnosis Leukoplakia, hairy leukoplakia, lichen planus, syphilitic mucous patches, white sponge nevus, chemical and traumatic lesions, cinnamon contact stomatitis, lupus erythematosus.

Treatment Topical antifungal agents (nystatin, azole derivatives, amphotericin B). Systemic azoles (ketoconazole, fluconazole, itraconazole).

Chronic Biting

Definition and etiology Mild chronic biting of the oral mucosa is relatively common in nervous individuals. These patients consciously bite the buccal mucosa, lips, and tongue, and detach the superficial epithelial layers.

Clinical features The lesions are characterized by a diffuse irregular white area of small furrows and desquamation of the epithelium (Fig. **22**). Rarely, erosions and petechiae may be seen. The diagnosis is made clinically.

Differential diagnosis Candidiasis, lichen planus, leukoplakia, hairy leukoplakia, white sponge nevus, leukoedema, cinnamon contact stomatitis.

Treatment Recommendation to stop the habit.

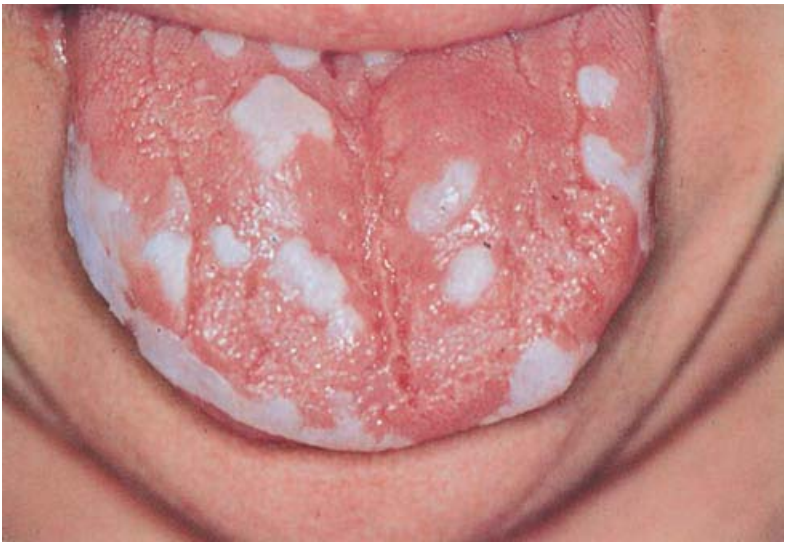


Fig. 21 Chronic mucocutaneous candidiasis: multiple lesions on the tongue.

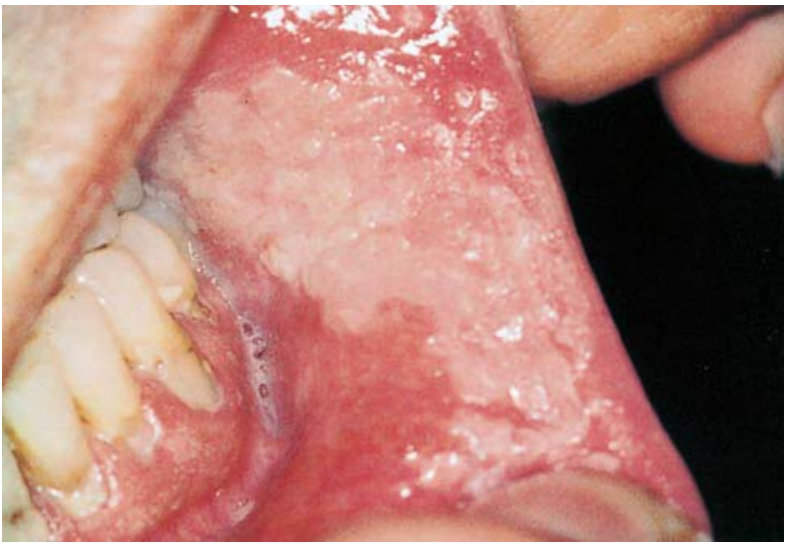


Fig. 22 Chronic biting of the buccal mucosa.

Geographic Tongue

Definition Geographic tongue, or erythema migrans, is a relatively common benign condition, primarily affecting the tongue and rarely other oral mucosa sites (*geographic stomatitis*) (Fig. **23**).

Etiology The exact etiology remains unknown. It may be genetic.

Clinical features Clinically, the condition is characterized by multiple, well-demarcated, erythematous, depapillated patches, typically surrounded by a slightly elevated whitish border, and usually restricted to the dorsum of the tongue (Figs. **24**, **25**). Characteristically, the lesions persist for a short time in one area, then disappear completely and reappear in another area. The condition is usually asymptomatic, and often coexists with fissured tongue. The diagnosis is made clinically.

Differential diagnosis Candidiasis, lichen planus, psoriasis, Reiter syndrome, syphilitic mucous patches.

Treatment Reassurance of the patient.

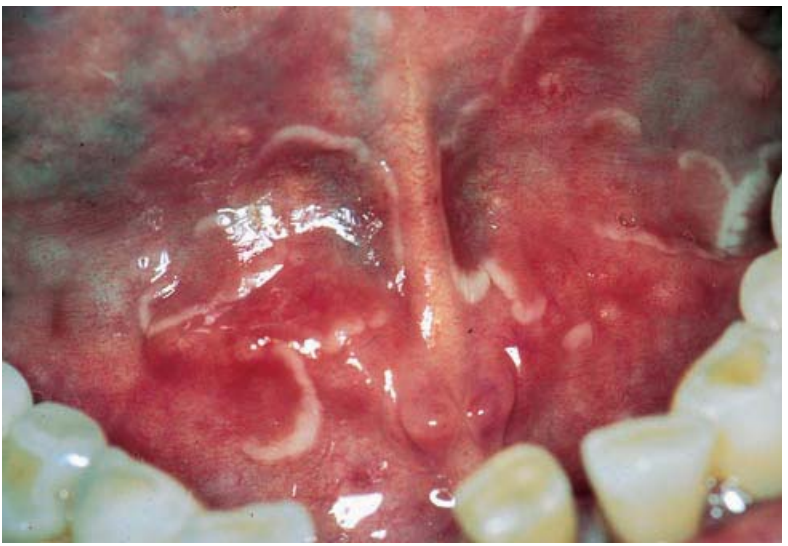


Fig. 23 Geographic stomatitis.

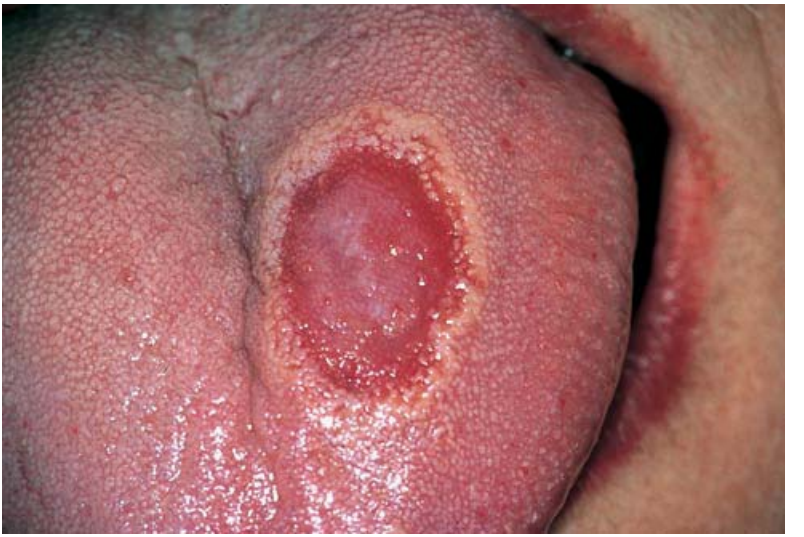


Fig. 24 Geographic tongue, localized lesion.

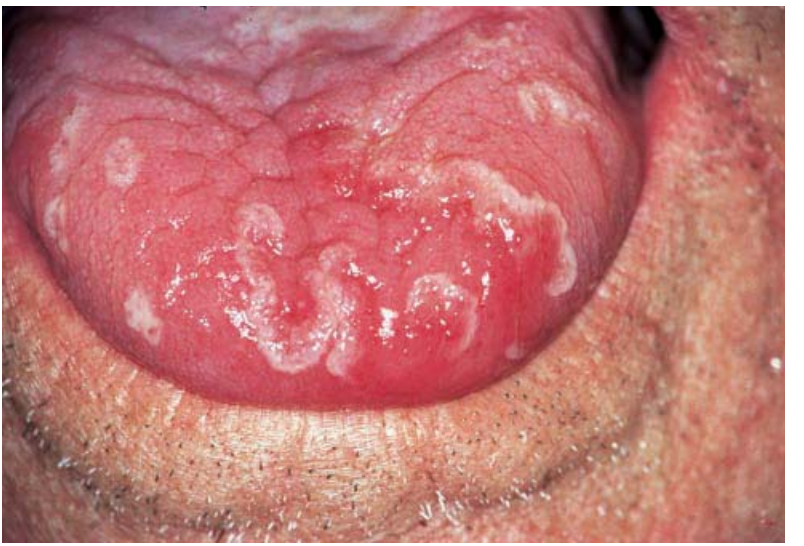


Fig. 25 Geographic tongue, with a prominent whitish border.

Hairy Tongue

Definition Hairy tongue is a relatively common disorder that is due to marked accumulation of keratin on the filiform papillae of the tongue, resulting in a hairlike pattern.

Etiology Unknown. Predisposing factors are poor oral hygiene, oxidizing mouthwashes, antibiotics, excessive smoking, radiation therapy, emotional stress, and bacterial and *Candida* species infections.

Clinical features Clinically, it is characterized by an asymptomatic elongation of the filiform papillae of the dorsum of the tongue, sometimes extending over several millimeters. The color may range from whitish (Figs. **26**, **27**, **28**) to brown or black. The diagnosis is made clinically.

Treatment Elimination of predisposing factors, brushing of the tongue, local use of keratolytic agents (trichloroacetic acid, podophyllin).

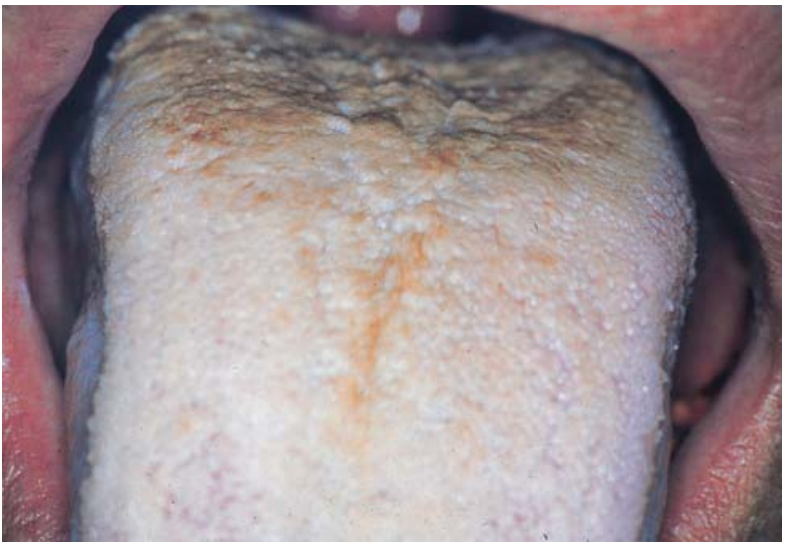


Fig. 26 Hairy tongue.

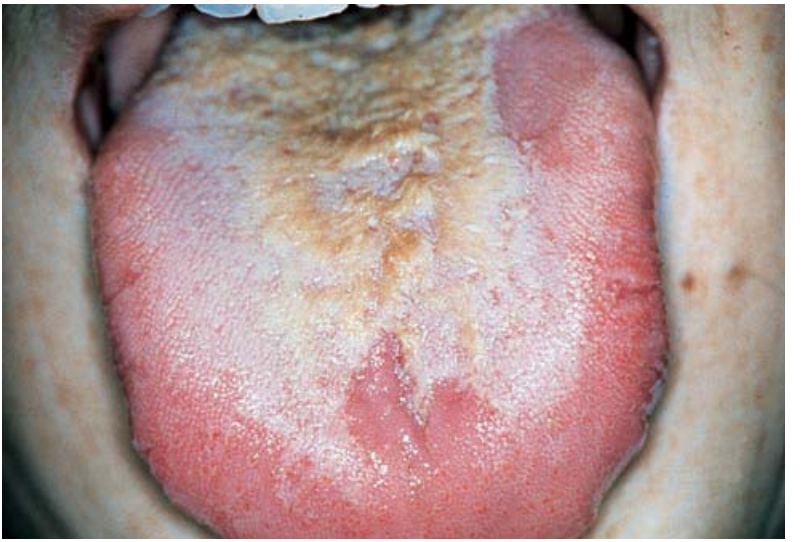


Fig. 27 Hairy tongue.

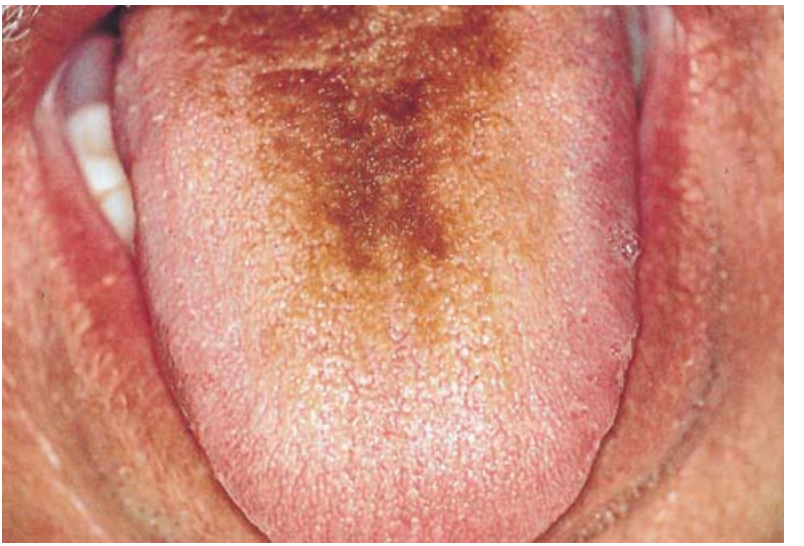


Fig. 28 Hairy tongue.

Furred Tongue

Definition Furred tongue is a relatively uncommon disorder, usually appearing during febrile illnesses.

Etiology The cause is not clear. Predisposing factors are febrile painful oral lesions, poor oral hygiene, dehydration, and soft diet.

Clinical features Clinically, it appears as a white or whitish-yellow thick coating on the dorsal surface of the tongue (Fig. **29**). The lesion is due to lengthening of the filiform papillae, by up to 3–4 mm, and accumulation of debris and bacteria. Characteristically, furred tongue appears and disappears within a short period. The diagnosis is made clinically.

Differential diagnosis Hairy tongue, hairy leukoplakia, candidiasis.

Treatment Therapy of the underlying illnesses and improvement of oral hygiene.

Materia Alba of the Gingiva

Definition and etiology Materia alba results from the accumulation of food debris, dead epithelial cells, and bacteria. It is common at the dentogingival margin. Rarely, materia alba may be seen along the vestibular surface of the attached gingiva in patients with poor oral hygiene.

Clinical features It presents as a soft, whitish plaque that is easily detached after slight pressure (Fig. **30**).

Differential diagnosis Candidiasis, chemical burn, leukoplakia.

Treatment Good oral hygiene.

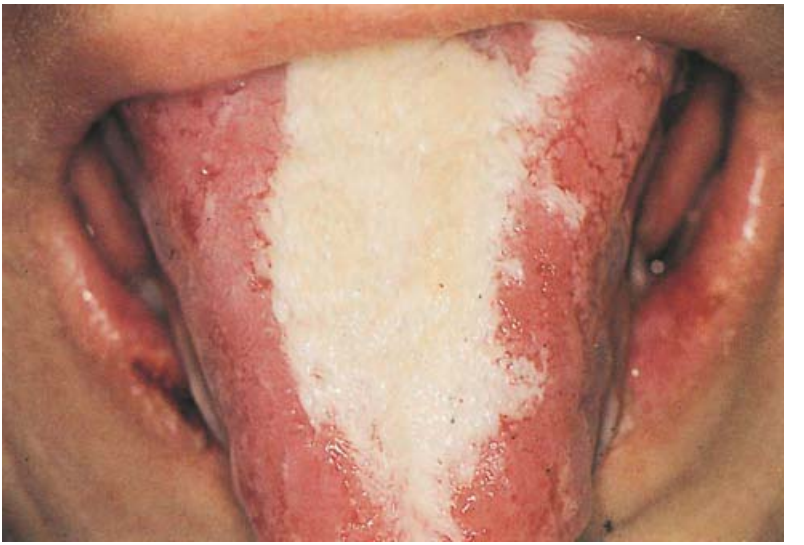


Fig. 29 Furred tongue.

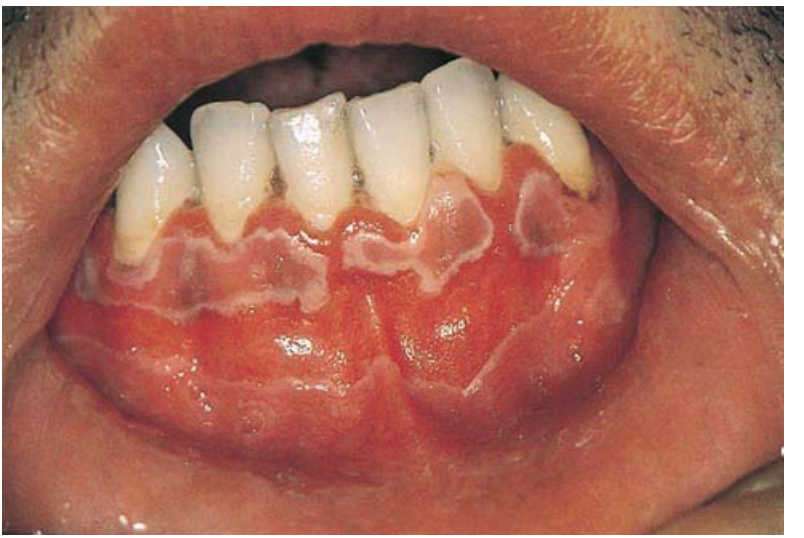


Fig. 30 White plaques on the attached gingiva and the alveolar mucosa, caused by materia alba accumulation.

Fordyce's Granules

Definition Fordyce's granules are ectopic sebaceous glands of the oral mucosa.

Etiology It is a normal anatomical variation.

Clinical features Clinically, the granules present as multiple, asymptomatic, slightly raised whitish-yellow spots (Fig. **31**). The vermilion border of the upper lip, the commissures, and the buccal mucosa are the sites of predilection. They occur in about 80% of adults of both sexes. The diagnosis is based on the clinical features alone.

Differential diagnosis Lichen planus, leukoplakia, candidiasis.

Treatment No treatment is required.

Leukoedema

Definition Leukoedema is a normal anatomical variation.

Etiology It is due to increased thickness of the epithelium and intracellular edema of the prickle-cell layer.

Clinical features Clinically, it is characterized by a grayish-white, opalescent pattern of the mucosa (Fig. **32**) and a slightly wrinkled surface, which characteristically disappears when the mucosa is everted and stretched. It usually occurs bilaterally on the buccal mucosa, and rarely on the tongue and lips.

Differential diagnosis Leukoplakia, hairy leukoplakia, lichen planus.

Treatment No treatment is required.

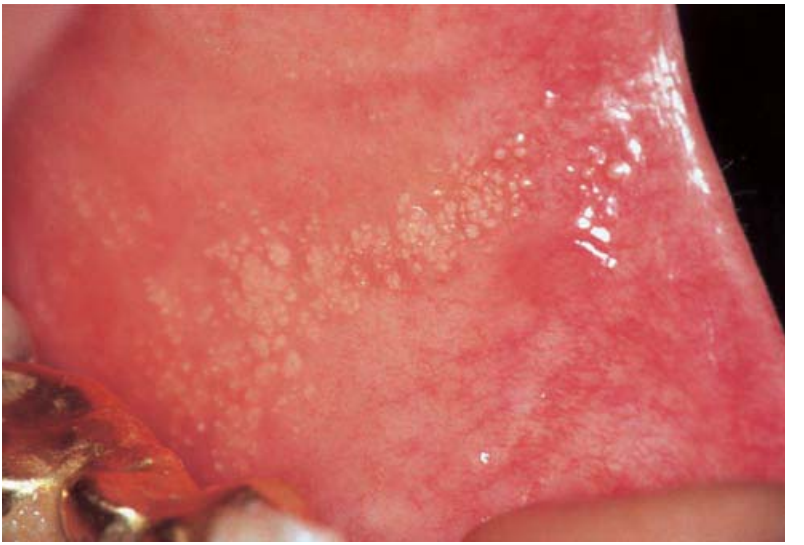


Fig. 31 Fordyce's granules on the buccal mucosa.

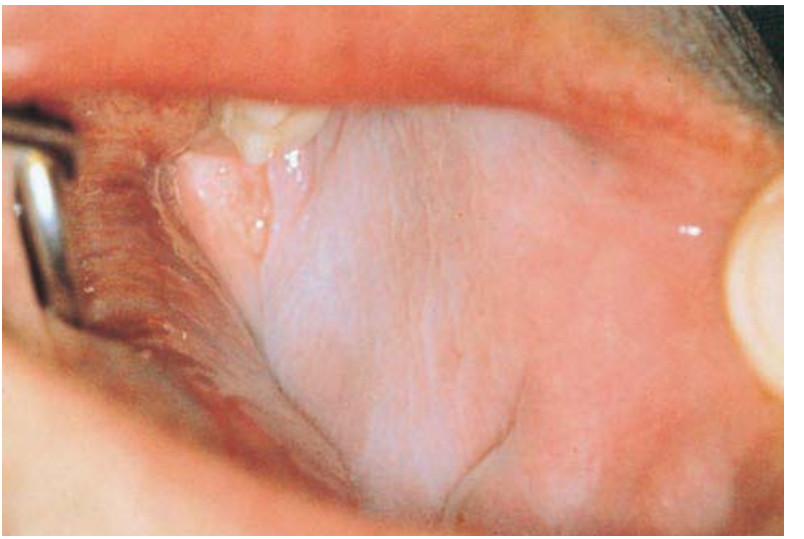


Fig. 32 Leukoedema of the buccal mucosa.

White Sponge Nevus

Definition White sponge nevus, or Cannon disease, is a relatively rare genodermatosis.

Etiology Genetic. It is inherited as an autosomal dominant trait.

Clinical features It presents as symmetrical white lesions with multiple furrows and a spongy texture (Fig. **33**). The lesions may appear at birth, or more commonly in early childhood. The buccal mucosa and the ventral surface of the tongue are the sites of predilection, although lesions may develop anywhere in the mouth, or even in the vaginal and rectal mucosa.

Laboratory tests Histopathological examination.

Differential diagnosis Leukoedema, leukoplakia, lichen planus, chronic biting, dyskeratosis congenita, pachyonychia congenita.

Treatment No treatment is required.

Dyskeratosis Congenita

Definition Dyskeratosis congenita, or Zinsser–Engman–Cole syndrome, is an uncommon disorder.

Etiology Genetic. It is probably inherited as a recessive autosomal and X-linked trait.

Clinical features It is characterized by hyperpigmentation, atrophic skin areas, telangiectasia, nail dystrophy, hyperhidrosis, skin and mucosal bullae, blepharitis and ectropion, anemia, and oral manifestations. The oral lesions consist of recurrent blisters, epithelial atrophy, and leukoplakia (Fig. **34**). Squamous-cell carcinoma may occur.

Differential diagnosis Leukoplakia, lichen planus, epidermolysis bullosa, pachyonychia congenita.

Treatment Supportive.

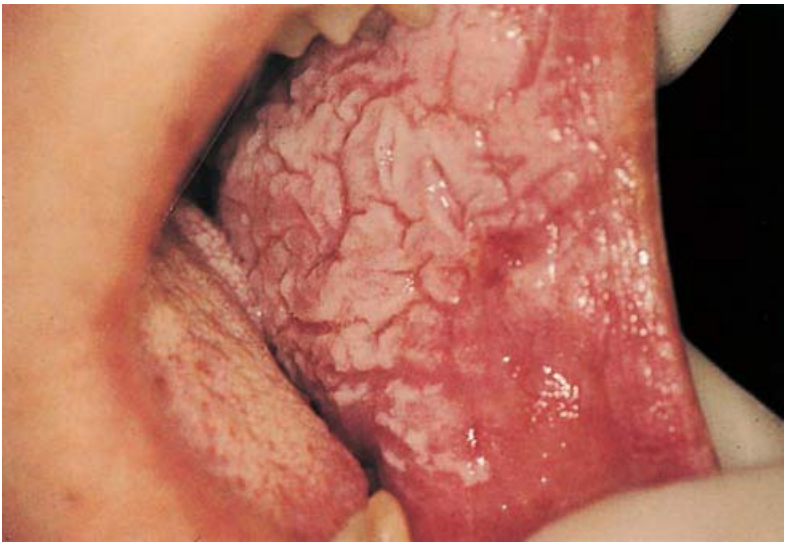


Fig. 33 White sponge nevus of the buccal mucosa.

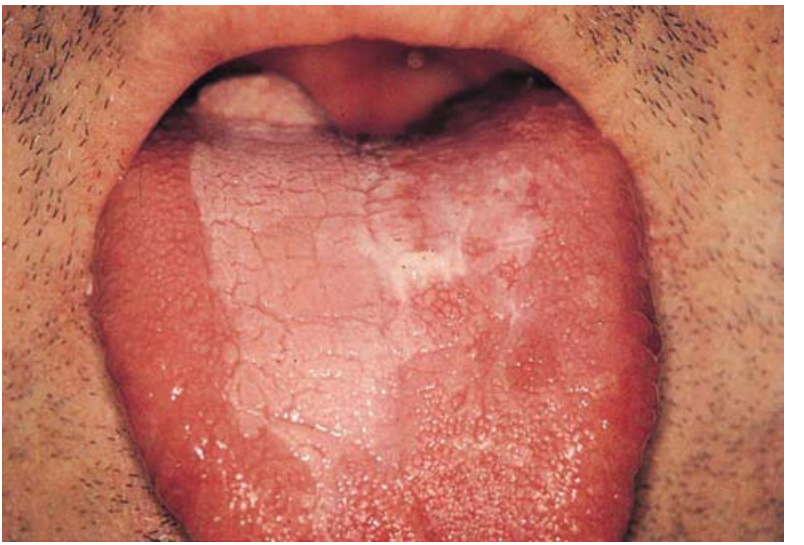


Fig. 34 Dyskeratosis congenita, leukoplakia, and verrucous carcinoma of the dorsal surface of the tongue.

Pachyonychia Congenita

Definition Pachyonychia congenita, or Jadassohn–Lewandowski syndrome, is an uncommon genodermatosis.

Etiology Genetic. It is inherited as an autosomal dominant trait.

Clinical features It is characterized by symmetrical nail thickening, palmoplantar hyperkeratosis, hyperhidrosis, blister formation, follicular keratosis, and oral lesions. The oral lesions appear at birth or shortly afterward, and present as thick and white or grayish-white plaques, usually on the buccal mucosa, the tongue, and the gingiva (Fig. **35**). The diagnosis is based on the history and the clinical features.

Differential diagnosis Dyskeratosis congenita, leukoplakia, lichen planus, white sponge nevus, and focal palmoplantar and oral mucosa hyperkeratosis syndrome.

Treatment Supportive.

Focal Palmoplantar and Oral Mucosa Hyperkeratosis Syndrome

Definition This is a rare mucocutaneous disorder.

Etiology Genetic. It is inherited as an autosomal dominant trait.

Clinical features The main clinical manifestations are focal hyperkeratosis on the weight-bearing and pressure-related regions of the palms, soles, and oral mucosa (Fig. **36**). Rarely, thickening of the nails and hyperhidrosis may be seen. The oral lesions present as white hyperkeratotic plaques (leukoplakia), mainly on the attached gingiva, the lateral border of the tongue, and the palate (Fig. **37**). The lesions usually develop in early childhood.

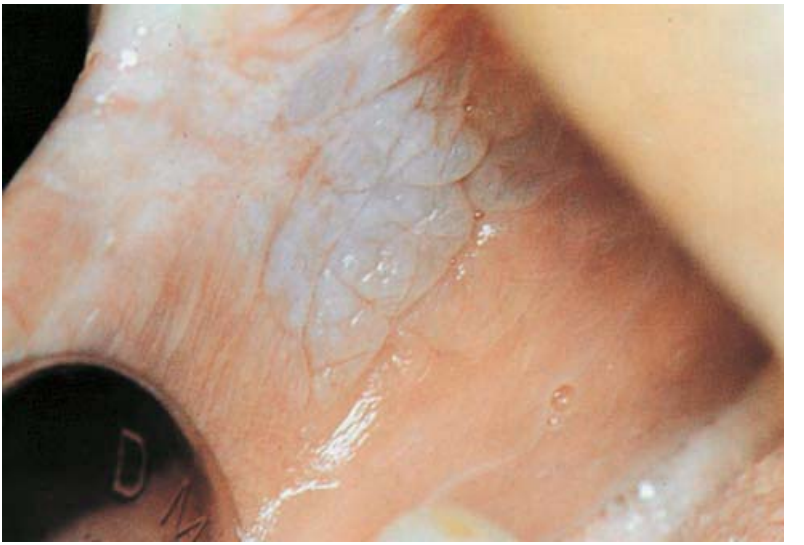


Fig. 35 Pachyonychia congenita: grayish-white lesion on the buccal mucosa.

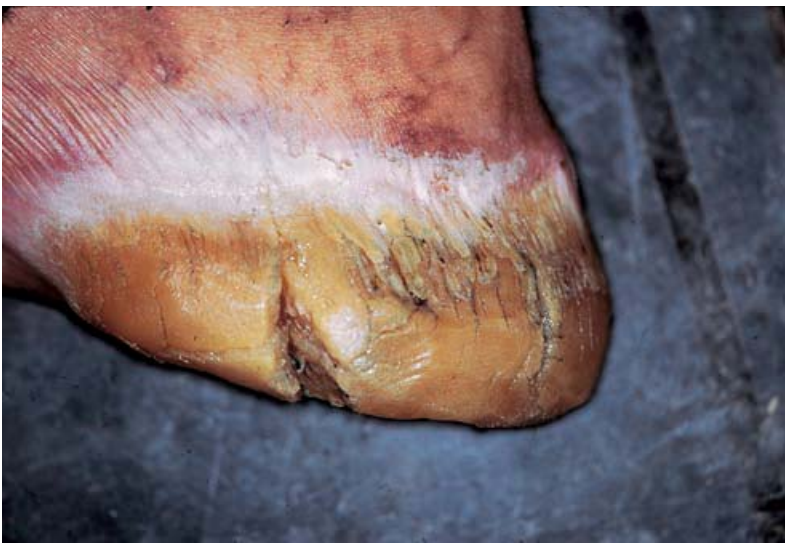


Fig. 36 Focal palmoplantar hyperkeratosis

Differential diagnosis Pachyonychia congenita, dyskeratosis congenita, leukoplakia.

Treatment Supportive. Retinoids may be helpful.

Papilloma

Papilloma (see p. 200) appears as an exophytic, painless, usually pedunculated growth. Characteristically, the tumor has a white or normal color, with numerous fingerlike projections that form a cauliflower pattern (Fig. **38**). Papilloma is usually solitary, with a size of 0.5–1 cm.

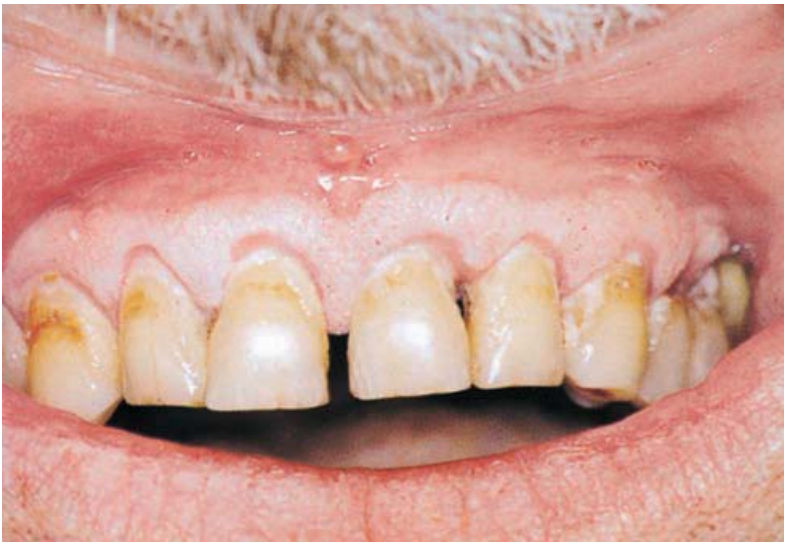


Fig. 37 Focal palmoplantar and oral mucosa hyperkeratosis syndrome: hyperkeratosis of the attached gingiva.

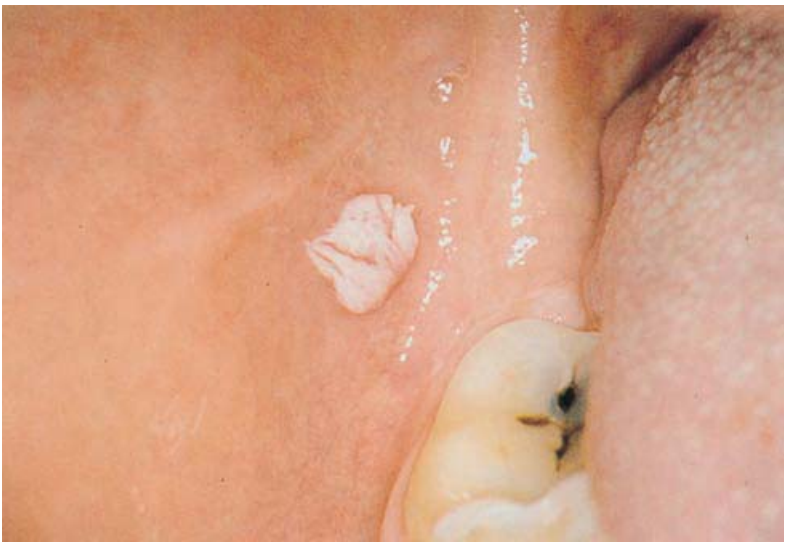


Fig. 38 Papilloma of the buccal mucosa.

Verrucous Carcinoma

Definition Verrucous carcinoma is a low-grade variant of squamous-cell carcinoma.

Etiology Human papillomavirus is presumably involved in the pathogenesis.

Clinical features Clinically, it presents as an exophytic white mass with a verrucous or pebbly surface (Fig. **39**). The size varies from 1 cm in the early stages to very extensive lesions. The buccal mucosa, palate, and alveolar mucosa are the most common sites of involvement. Verrucous carcinoma mainly develops in smokers over 60 years of age.

Laboratory tests Histopathological examination.

Differential diagnosis Verrucous leukoplakia, papilloma, verruciform xanthoma, white sponge nevus, squamous-cell carcinoma.

Treatment Surgical excision.

Squamous-Cell Carcinoma

Squamous-cell carcinoma has a wide spectrum of clinical features (see p. 172). In about 5–8% of cases, it appears in the early stages as a white asymptomatic plaque identical to leukoplakia (Fig. **40**). Biopsy and histopathological examination are important for the diagnosis in these cases.

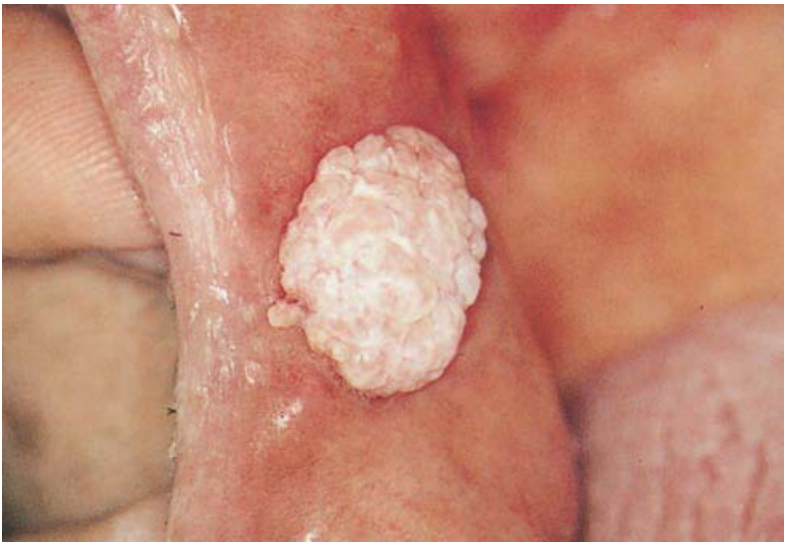


Fig. 39 Early verrucous carcinoma of the buccal mucosa.

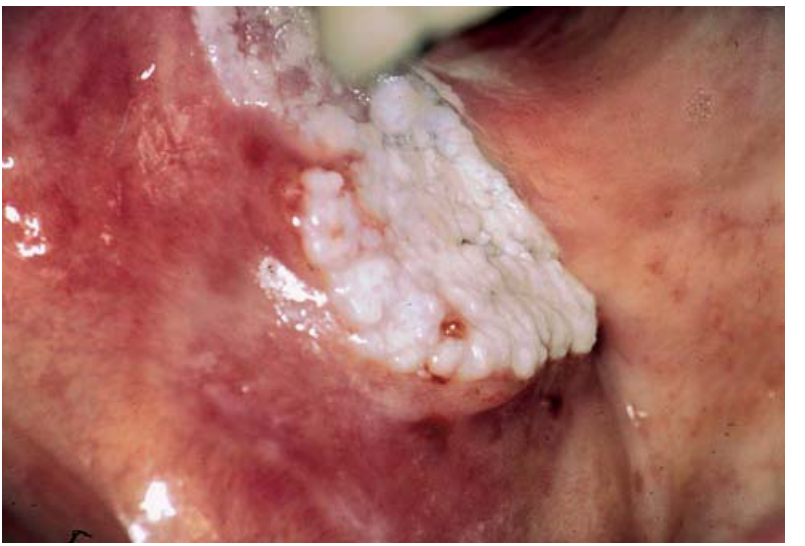


Fig. 40 Early squamous-cell carcinoma, presenting as a white plaque.

Skin and Mucosal Grafts

Definition Skin and mucosal grafts are often utilized in the oral cavity to cover mucosal defects after extensive surgery for benign and malignant tumors, or as free gingival graft.

Clinical features Clinically, both forms of grafts (skin and mucosal) usually present as a whitish, or gray-white plaque (Figs. **41**, **42**). The size of the plaque depends on the size of the graft. Occasionally, the color of the skin graft is black, due to melanin overproduction. If the graft contain hair follicles, hairs may develop in the oral cavity. The tongue, buccal mucosa, palate, gingiva and alveolar mucosa are the most common sites where skin and mucosal grafts are placed. Skin graft into the oral cavity may be associated with unpleasant feelings. The diagnosis is based on the history and the clinical features.

Differential diagnosis Leukoplakia, traumatic scar, epidermolysis bullosa.

Treatment No treatment is required.

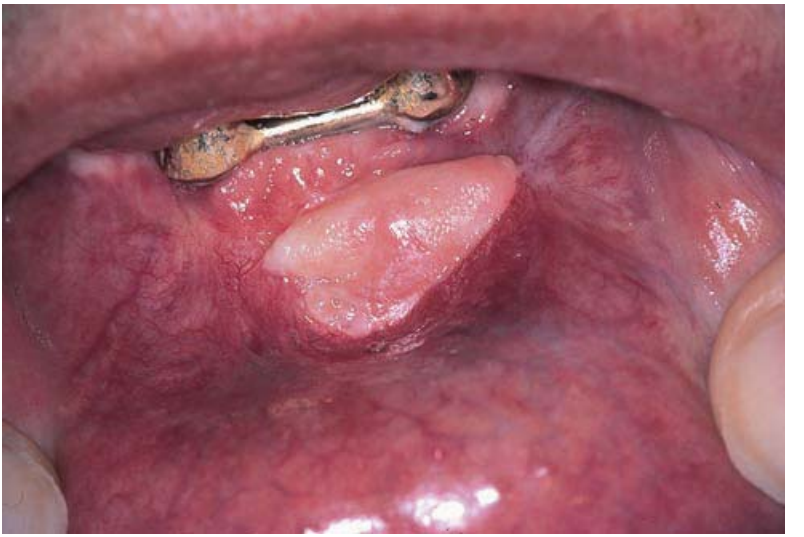


Fig. 41 Mucosal graft.

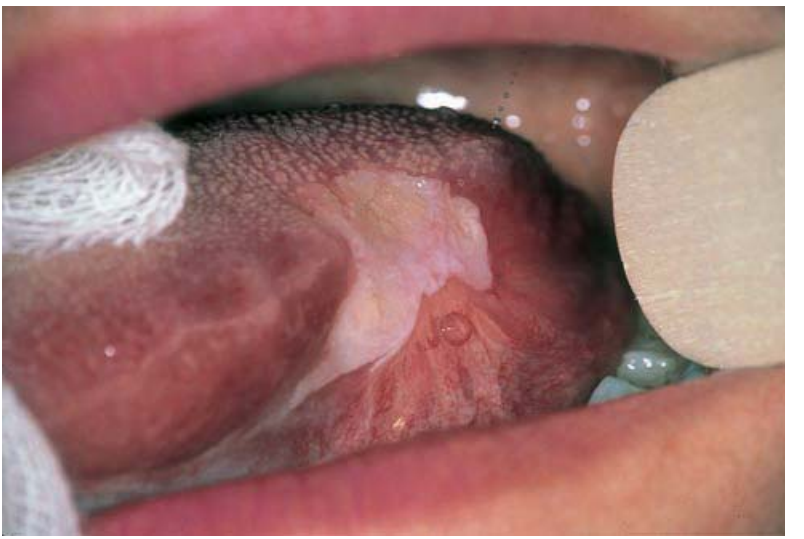


Fig. 42 Skin graft presenting as a white plaque on the lateral border of the tongue.

Epithelial Peeling

Definition Epithelial peeling is a relatively common superficial desquamation (epitheliolysis) of the oral mucosa.

Etiology It is caused by the direct irritating effect of toothpastes that contain sodium lauryl sulfate or pyrophosphates. The same phenomenon may be associated with chlorhexidine mouthwash. Sometimes the lesions are idiopathic.

Clinical features Clinically, epithelial peeling presents as superficial painless white plaques or dots that can be easily lifted from the oral mucosa (Figs. **43**, **44**). The buccal mucosa, lip mucosa, and mucobuccal and mucolabial folds are more frequently affected. The lesions usually disappear when the individual stops using these toothpastes or mouthwashes. The diagnosis is based entirely on the history and the clinical features.

Differential diagnosis Chemical burn, chronic biting, candidiasis, leukoplakia.

Treatment Discontinuation of responsible toothpastes or mouthwashes.

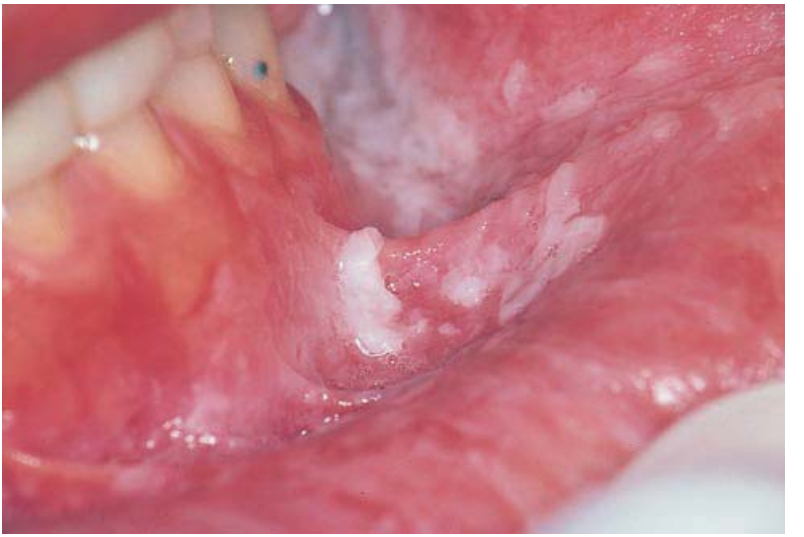


Fig. 43 Mucosal peeling.

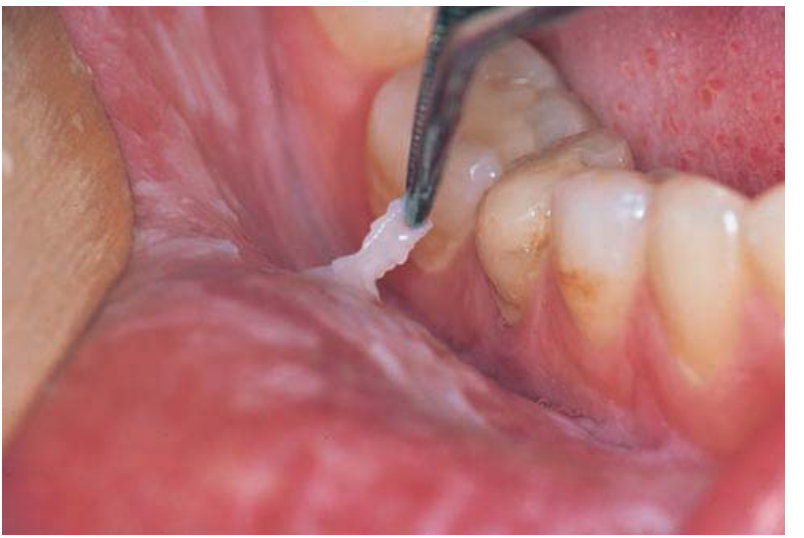
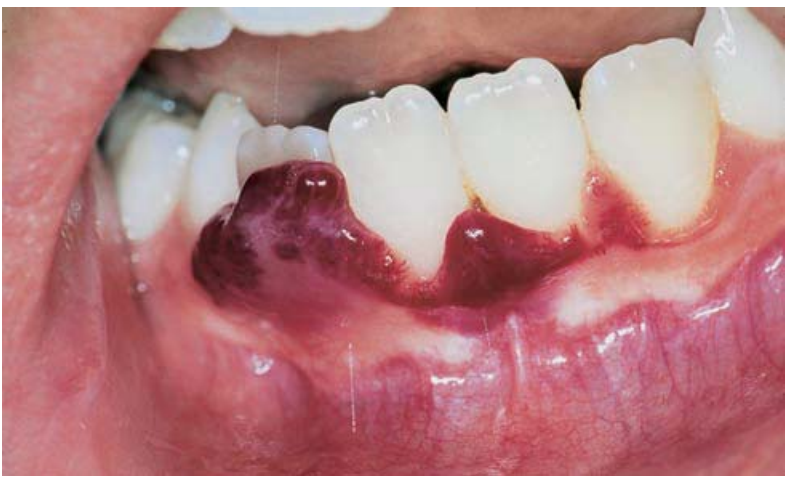


Fig. 44 Mucosal peeling.

2 Red Lesions

Red lesions are a large, heterogeneous group of disorders of the oral mucosa. Traumatic lesions, infections, developmental anomalies, allergic reactions, immunologically mediated diseases, premalignant lesions, malignant neoplasms, and systemic diseases are included in this group. The red color of the lesions may be due to thin epithelium, inflammation, dilatation of blood vessels or increased numbers of blood vessels, and extravasation of blood into the oral soft tissues.

- Traumatic erythema
- Thermal burn
- Radiation mucositis
- Fellatio
- Geographic tongue
- Median rhomboid glossitis
- Denture stomatitis
- Erythematous candidiasis
- Squamous-cell carcinoma
- Erythroplakia
- Plasma-cell gingivitis
- Granulomatous gingivitis
- Desquamative gingivitis
- Linear gingival erythema
- Contact allergic stomatitis
- Gonococcal stomatitis
- Hemangioma
- Lupus erythematosus
- CREST syndrome
- Hereditary hemorrhagic telangiectasia
- Anemia
- Thrombocytopenic purpura
- Infectious mononucleosis
- Reiter disease
- Peripheral ameloblastoma
- Sturge–Weber angiomatosis



Traumatic Erythema

Definition and etiology Traumatic erythema occurs when a traumatic effect results in hemorrhage within the oral tissues.

Clinical features Traumatic erythema can present either as an ecchymosis or as a hematoma. Clinically, it appears as an irregular, usually flat, area with a bright or deep red color (Fig. **45**). The lips, tongue, and buccal mucosa are the most common areas affected. The diagnosis is based on the history and the clinical features.

Differential diagnosis Hematomas due to anticoagulants, thrombocytopenia, thrombasthenia.

Treatment No treatment is required.

Thermal Burn

Definition and etiology Thermal burns to the oral mucosa are fairly common, usually due to contact with very hot foods, liquids, or hot metal objects.

Clinical features Clinically, the condition appears as a red, painful erythema that may undergo desquamation, leaving erosions (Fig. **46**). The lesions heal spontaneously in about a week. The diagnosis is made exclusively on clinical grounds.

Differential diagnosis Chemical burn, traumatic lesions, herpes simplex, aphthous ulcers, drug reactions.

Treatment No treatment is required.

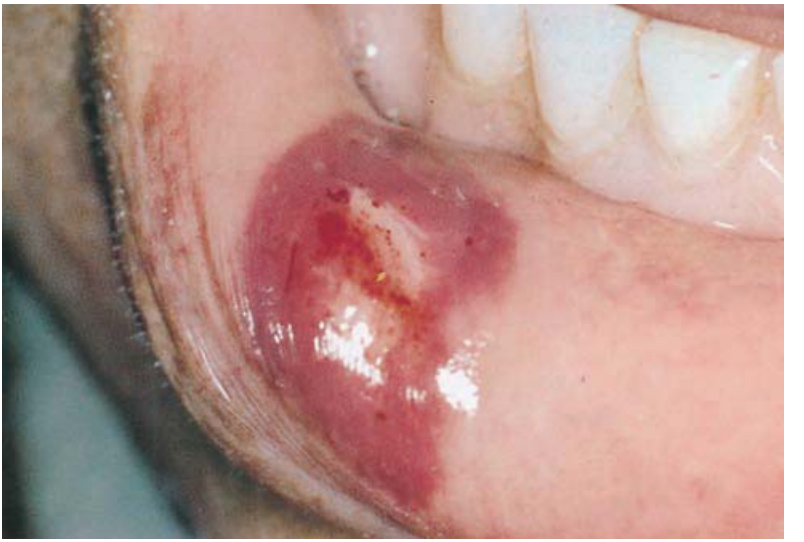


Fig. 45 Traumatic hematoma on the lower lip.

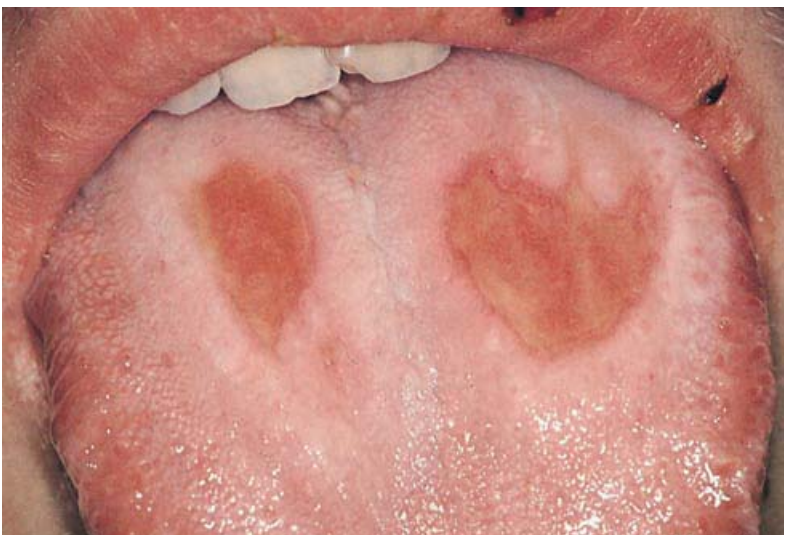


Fig. 46 Erosions on the dorsum of the tongue, caused by very hot food.

Radiation Mucositis

Definition and etiology Oral radiation mucositis is a side effect of radiation treatment of head and neck tumors.

Clinical features The oral lesions are classified as early and late. Early reactions may begin at the end of the first week of radiotherapy, and consist of erythema and edema of the oral mucosa (Fig. **47**). Soon after, erosions or ulcers may develop, covered by a whitish-yellow exudate. Xerostomia, loss of taste, and burning and pain during mastication, swallowing, and speech are common. The diagnosis is made clinically.

Differential diagnosis Mycositis due to chemotherapy, graft-versus-host disease, erythema multiforme, herpetic stomatitis, lichen planus.

Treatment Supportive. Cessation of the radiation treatment, B-complex vitamins, and sometimes low doses of steroids are indicated.

Lesions secondary to Fellatio

Definition Fellatio is a practice of oral sex.

Etiology Orogenital sex and the negative pressure or repeated "irritation" applied during fellatio.

Clinical features The lesions present as petechiae, erythema, or ecchymoses usually at the junction of the soft and hard palate (Fig. **48**). They disappear spontaneously within a week, and the diagnosis is made on the basis of the history and the clinical features.

Differential diagnosis Thermal burn, trauma, erythematous candidiasis, infectious mononucleosis, thrombocytopenic purpura, leukemia.

Treatment No treatment is required.

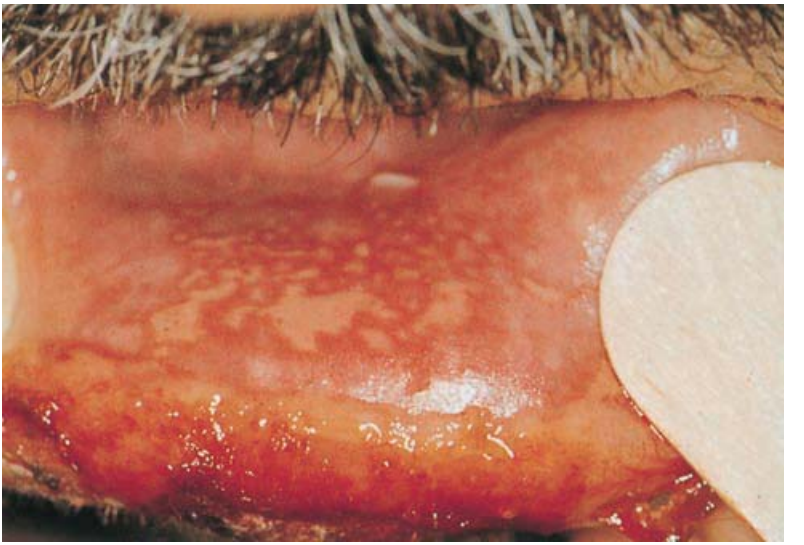


Fig. 47 Erythema and erosions on the lower lip, caused by ionizing radiation.

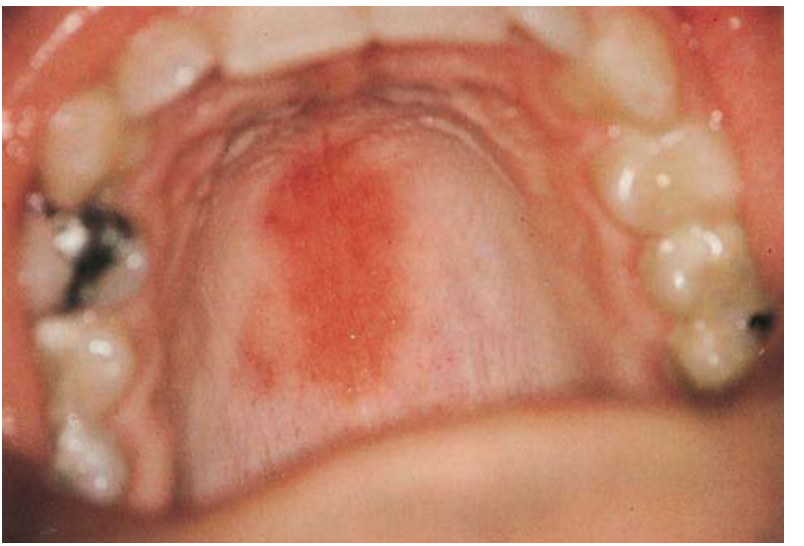


Fig. 48 Erythema on the palate, caused after fellatio.

Geographic Tongue

Geographic tongue or erythema migrans (see also p. 22) presents as multiple, well-demarcated patches of erythema surrounded by a thin, raised, whitish border (Fig. **49**). Characteristically, the lesions persist for a short time in one area, disappear within a few days, and then develop in another area. The dorsal surface of the tongue is the site of predilection, but infrequently the lesions may appear at other mucosal sites. The diagnosis is made on the basis of clinical criteria.

Differential diagnosis Psoriasis, Reiter syndrome, plasma-cell stomatitis, mucous patches of secondary syphilis, candidiasis.

Treatment No treatment is required.

Median Rhomboid Glossitis

Definition Median rhomboid glossitis is a rare condition that occurs exclusively on the dorsum of the tongue.

Etiology Presumably developmental. *Candida albicans* may also be involved.

Clinical features It presents as a well-demarcated erythematous rhomboid area along the midline of the dorsum of the tongue, immediately anterior to the circumvallate papillae (Fig. **50**). The surface of the lesion may be smooth or lobulated.

Differential diagnosis Candidiasis, lymphangioma, geographic tongue, syphilis, hemangioma, non-Hodgkin lymphoma.

Treatment No treatment is required.

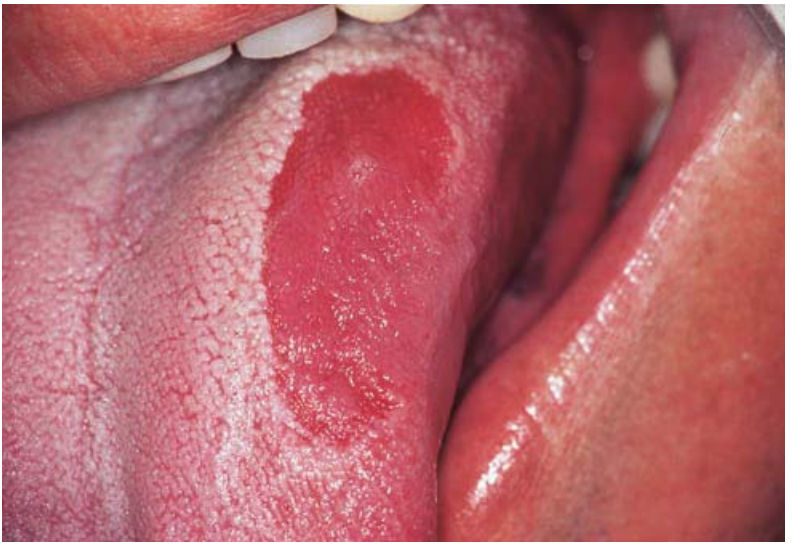


Fig. 49 Geographic tongue: well-demarcated red patch on the tongue.

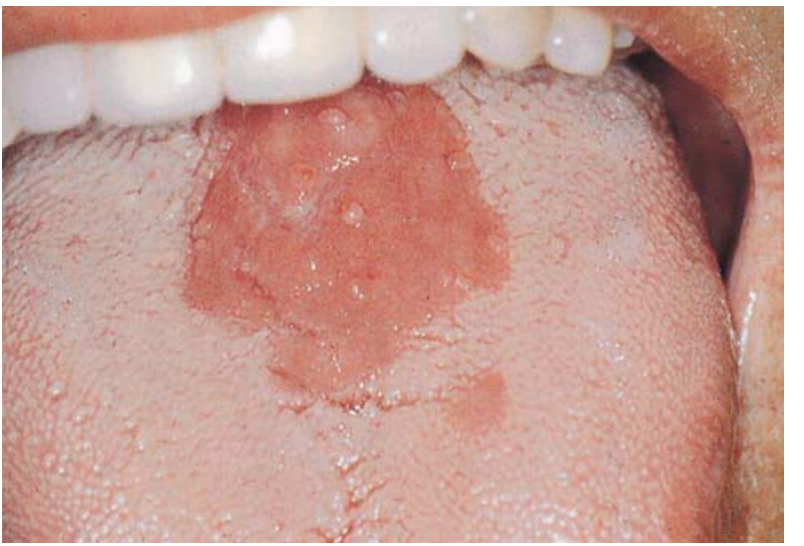


Fig. 50 Median rhomboid glossitis.

Denture Stomatitis

Definition Denture stomatitis, or denture sore mouth, is a frequent condition in patients who wear dentures continuously for extended times.

Etiology Mechanical irritation from dentures, *Candida albicans*, or a tissue response to microorganisms living beneath the dentures.

Clinical features The condition is characterized by diffuse erythema, edema, and sometimes petechiae and white spots that represent accumulations of candidal hyphae, almost always located in the denture-bearing area of the maxilla (Fig. **51**). The condition is usually asymptomatic. The diagnosis is based on clinical criteria.

Differential diagnosis Allergic contact stomatitis due to acrylic.

Treatment Improvement of denture fit, oral hygiene, and topical antimycotics.

Erythematous Candidiasis

Erythematous candidiasis is a relatively common form of candidiasis, with a high incidence in HIV-infected patients and rarely in patients receiving broad-spectrum antibiotics or steroids (see also p. 18). It may be acute or chronic. Clinically, it is characterized by erythematous patches or large areas, usually located on the dorsum of the tongue and palate (Fig. **52**). A burning sensation is a common symptom.

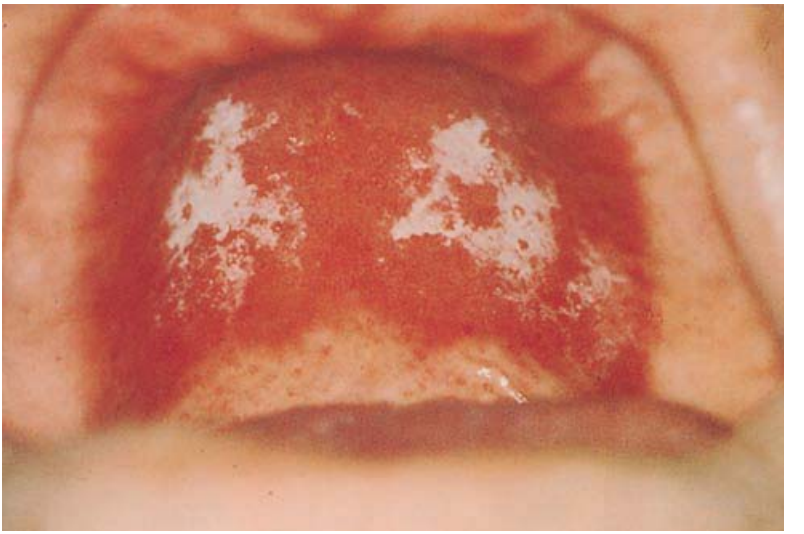


Fig. 51 Denture stomatitis.

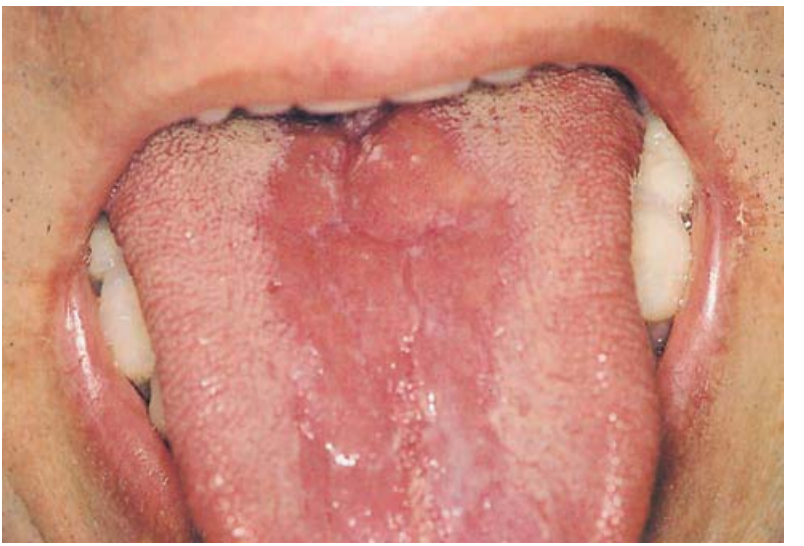


Fig. 52 HIV infection: erythematous candidiasis on the dorsum of the tongue.

Squamous-Cell Carcinoma

The early stage of squamous-cell carcinoma (see also p. 172) may present as an asymptomatic, atypical red patch (Figs. **53**, **54**, **55**). The clinical features are identical to erythroplakia, erythematous candidiasis, or contact reactions to dental materials. In these cases, a biopsy should be taken to allow a conclusive diagnosis.

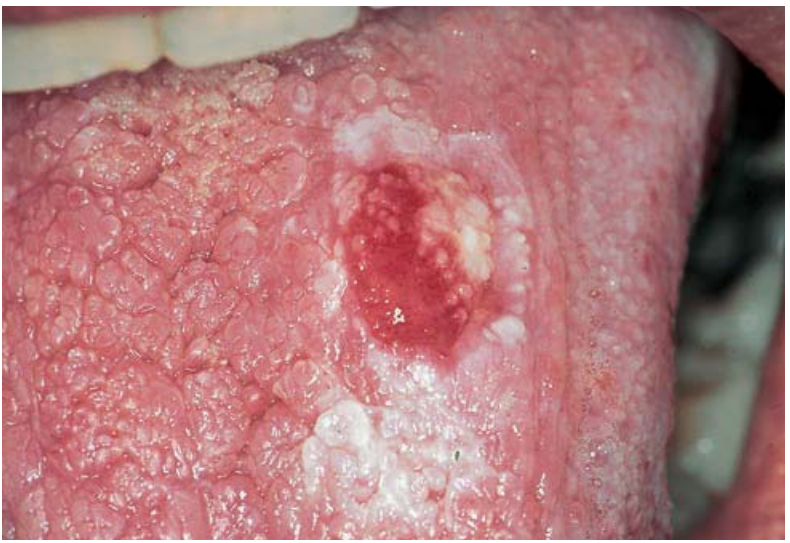


Fig. 53 Early squamous cell carcinoma presenting as a red patch on the tongue.

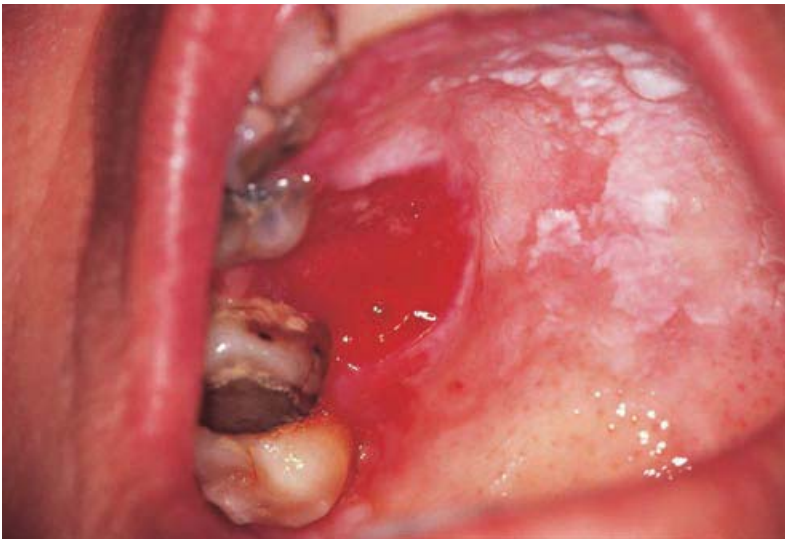


Fig. 54 Squamous-cell carcinoma presenting as a red patch on the palate.

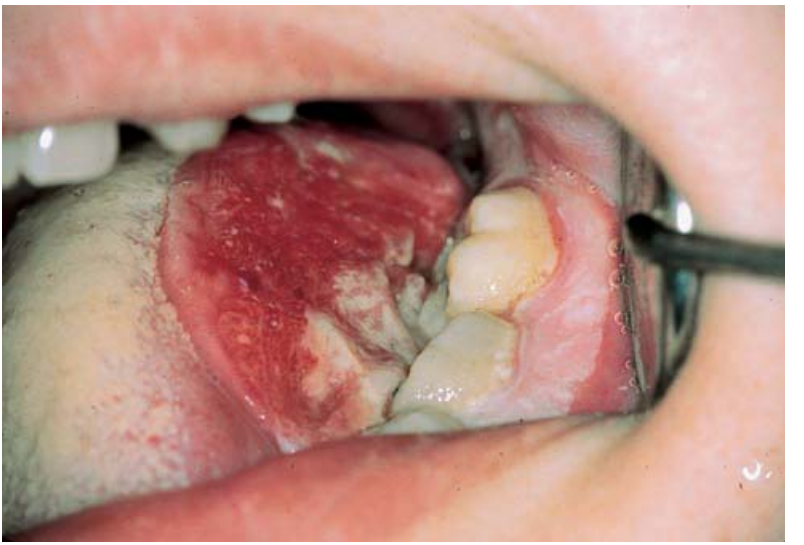


Fig. 55 Squamous cell carcinoma presenting as a red mass on the lateral border of the tongue.

Erythroplakia

Definition Erythroplakia, or Queyrat erythroplasia, is a premalignant lesion frequently occurring on the glans penis, and rarely on the oral mucosa. It is defined as a red, nonspecific patch or plaque that cannot be classified clinically and pathologically under any other disease.

Etiology Unknown.

Clinical features It appears as a usually asymptomatic, fiery red, well-demarcated plaque, with a smooth and velvety surface (Figs. **56**, **57**, **58**). The red lesions may be associated with white spots or small plaques. The floor of the mouth, retromolar area, soft palate, and tongue are the most common sites of involvement. Erythroplakia occurs more frequently between the ages of 50 and 70 years. Over 91% of erythroplakias histologically demonstrate severe dysplasia, carcinoma in situ, or early invasive squamous-cell carcinoma at the time of diagnosis.

Laboratory tests Histopathological examination.

Differential diagnosis Erythematous candidiasis, lichen planus, discoid lupus erythematous, early squamous-cell carcinoma, local irritation.

Treatment Surgical excision.

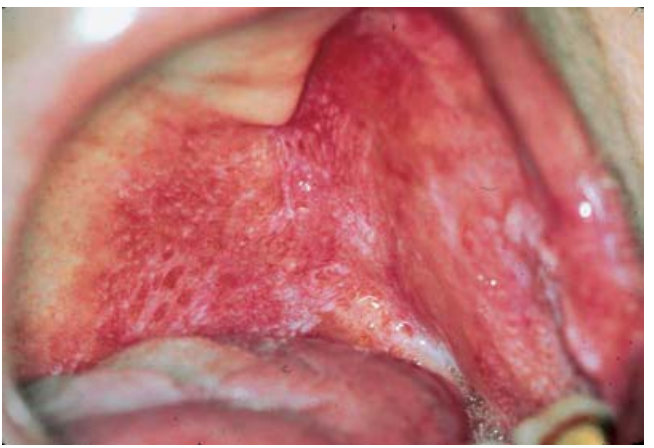


Fig. 56 Erythroplakia of the buccal mucosa.

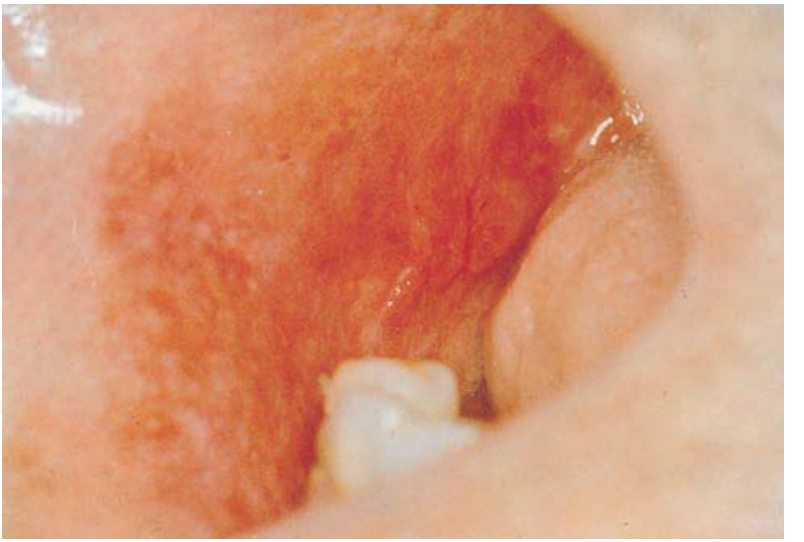


Fig. 57 Erythroplakia of the buccal mucosa.

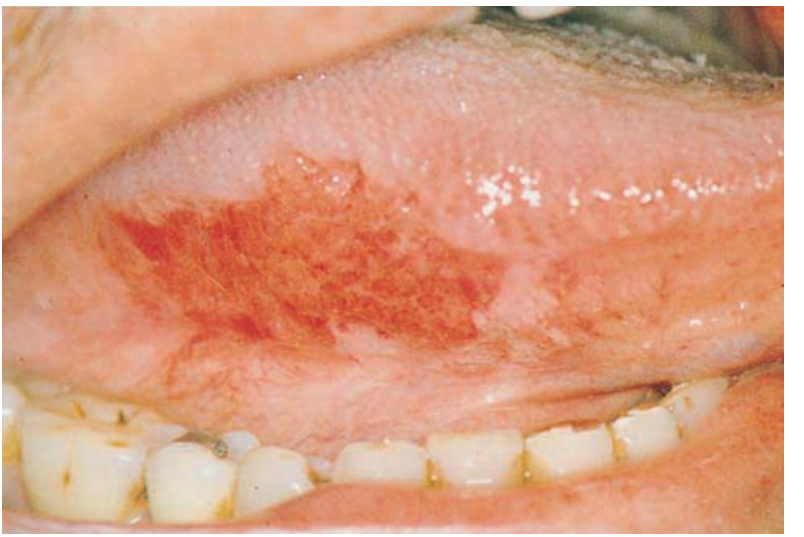


Fig. 58 Erythroplakia of the lateral margin of the tongue.

Plasma-Cell Gingivitis

Definition Plasma-cell gingivitis is a rare and unique gingival disorder, characterized histopathologically by a dense chronic inflammatory infiltration of the lamina propria, mainly of plasma cells.

Etiology Unknown. Reactions to local allergens, chronic infections, and plasma-cell dyscrasias have been considered as possible causes.

Clinical features Clinically, both free and attached gingiva are bright red and edematous, with a loss of normal stippling (Fig. **59**). The gingivitis may be localized or widespread, and is frequently accompanied by a burning sensation. Rarely, similar lesions may be seen on the tongue and lips.

Laboratory tests Histopathological and histochemical examination, immunoelectrophoresis.

Differential diagnosis Desquamative gingivitis, psoriasis, candidiasis, soft-tissue plasmacytoma, erythroplakia, granulomatous gingivitis.

Treatment Remove the allergens if possible. Topical or systemic steroids.

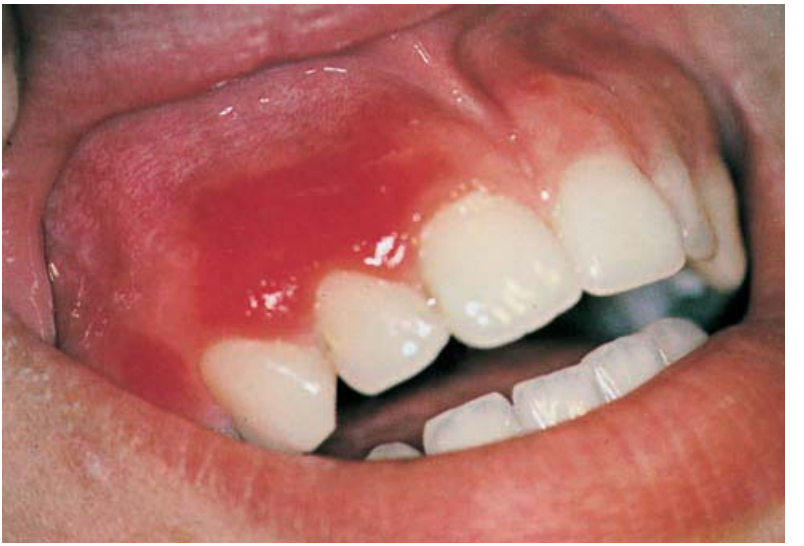


Fig. 59 Plasma-cell gingivitis.

Granulomatous Gingivitis

Definition Granulomatous gingivitis is a relatively rare, chronic inflammatory disorder with a specific histopathological pattern.

Etiology Foreign body reaction, local bacterial or fungal infection, reactions to food additives and systemic granulomatous disorders (Crohn disease, sarcoidosis, Melkersson–Rosenthal syndrome, Wegener granulomatosis) may be the cause.

Clinical features Granulomatous gingivitis presents as a diffuse erythematous and slightly edematous area of the free and attached gingiva, and of the interdental papillae (Figs. **60**, **61**). The lesions may be localized in one area or multiple areas. Sensitivity and mild pain are common symptoms. The lesions resist conventional local treatment. In cases of systemic granulomatous disease, other areas of the mouth may be involved. The clinical diagnosis should be confirmed by a biopsy and histopathological examination.

Differential diagnosis Plaque-related chronic gingivitis, desquamative gingivitis, linear gingiva erythema, trauma, plasma-cell gingivitis, drug reactions, candidiasis, erythroplakia, non-Hodgkin lymphoma, leukemia, amyloidosis, orofacial granulomatosis.

Treatment Local or systemic corticosteroids is the treatment of choice. In case of reaction to foreign material, conservative surgical excision is suggested.

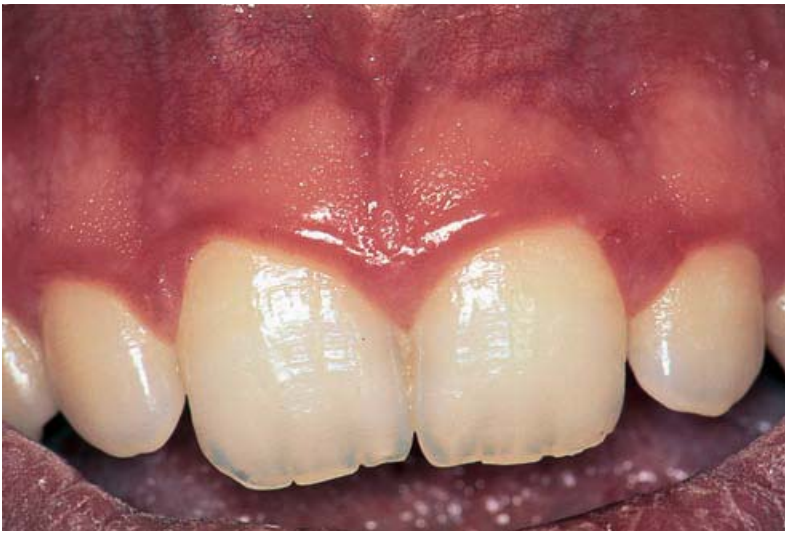


Fig. 60 Orofacial granulomatosis, gingival swelling.

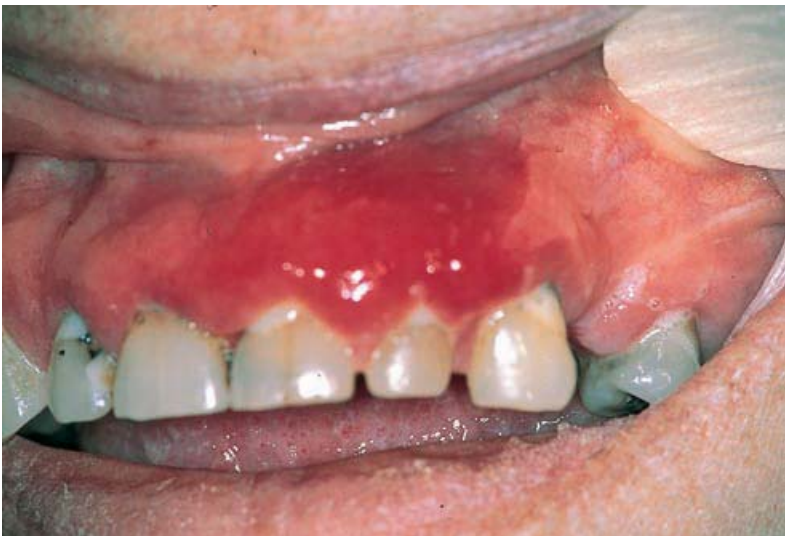


Fig. 61 Granulomatous gingivitis localized

Desquamative Gingivitis

Definition Desquamative gingivitis is a clinical descriptive term used for nonspecific gingival manifestation of several chronic mucocutaneous diseases.

Etiology With rare exceptions, an autoimmune mechanism is responsible. Cicatricial pemphigoid and lichen planus are the most common diseases related to desquamative gingivitis. Less frequently, bullous pemphigoid, pemphigus, linear IgA disease, epidermolysis bullosa acquisita, chronic ulcerative stomatitis, discoid lupus erythematosus, and psoriasis may be the underlying disease entity.

Clinical features It presents as erythema and edema of the marginal and attached gingiva (Figs. **62**, **63**). The facial surface is more frequently affected than the lingual gingiva. Spontaneous desquamation of the epithelia, blister formation, and areas of superficial erosions are common. Characteristically, after mild pressure on the affected gingiva, desquamation of the epithelium or hemorrhagic blister formation usually occur. The lesions may be either localized or generalized. Desquamative gingivitis may be the only oral manifestation or may be associated with additional oral lesions of the underlying chronic bullous dermatosis. Women over 40 years of age are more frequently affected. The clinical diagnosis should be confirmed by histopathological and immunological examinations.

Differential diagnosis Necrotizing ulcerative gingivitis, plasma cell gingivitis, plaque related gingivitis, drug reactions, granulomatous gingivitis, oral psoriasis.

Treatment Good oral hygiene, avoidance of any mechanical pressure on the gingiva. Systemic treatment (corticosteroids, immunosuppressants, dapsone) depends on the identification of the underlying disease.

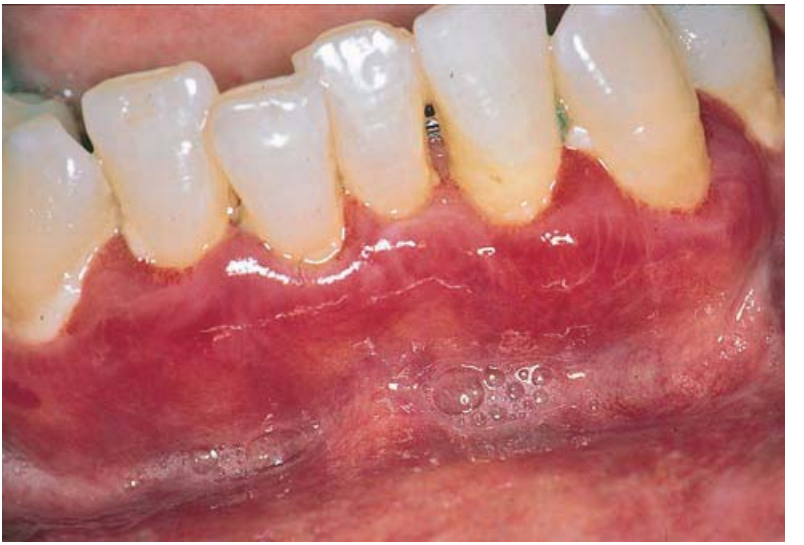


Fig. 62 Desquamative gingivitis as a manifestation of cicatricial pemphigoid

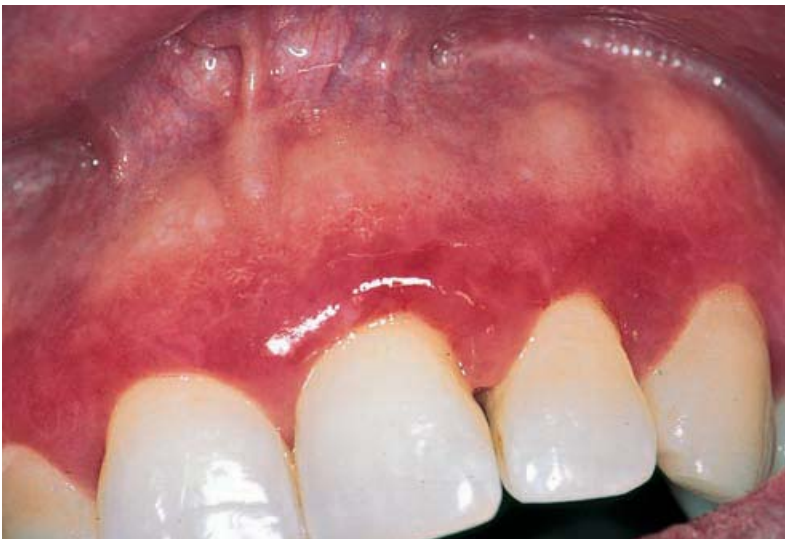


Fig. 63 Desquamative gingivitis as a manifestation of lichen planus

Linear Gingival Erythema

Definition Linear gingival erythema is a relatively uncommon gingival disorder usually following HIV infection.

Etiology The exact etiology remains unclear. However, a close association of the disorder with *Candida* infection is common.

Clinical features Characteristically, linear gingival erythema appears as a fiery red band (2–4 mm wide) along the margin of the gingiva and a punctate or diffuse erythema of the attached gingiva (Fig. **64**). Gingival bleeding is rare. The lesion does not respond to plaque control measures or root planing and scaling. The diagnosis is mainly based on the history, the clinical features, and laboratory tests for HIV infection.

Differential diagnosis Plaque-related gingivitis, herpetic gingivitis desquamative gingivitis, granulomatous gingivitis, plasma-cell gingivitis, leukemia.

Treatment High level of oral hygiene and plaque control. Systemic antifungals such as itraconazole or fluconazole are usually useful.

Contact Allergic Stomatitis

Definition Contact allergic stomatitis is a rare acute or chronic allergic reaction.

Etiology Denture base materials, restorative materials, mouthwashes, dentifrices, chewing gums, foods, and other substances may be responsible.

Clinical features Clinically, in the acute form, the affected mucosa presents with diffuse erythema and edema, and occasionally small vesicles and erosions (Fig. **65**). A burning sensation is a common symptom. In the chronic form, hyperkeratotic white lesions may be seen in addition to erythema.

Laboratory tests Mucosal and skin patch tests.

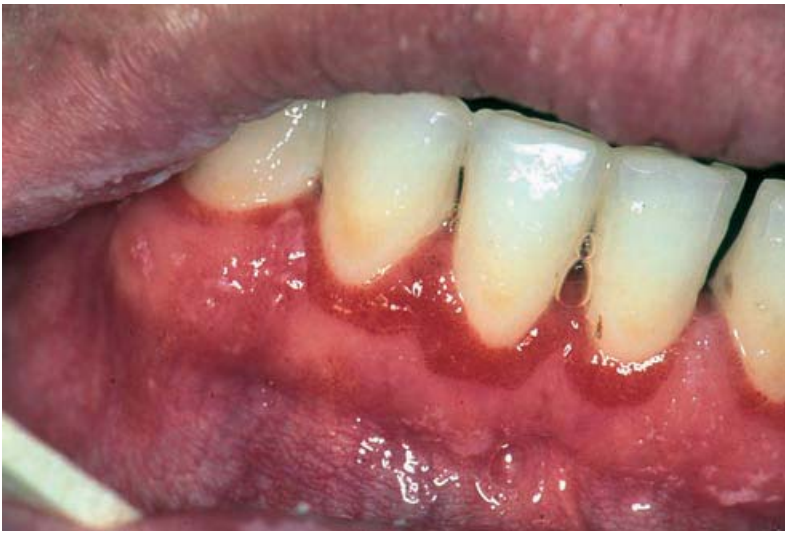


Fig. 64 Linear gingival erythema, fiery red band along the margin of the gingiva.

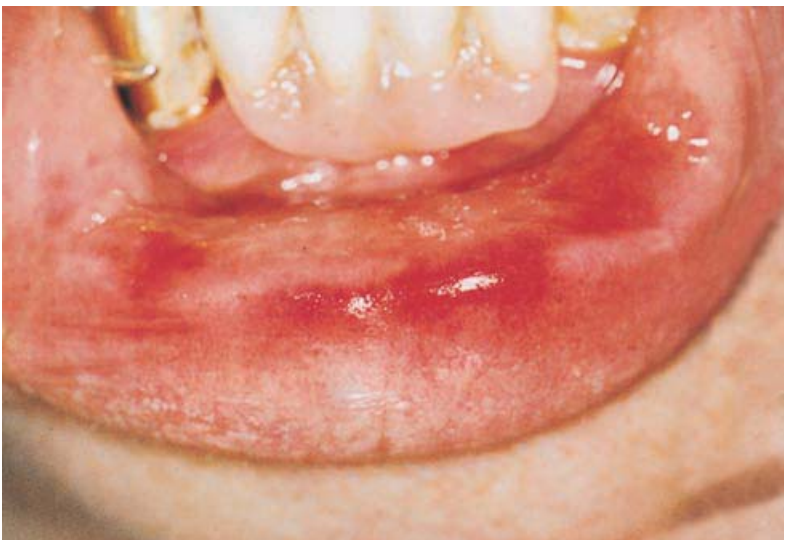


Fig. 65 Allergic stomatitis caused by acrylic resin.

Differential diagnosis Denture stomatitis, erythematous candidiasis, erythroplakia, leukoplakia, drug reactions.

Treatment Removal of suspected allergens, topical or systemic steroids, antihistamines.

Gonococcal Stomatitis

Definition Gonococcal stomatitis is a rare manifestation of gonococcal infection. It is a sexually transmitted disease that primarily involves the urinary tract and anorectal area.

Etiology *Neisseria gonorhoeae*. Gonococcal stomatitis is usually the result of orogenital sex (fellatio, cunnilingus). Accordingly, gonococcal stomatitis is more common in women and homosexual men.

Clinical features The oral manifestations of gonococcal infection appear as atypical fiery erythema and edema with or without superficial ulceration covered with a grayish or yellowish-exudate (Fig. **66**). A burning, mild pain and sore throat are common symptoms. The pharyngeal area, tonsils, uvula, and soft palate are the most common sites of involvement. Rarely, lesions may develop on the tongue, buccal mucosa, and gingiva. Submandibular and cervical lymph node enlargement may occur. The diagnosis is based on the history and the clinical features, and should be confirmed by identification of the microorganism.

Differential diagnosis Streptococcal stomatitis, herpetic stomatitis, erythematous candidiasis, mechanical trauma, thermal burn.

Treatment Frequently the oral lesions are self-limited. Systemic penicillin or tetracycline are the drugs of choice.

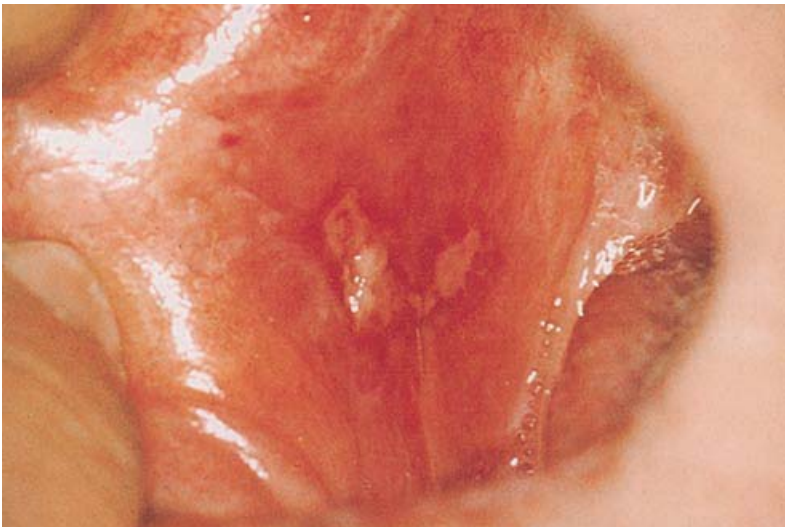


Fig. 66 Gonococcal stomatitis, erythema, and erosion on the buccal mucosa.

Hemangioma

Definition Hemangioma is a relatively common benign proliferation of blood vessels that primarily develops during childhood.

Etiology Developmental.

Clinical features Two main forms of hemangioma are recognized: *capillary* and *cavernous.* The capillary form presents as a flat red area consisting of numerous small capillaries (Fig. **67**). Cavernous hemangioma appears as an elevated lesion of a deep red color, and consists of large dilated sinuses filled with blood (Fig. **68**). A characteristic sign of hemangioma is that the red color disappears on pressure, and returns when the pressure is released.

Laboratory tests Histopathological examination.

Differential diagnosis Pyogenic granuloma, lymphangioma, traumatic hematoma, Kaposi sarcoma, malignant melanoma.

Treatment Surgical excision, or cryotherapy or laser therapy. Some capillary hemangiomas may regress spontaneously.

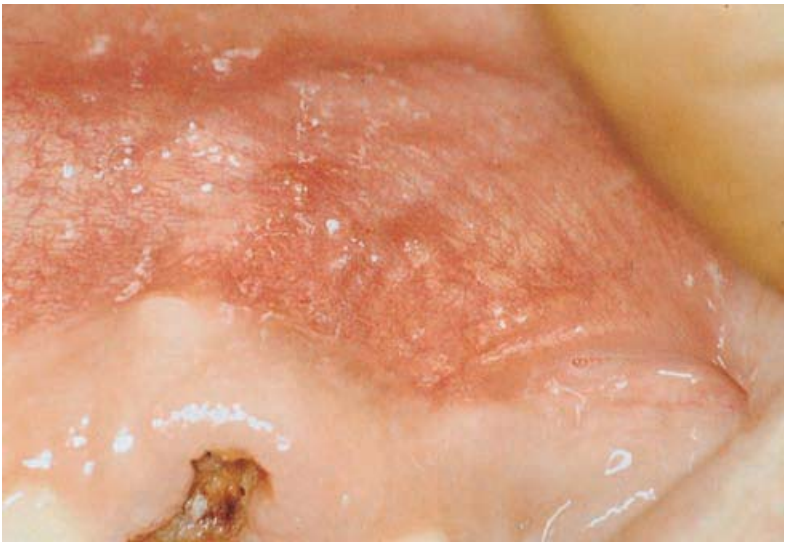


Fig. 67 Capillary hemangioma.

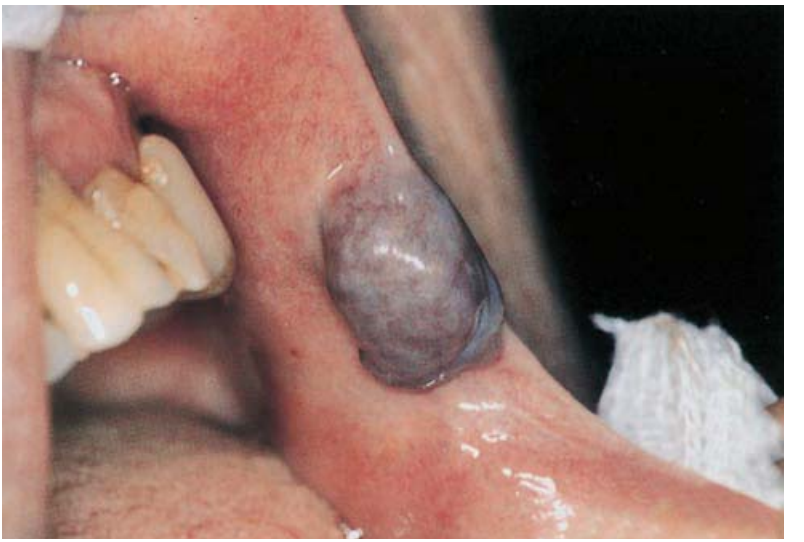


Fig. 68 Cavernous hemangioma.

Lupus Erythematosus

Definition Lupus erythematosus is a chronic immunologically mediated disease.

Etiology Autoimmune.

Clinical features Two main forms of the disease are recognized: *discoid* (DLE) and *systemic* (SLE). Oral lesions develop in 15–25% of cases in DLE and in 30–45% of cases in SLE, usually in association with skin lesions. The oral lesions are characterized by a well-defined central atrophic red area surrounded by a sharp elevated border of irradiating whitish striae (Fig. **69**). Telangiectasia, petechiae, edema, erosions, ulcerations, and white hyperkeratotic plaques may be seen.

Laboratory tests Histopathological examination, direct immunofluorescence.

Differential diagnosis Lichen planus, geographic glossitis, speckled leukoplakia, erythroplakia, cicatricial pemphigoid, syphilis.

Treatment Steroids, antimalarials.

CREST Syndrome

CREST syndrome is a clinical variant of scleroderma characterized by a combination of **C**alcinosis cutis, **R**eynaud phenomenon, **E**sophageal dysfunction, **S**clerodactyly, and **T**elangiectasia. Telangiectasia may occur on the lips and oral mucosa, and presents as red dots or plaques (Fig. **70**).

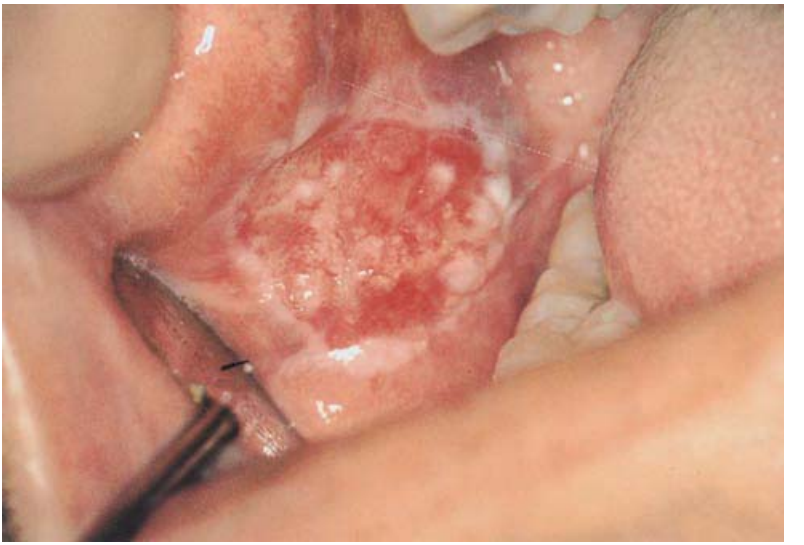


Fig. 69 Discoid lupus erythematosus: typical lesion on the buccal mucosa.

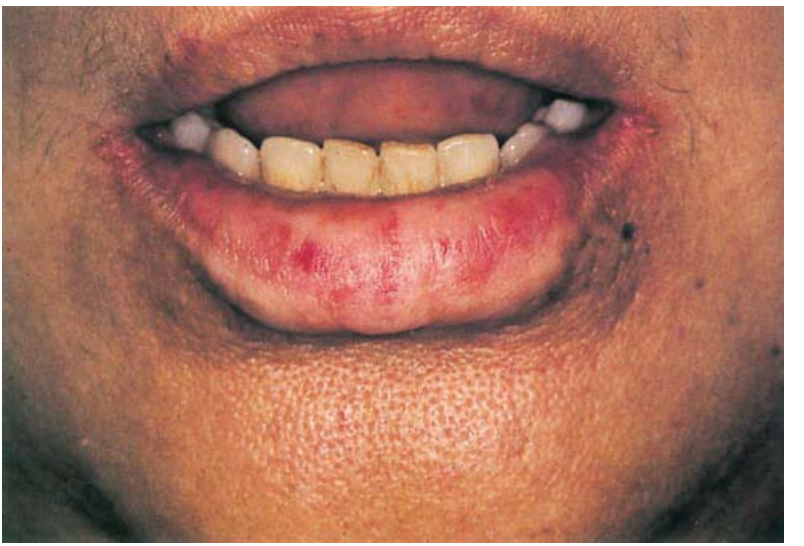


Fig. 70 CREST syndrome: lip telangiectasia.

Hereditary Hemorrhagic Telangiectasia

Definition Hereditary hemorrhagic telangiectasia, or Osler–Rendu–Weber disease, is a rare mucocutaneous disorder characterized by dysplasia of the capillaries and small vessels.

Etiology Inherited as an autosomal dominant trait.

Clinical features The oral mucosa is frequently involved and the lesions present as multiple bright red papules, 1–2 mm in size, which disappear on pressure from a glass slide (Fig. **71**). Nodules and spiderlike lesions may also be seen. Hemorrhage is common after minimal mechanical damage. The lips, tongue, buccal mucosa, and palate are most frequently involved. Epistaxis and gastrointestinal bleeding are common.

Laboratory tests Histopathological examination.

Differential diagnosis CREST syndrome, varicosities, Maffucci syndrome, multiple hemangiomas.

Treatment Supportive.

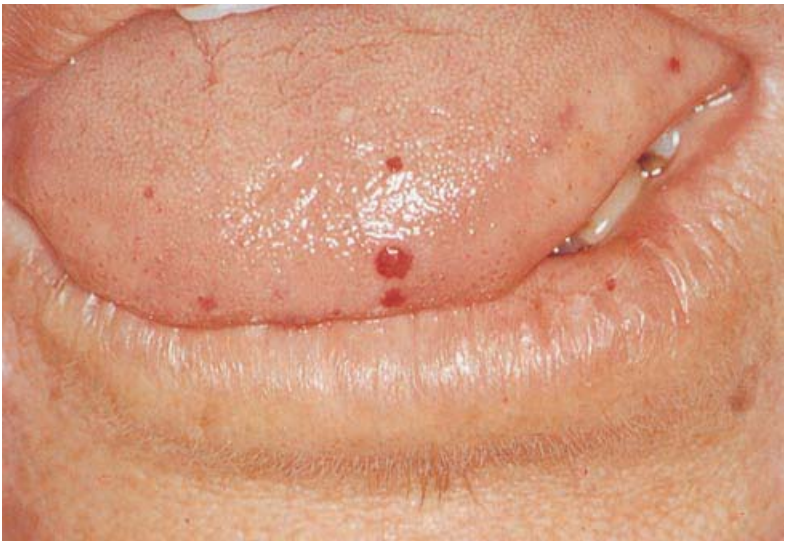


Fig. 71 Hereditary hemorrhgic telangiectasia: multiple lesions on the tongue.

Anemia

Pernicious anemia, iron deficiency anemia, and Plummer–Vinson syndrome usually affect the oral mucosa. The oral manifestations are early and common, and are characterized by an atrophic, smooth and red tongue (Figs. **72**, **73**). A burning sensation, taste loss, angular cheilitis, and rarely erosions may be present. The differential diagnosis includes atrophic lichen planus and malnutrition disorders. The diagnosis is based on hematological laboratory tests.

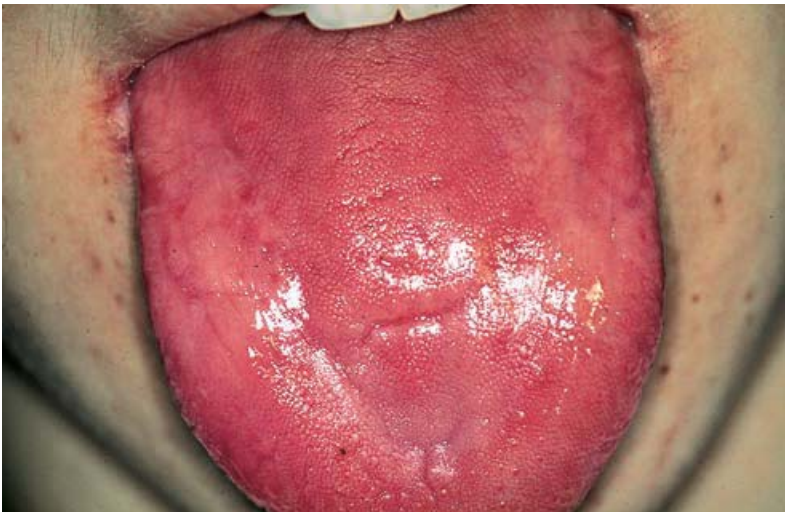


Fig. 72 Pernicious anemia: red and smooth dorsum of the tongue

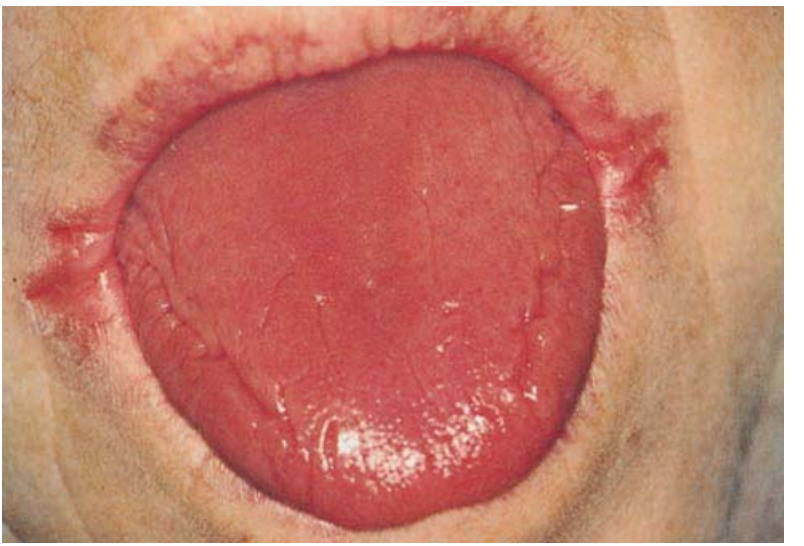


Fig. 73 Plummer–Vinson syndrome: redness and atrophy of the lingual papillae, associated with angular cheilitis.

Thrombocytopenic Purpura

Definition Thrombocytopenic purpura is a hematological disorder characterized by a decrease in platelets in the peripheral blood.

Etiology Presumably a nonspecific viral infection, myelotoxic agents.

Clinical features The oral manifestations consist of red lesions in the form of petechiae, ecchymoses, or even hematomas, usually located on the palate and buccal mucosa (Fig. **74**). Spontaneous gingival bleeding is a constant early finding. Purpuric skin rash, epistaxis, and bleeding from the gastrointestinal and urinary tract are common.

Laboratory tests Peripheral platelet count, bone-marrow aspiration, bleeding and clotting times.

Differential diagnosis Aplastic anemia, leukemias, polycythemia vera, agranulocytosis, macroglobulinemia, drug reactions.

Treatment Steroids, platelet transfusions, cessation of drug treatment if it is drug-related.

Infectious Mononucleosis

Definition Infectious mononucleosis is an acute, self-limited infectious disease that primarily affects children.

Etiology Epstein–Barr virus transmitted through saliva transfer.

Clinical features The oral manifestations are early and common, and consist of palatal petechiae, uvular edema, tonsillar exudate, gingivitis, and rarely ulcers (Fig. **75**). Generalized lymphadenopathy, hepatosplenomegaly, maculopapular skin rash, and sore throat are common. Prodromal symptoms such as anorexia, malaise, headache, fatigue, and later fever occur before the clinical manifestations.

Laboratory tests Heterophile antibody tests, and other specific antibody tests (Paul–Bunnell test, monospot test).

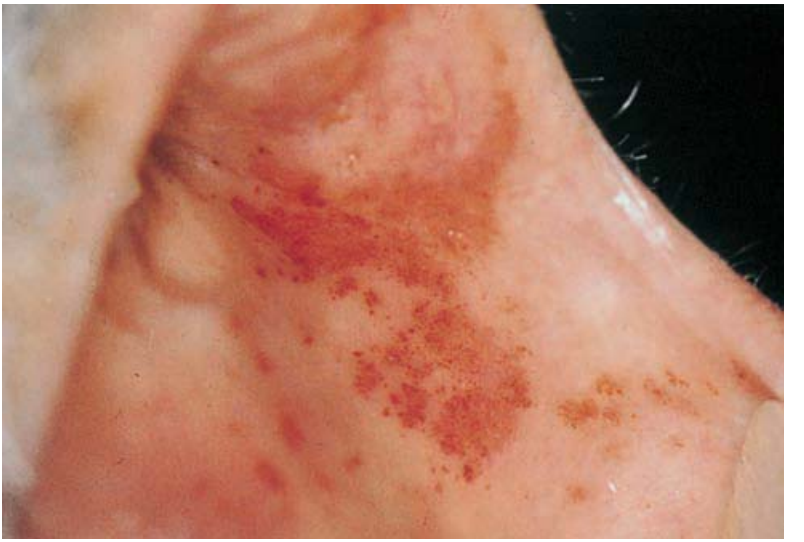


Fig. 74 Idiopathic thrombocytopenic purpura: petechiae and ecchymoses of the buccal mucosa.

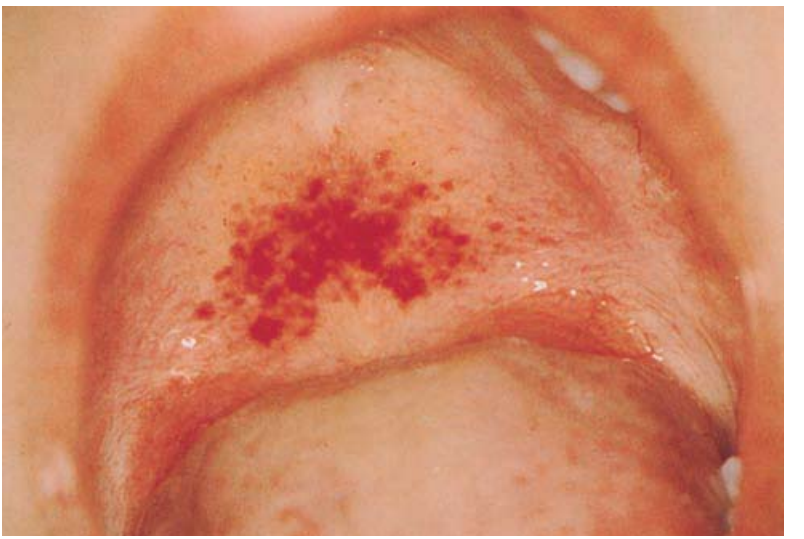


Fig. 75 Infectious mononucleosis: petechiae on the palate.

Differential diagnosis Leukemias, secondary syphilis, diphtheria, fellatio, thrombocytopenic purpura, traumatic hematoma.

Treatment Symptomatic.

Reiter Disease

Definition Reiter disease is an uncommon multisystemic disorder that predominantly affects young men aged 20–30 years.

Etiology The exact etiology remains unknown, although the pathogenesis is mediated by an immunological mechanism. The disease may be triggered by an infectious agent in a genetically susceptible individual.

Clinical features The main clinical manifestations are nongonococcal urethritis, cyclic balanitis, symmetrical arthritis of six to seven joints, conjunctivitis, prostatitis, cervicitis, and mucocutaneous lesions. The cutaneous manifestations appear as macular, vesicular, or pustular lesions involving mainly the palms and soles. Psoriasiform lesions, keratoderma, and nail changes are common. Oral lesions occur in 20–40% of the cases and are characterized by diffuse erythematous areas intermixed with thin whitish dots or lines and painful superficial erosions (Figs. **76**, **77**). The buccal mucosa, gingiva, palate, lips, and tongue are more frequently affected. The tongue lesions may mimic geographic tongue. The clinical diagnosis should be confirmed by biopsy and histopathological examination.

Differential diagnosis The differential diagnosis of oral lesions includes Behçet disease, erythema multiforme, geographic tongue, and drug reactions.

Treatment Systemic corticosteroids and nonsteroidal anti-inflammatory agents are the drugs of choice.

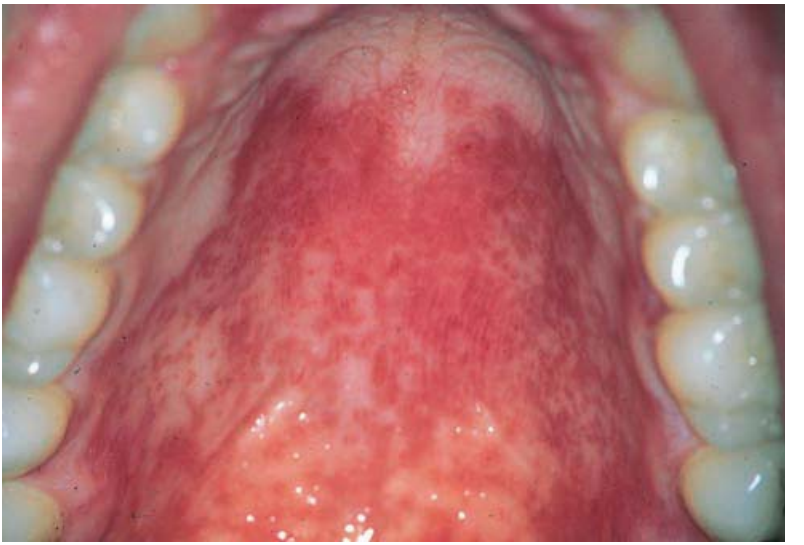


Fig. 76 Reiter disease, diffuse erythema on the palate

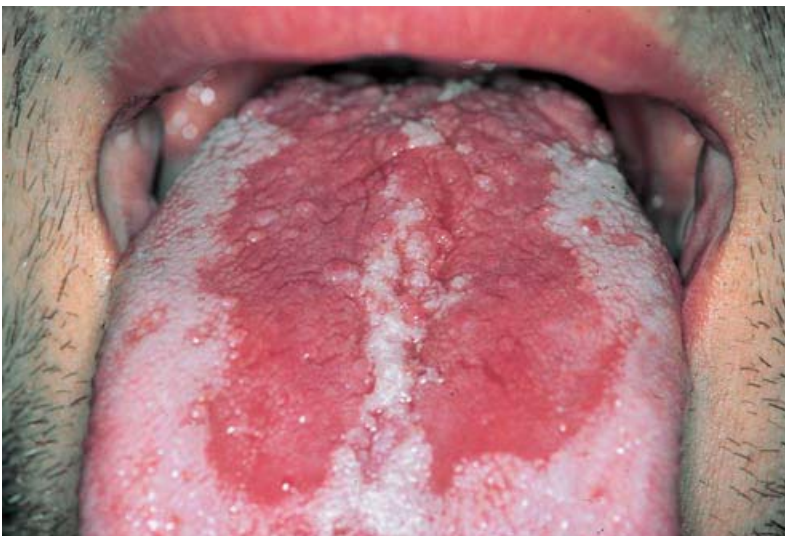


Fig. 77 Reiter disease, erythema and superficial erosions on the tongue

Peripheral Ameloblastoma

Definition Ameloblastoma is the most common tumor of odontogenic epithelial origin that primarily affects the jaws.

Etiology Unknown. The peripheral ameloblastoma probably arises from dental lamina rests or from basal epithelial cells.

Clinical features Peripheral ameloblastoma is rare and accounts for about 1–2% of all ameloblastomas. It usually presents as a painless, slow-growing, nonulcerated, sessile red mass (Fig. **78**). The size of the lesion varies between 1 and 2 cm. The posterior alveolar mucosa and the gingiva of the mandible are more frequently affected. The lesion causes little or no bone erosion. The clinical diagnosis should be confirmed by a biopsy and histopathological examination.

Differential diagnosis Pyogenic granuloma, peripheral giant cell granuloma, fibroma, squamous-cell carcinoma, extraosseous calcifying epithelial odontogenic tumor, extraosseous calcifying epithelial odontogenic cyst, odontogenic myxoma.

Treatment Local surgical excision.

Sturge–Weber Angiomatosis

Definition Sturge–Weber angiomatosis, or encephalotrigeminal angiomatosis, is a relatively rare, sporadic congenital capillary vascular malformation typically involving areas innervated by the trigeminal nerve.

Etiology Developmental abnormality.

Clinical features The main clinical features are characterized by unilateral hemangiomas of the facial skin, oral mucosa, and leptomeninges, brain calcification, ocular disorders, epilepsy, and occasionally mild mental handicap. Oral hemangiomas have a bright red or purple color and are usually flat but may also be raised, causing tissue enlargement (Fig. **79**). Dentists and oral surgeons must be careful during tooth extraction and periodontal surgery so as to avoid bleeding complications. Facial hemangiomas have a bright red color and are asymptomatic

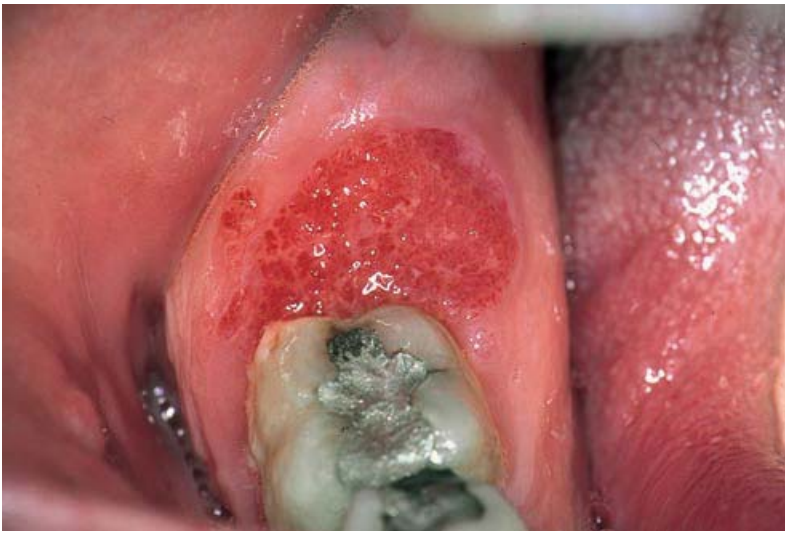


Fig. 78 Peripheral ameloblastoma, red mass on the posterior alveolar mucosa.

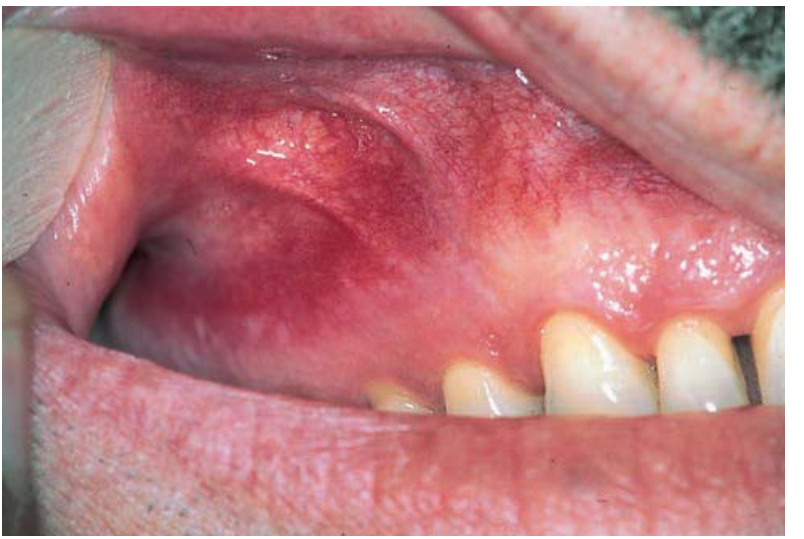


Fig. 79 Sturge–Weber angiomatosis, oral hemangiomas on the alveolar mucosa.

(Fig. **80**). Facial and oral hemangiomas are usually obvious at birth. The diagnosis is usually based on clinical criteria.

Differential diagnosis Solitary hemangioma, Klippel–Trénaunay–Weber syndrome.

Treatment Laser therapy is recommended.

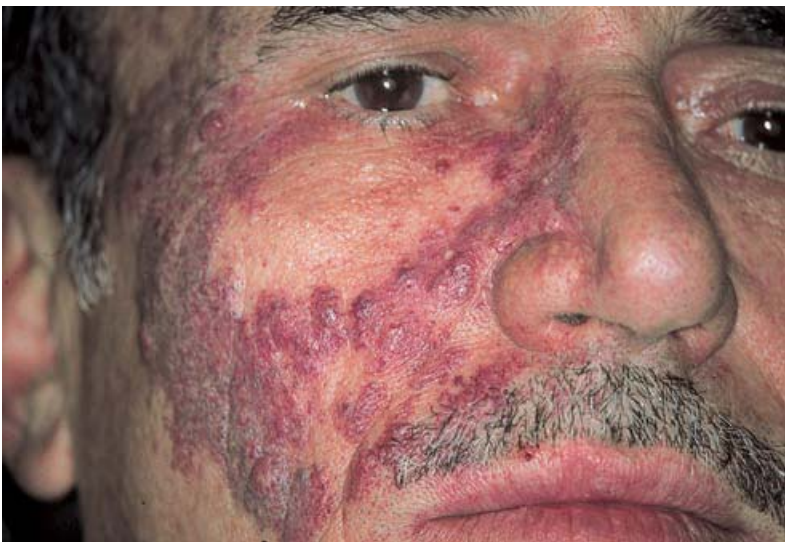
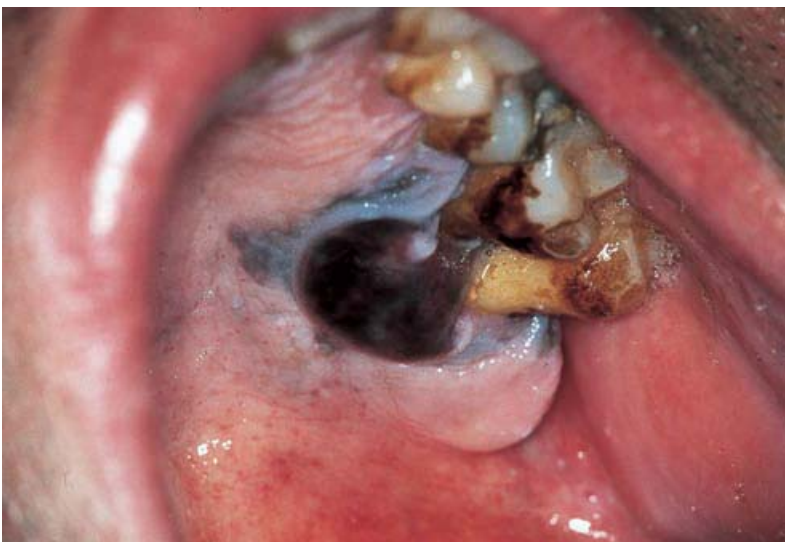


Fig. 80 Sturge–Weber angiomatosis, facial hemangiomas

3 Black and Brown Lesions

Pigmented oral lesions are a large group of disorders in which the dark or brown color is the essential clinical characteristic. Usually, the dark color of the lesions is due to melanin production by either melanocytes or nevus cells. In addition, exogenous deposits and pigment-producing bacteria can also produce pigmented lesions. Benign disorders, deposits, benign and malignant neoplasms, and systemic diseases are included in the group of pigmented lesions.

- Normal pigmentation
- Amalgam tattoo
- Heavy-metal deposition
- Drug-induced pigmentation
- Smoker's melanosis
- Black hairy tongue
- Ephelis
- Lentigo
- Lentigo maligna
- Pigmented nevi
- Nevus of Ota
- Melanoma
- Addison disease
- Peutz–Jeghers syndrome



Normal Pigmentation

Definition and etiology Increased melanin production and deposition in the oral mucosa may often be a physiological finding, particularly in dark-skinned individuals.

Clinical features This type of pigmentation is persistent and symmetrical, and clinically presents as asymptomatic black or brown areas of varying size. The gingiva are most commonly affected, followed by the buccal mucosa, palate, and lips (Fig. **81**). The pigmentation is more prominent in areas of pressure or friction, and usually becomes more intense with increasing age.

Laboratory tests Histopathological examination.

Differential diagnosis Addison disease, smoker's melanosis, drug-induced pigmentation, pigmented nevi, melanoma, amalgam tattoo.

Treatment No treatment is required.

Amalgam Tattoo

Definition Amalgam deposition (tattoo) is a common oral disorder.

Etiology Implantation of dental amalgam into the oral mucosa.

Clinical features The condition presents as a well-defined irregular or diffuse flat area, with a bluish-black discoloration of varying size (Fig. **82**). The most common sites of involvement are the gingiva, alveolar mucosa, and buccal mucosa. The diagnosis is usually made at the clinical level.

Laboratory tests Histopathological examination and radiographs.

Differential diagnosis Pigmented nevi, lentigo, freckles, melanoma, normal pigmentation, other metal tattoo.

Treatment No treatment is required.

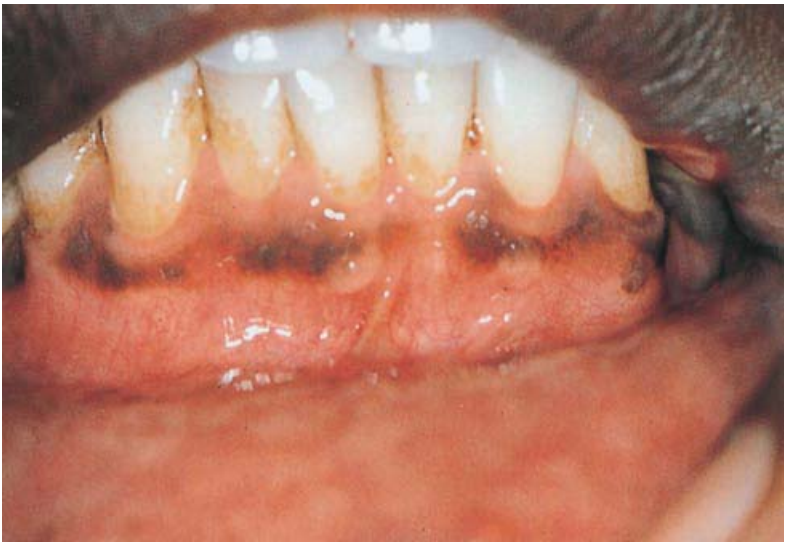


Fig. 81 Normal pigmentation of the gingiva.

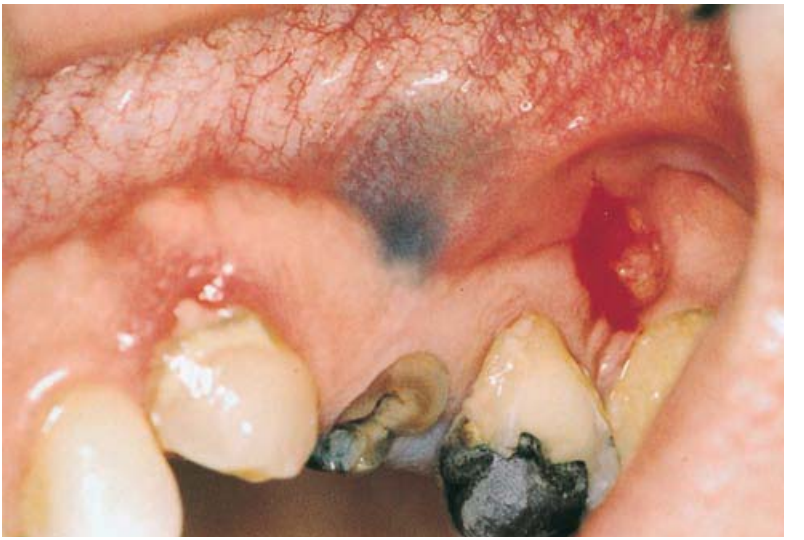


Fig. 82 Amalgam tattoo.

Heavy-Metal Deposition

Definition and etiology Heavy-metal deposition is a rare oral condition caused by ingestion or exposure to bismuth, lead, silver, mercury, and other heavy metals.

Clinical features Clinically, the most common pattern (bismuth, lead) is a bluish line along the marginal gingiva, or similar spots within the gingival papillae (Fig. **83**). Rarely, diffuse bluish-black discoloration may be seen (silver). The diagnosis is based on the history and the clinical features.

Differential diagnosis Normal pigmentation, amalgam tattoo.

Treatment No treatment is required for oral lesions.

Drug-Induced Pigmentation

Definition Drug-induced oral pigmentation is a relatively common condition, caused by increased melanin production or drug metabolite deposition.

Etiology Antimalarials, tranquilizers, minocycline, azidothymidine, ketoconazole, phenolphthalein, and others are the most common drugs that induce pigmentation.

Clinical features The clinical picture varies, and the condition may appear as irregular brown or black macules or plaques, or diffuse melanosis (Fig. **84**). The buccal mucosa, tongue, palate, and gingiva are the most commonly affected sites. The diagnosis is made on the basis of the history and clinical criteria.

Differential diagnosis Normal pigmentation, Addison disease, Peutz–Jeghers syndrome.

Treatment No treatment is required.

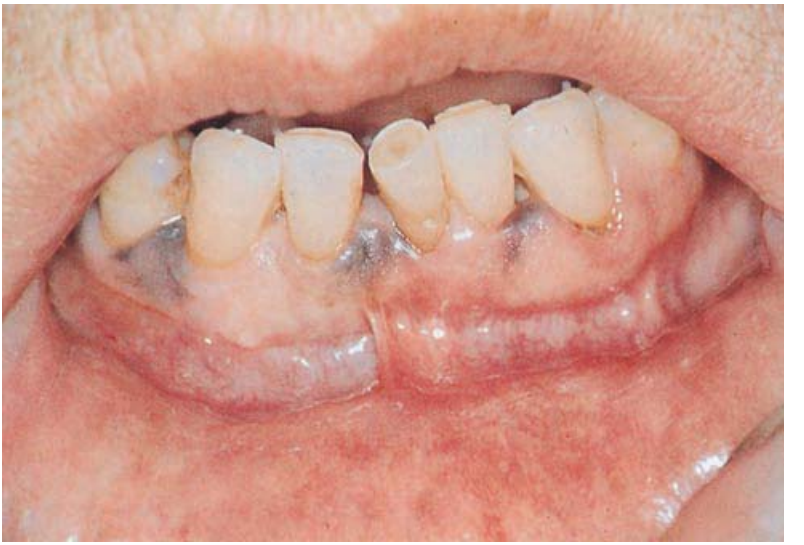


Fig. 83 Bismuth deposition within the gingival papillae.

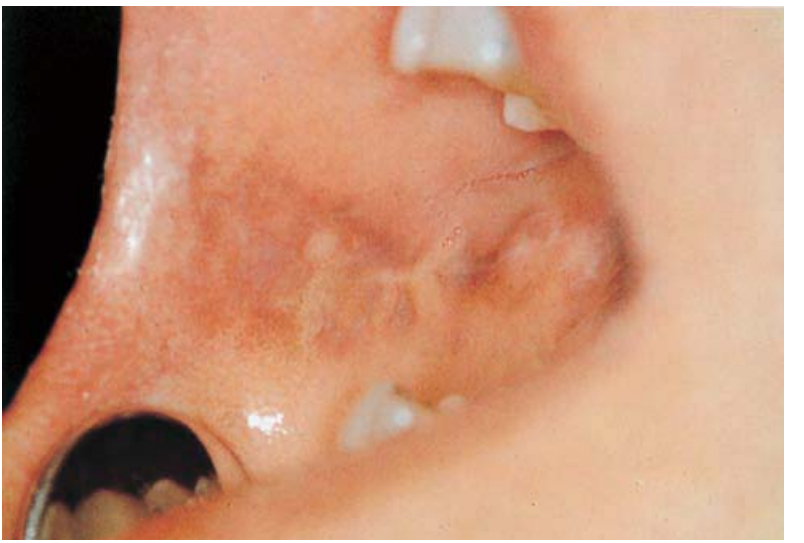


Fig. 84 Pigmentation of the buccal mucosa caused by chloroquine.

Smoker's Melanosis

Definition Smoker's melanosis, or smoking-associated melanosis, is a benign abnormal melanin pigmentation of the oral mucosa.

Etiology Tobacco smoke that stimulates melanocytes.

Clinical features Clinically, it appears as multiple brown pigmented areas, usually located on the anterior labial gingiva of the mandible (Fig. **85**). Pigmentation of the buccal mucosa and palate has been associated with pipe smoking. The intensity of pigmentation is related to time and dose. Women are more commonly affected.

Differential diagnosis Normal pigmentation, drug-induced pigmentation, pigmented nevi, melanoma, Addison disease.

Treatment No treatment is required. Cessation of smoking is usually associated with a return of normal mucosal pigmentation.

Black Hairy Tongue

Hairy tongue (see also p. 24) may occasionally appear black as a result of the growth of pigment-producing bacteria that colonize the elongated filiform papillae (Fig. **86**). In addition, the black color may also be due to staining from food and tobacco. The diagnosis is made on the basis of clinical criteria.

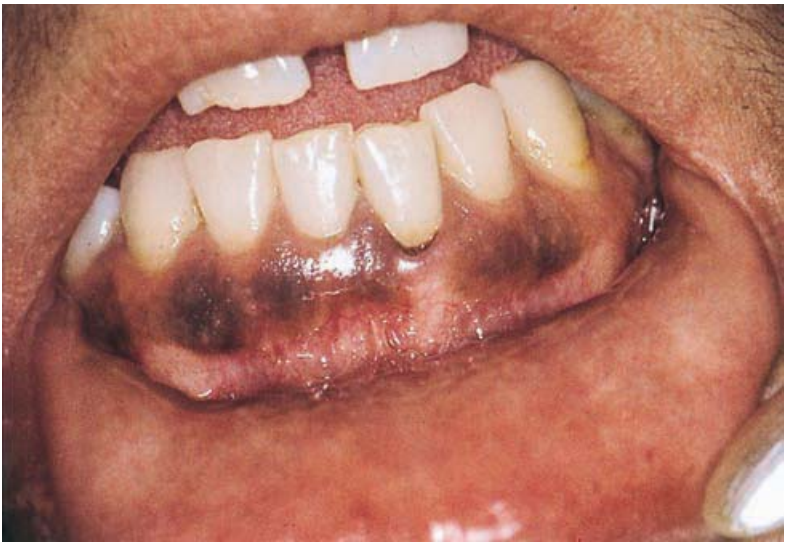


Fig. 85 Smoker's melanosis of the gingiva.

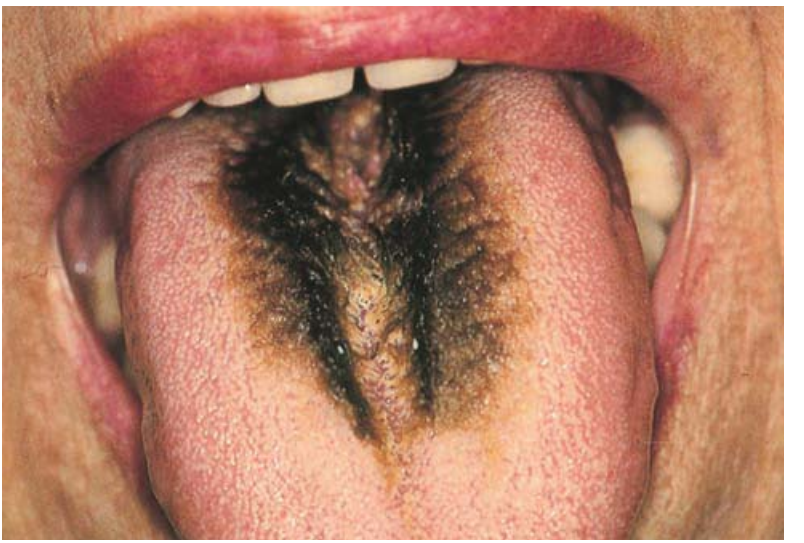


Fig. 86 Black hairy tongue.

Ephelis

Definition Ephelides, or freckles, are discrete brown macules, commonly seen on sun-exposed skin and rarely in the mouth.

Etiology Unknown. They are due to increased melanin production.

Clinical features Clinically, the lesions appear as solitary and well-demarcated asymptomatic round brown macules, less than 5 mm in diameter (Fig. **87**). The vermilion border of the lower lip is the most common site of development.

Laboratory tests Histopathological examination.

Differential diagnosis Lentigo, pigmented nevi, melanoma, drug-associated pigmentation, Peutz–Jeghers syndrome, Albright syndrome.

Treatment No treatment is required, except for aesthetic or diagnostic considerations.

Lentigo

Definition Lentigo is a rare oral disorder of pigmentation.

Etiology Increased number of epidermal melanocytes.

Clinical features The condition presents as small round flat spots, brown or dark brown in color, usually less than 0.5 cm in diameter (Fig. **88**). It is a rare lesion intraorally.

Laboratory tests Histopathological examination.

Differential diagnosis Ephelis, pigmented nevi, melanoma, Peutz–Jeghers syndrome.

Treatment No treatment is required.

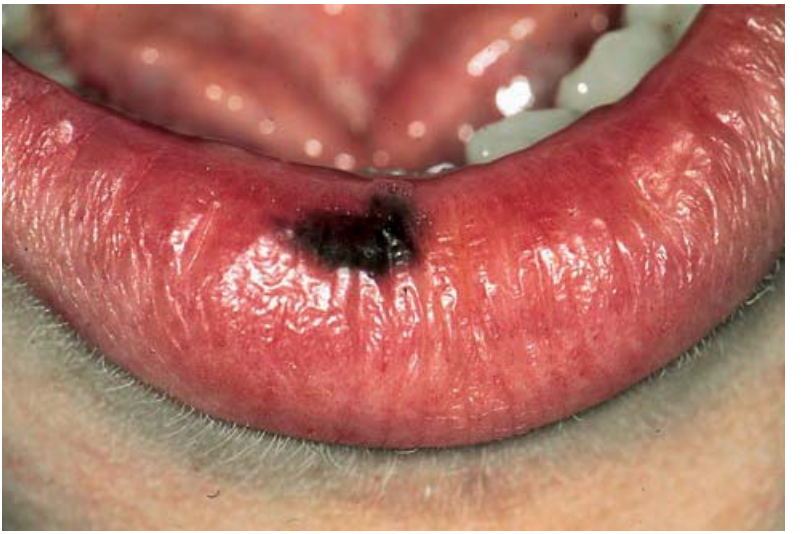


Fig. 87 Ephelis on the vermilion border of the lower lip.

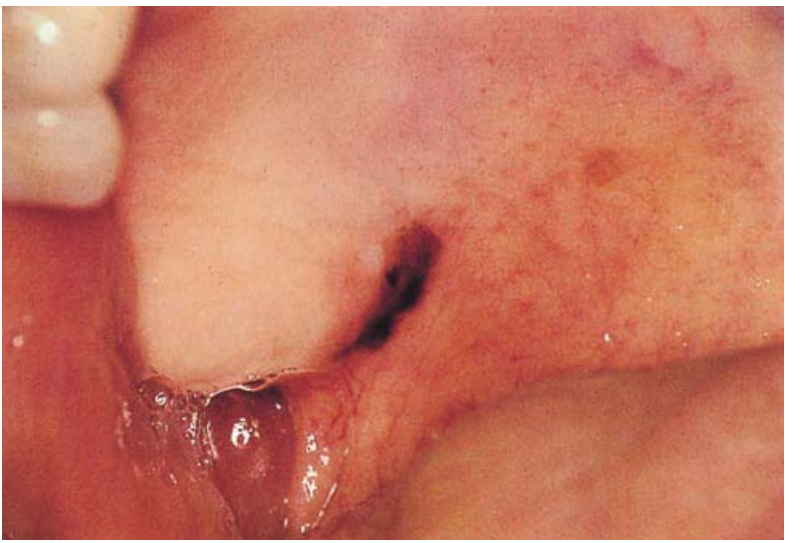


Fig. 88 Lentigo of the palate.

Lentigo Maligna

Definition Lentigo maligna, or Hutchinson's freckle, is a premalignant lesion of melanocytes that probably represents in-situ melanoma.

Etiology Unknown.

Clinical features Lentigo maligna is very rare intraorally. Clinically, it appears as a slowly expanding black or brown plaque, with irregular borders (Fig. **89**). In 5–15 years, it ultimately progresses into invasive melanoma. The lips, buccal mucosa, palate, and floor of the mouth are the common sites affected.

Laboratory tests Histopathological examination.

Differential diagnosis Melanoma, pigmented nevi, amalgam tattoo.

Treatment Surgical excision, radiotherapy.

Pigmented Nevi

Definition Pigmented cellular nevi are benign malformations of melanocytes and "nevus cells," common in the skin and rare in the oral mucosa.

Etiology Developmental. Melanocytes and nevus cells of neural crest origin.

Clinical features Based on histological criteria, oral pigmented nevi are classified into four types: *intramucosal*, *junctional*, *compound*, and *blue*. Clinically, the lesion appears as an asymptomatic, well-demarcated, flat or slightly elevated, brown, black, or blue spot or plaque (Fig. **90**). The lesion is usually solitary, with a diameter of less than 1 cm. The palate, gingiva, buccal mucosa, and lips are the sites of predilection.

Laboratory tests Histopathological examination.

Differential diagnosis Ephelis, lentigo, melanoma, amalgam tattoo.

Treatment Usually, no treatment is required. Conservative surgical excision is carried out in some cases.

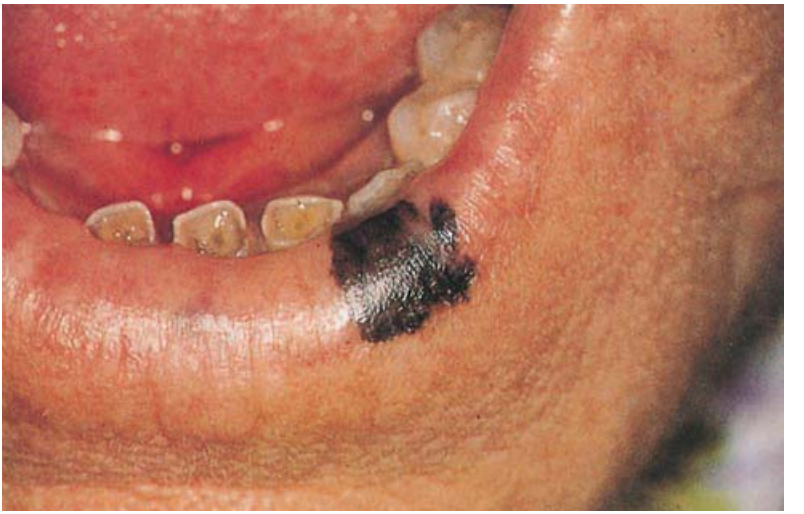


Fig. 89 Lentigo maligna on the vermilion border of the lower lip.

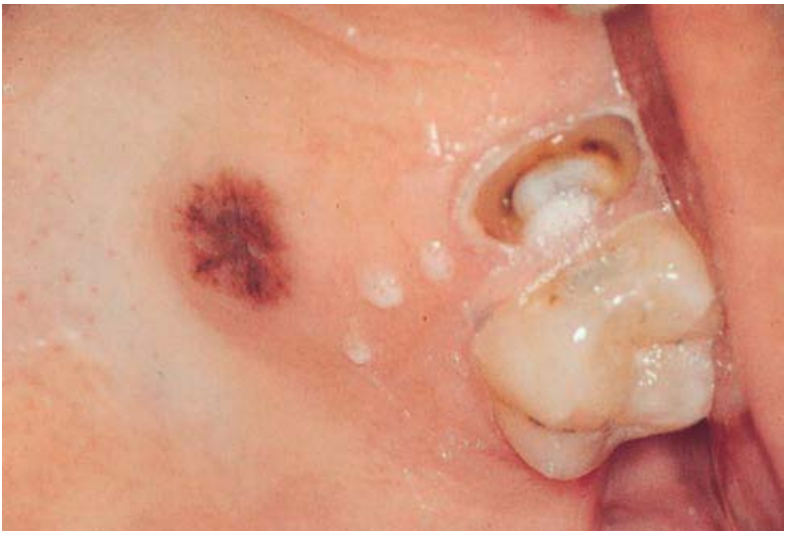


Fig. 90 Compound nevus of the palate.

Nevus of Ota

Definition Nevus of Ota, or oculodermal melanocytosis, is a hamartomatous disorder of the melanocytes that predominantly involves the skin of the face and eyes, and mucous membranes. Characteristically, the lesions follow the distribution of the first and second branches of the trigeminal nerve.

Etiology Developmental. Hyperpigmentation is due to melanin-producing melanocytes in the dermis that have failed to reach the epidermis or epithelium during fetal life.

Clinical features The skin lesions present as multiple mottled black or brown macules varying in size from 1 mm to several millimeters (Fig. **91**). The oral lesion presents as asymptomatic blue or blue-black dots or patches that usually involve the palate and buccal mucosa (Fig. **92**). Hyperpigmentation of ipsilateral sclera is a common sign, while involvement of the cornea, iris, fundus, oculi, and retina is rare. Other sites such as nasal mucosa, pharynx, and tympanum may be less commonly affected. The disorder usually appears in early childhood before the age of 1 year and around puberty. About 70–80% of the cases are female. Malignant transformation of nevus of Ota is very rare. The diagnosis is mainly based on the history and the clinical features.

Laboratory tests Histopathological examination.

Treatment Laser and camouflage of face lesions.

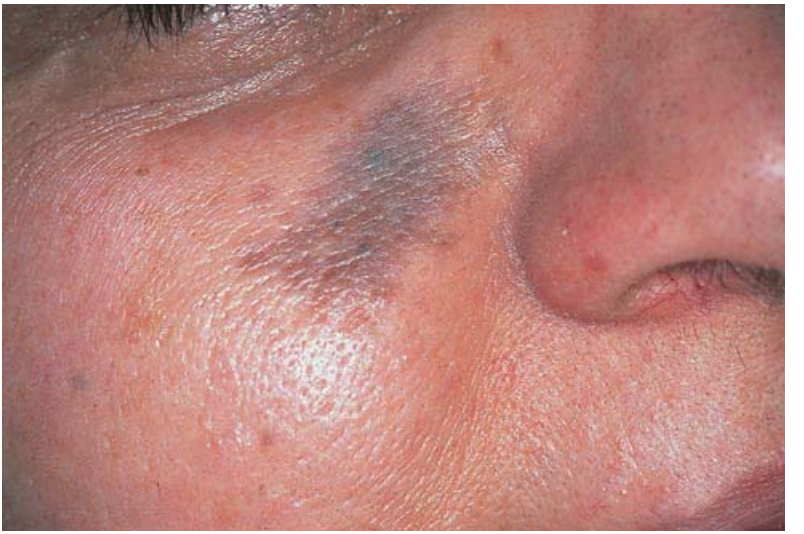


Fig. 91 Nevus of Ota, skin hyperpigmentation.

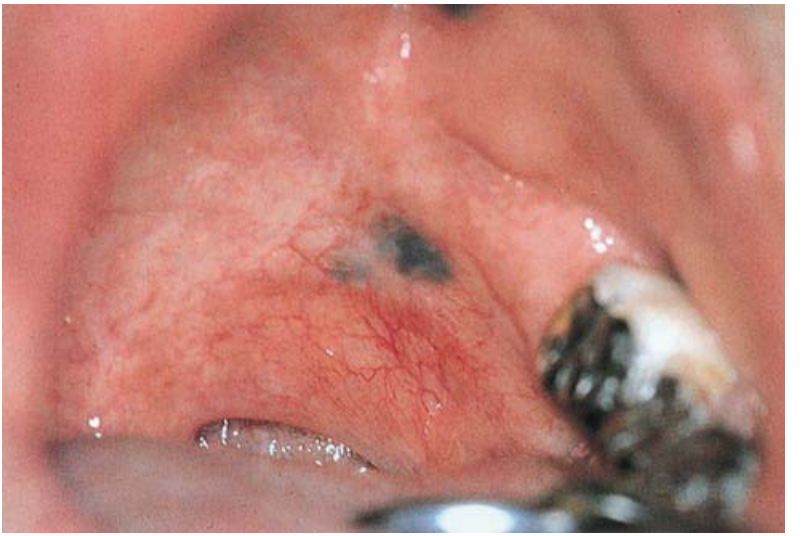


Fig. 92 Nevus of Ota, pigmented spots on the palate.

Melanoma

Definition Melanoma is a malignant neoplasm originating either de novo from melanocytes, or from a benign melanocytic lesion.

Etiology Unknown. Ultraviolet radiation is an important causative factor for skin melanoma.

Clinical features Primary oral melanoma is uncommon, representing 0.5–1.5% of melanomas. Clinically, it presents as a black or brown macule, plaque, or nodule that may be ulcerated (Figs. **93**, **94**, **95**). The lesions are usually characterized by an irregular margin and a tendency to spread. Based on clinical and histopathological criteria, oral melanoma is classified into three forms: *lentigo maligna melanoma* (best prognosis), *superficial spreading melanoma* (good prognosis), and *nodular melanoma* (poor prognosis). The palate, upper gingiva, and alveolar mucosa are most commonly affected.

Laboratory tests Histopathological examination.

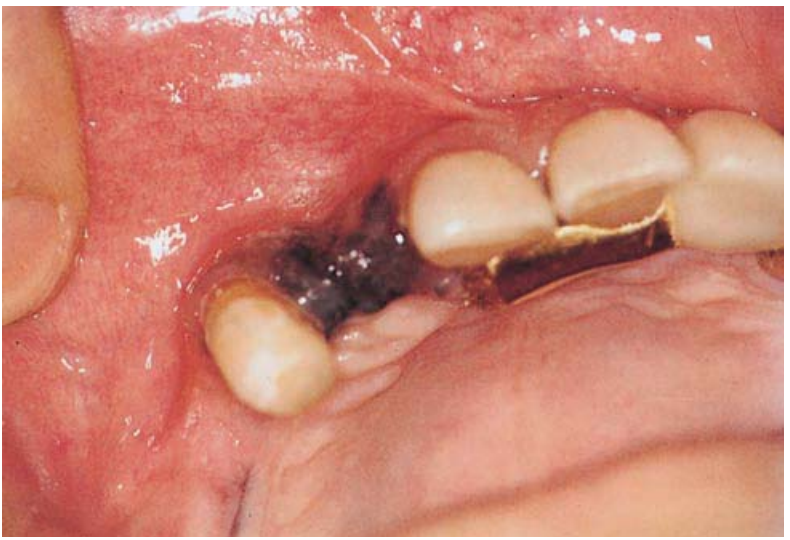


Fig. 93 Early nodular malignant melanoma of the alveolar mucosa.

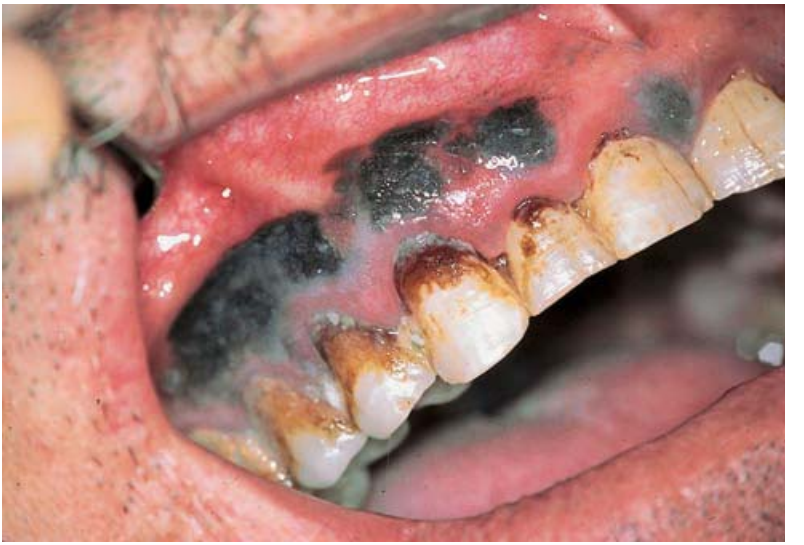


Fig. 94 Multiple nodular malignant melanomas of the alveolar mucosa of the maxilla

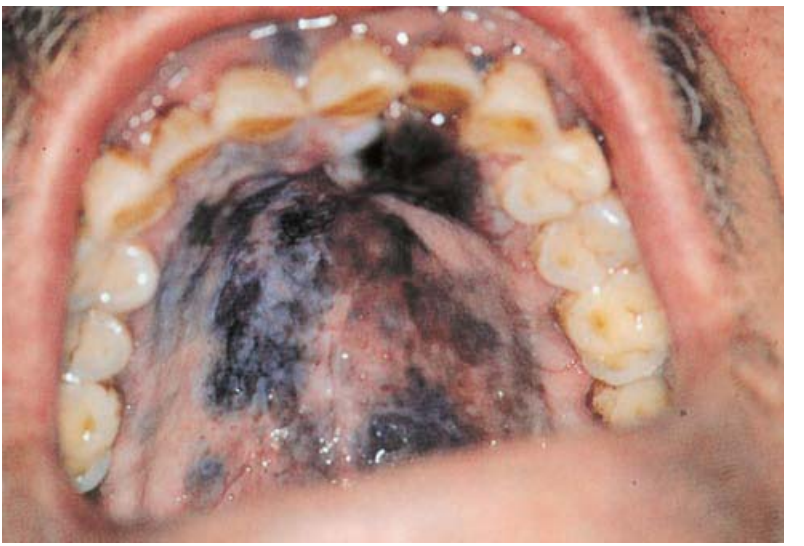


Fig. 95 Extensive superficial spreading melanoma of the palate.

Differential diagnosis Pigmented nevi, ephelis, lentigo, lentigo maligna, amalgam tattoo, pyogenic granuloma, Kaposi sarcoma.

Treatment Surgical excision, radiotherapy, chemotherapy.

Addison Disease

Definition Addison disease is a relatively uncommon insufficiency of adrenal corticosteroid hormones.

Etiology Adrenal cortex destruction, usually caused by autoimmunity, infections, tumors, amyloidosis.

Clinical features The oral manifestations are common and early, and present as diffuse or patchy dark brown pigmentation, due to melanin production (Figs. **96**, **97**). The buccal mucosa, palate, lips, and gingiva are the most common sites of involvement.

Laboratory tests Measurement of plasma adrenocorticotropic hormone (ACTH) and serum cortisol levels.

Differential diagnosis Normal pigmentation, drug-induced pigmentation, Peutz–Jeghers syndrome.

Treatment Steroid replacement.

Peutz–Jeghers Syndrome

Definition Peutz–Jeghers syndrome is a rare genetically transmitted disorder, characterized by mucocutaneous pigmentation and intestinal polyposis.

Etiology Inherited as an autosomal dominant trait.

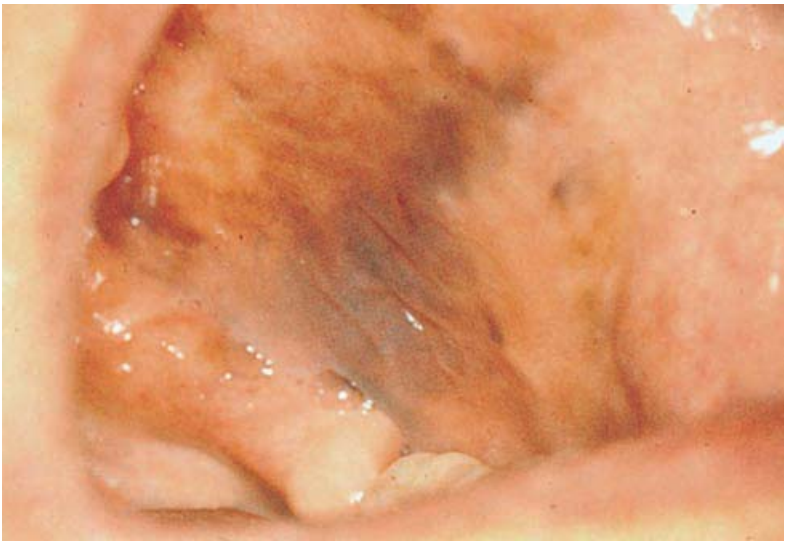


Fig. 96 Addison disease: pigmentation of the buccal mucosa.

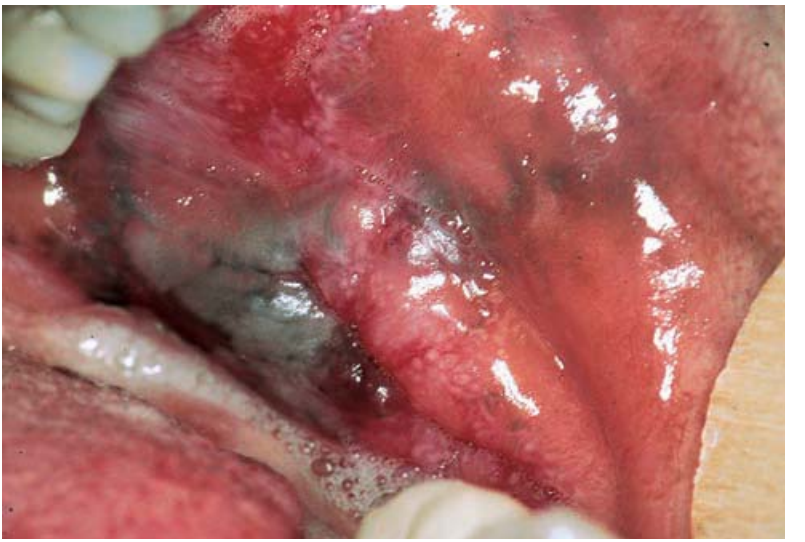


Fig. 97 Addison disease: diffuse pigmentation of the buccal mucosa

Clinical features The oral manifestations are the most important diagnostic findings, and consist of oval or round, brown or black macules or spots, 1–10 mm in diameter (Figs. **98**, **99**). The perioral skin, lips, buccal mucosa, and tongue are the most common sites affected. The skin lesions consist of numerous, usually perioral, dark spots (Fig. **100**). Intestinal polyps (hamartomas) are constant findings, usually in the jejunum and ileum.

Laboratory tests Histopathological examination, radiography of the gastrointestinal tract.

Differential diagnosis Ephelides, lentigo, normal pigmentation, Addison disease.

Treatment Supportive; surgical intervention in some cases.

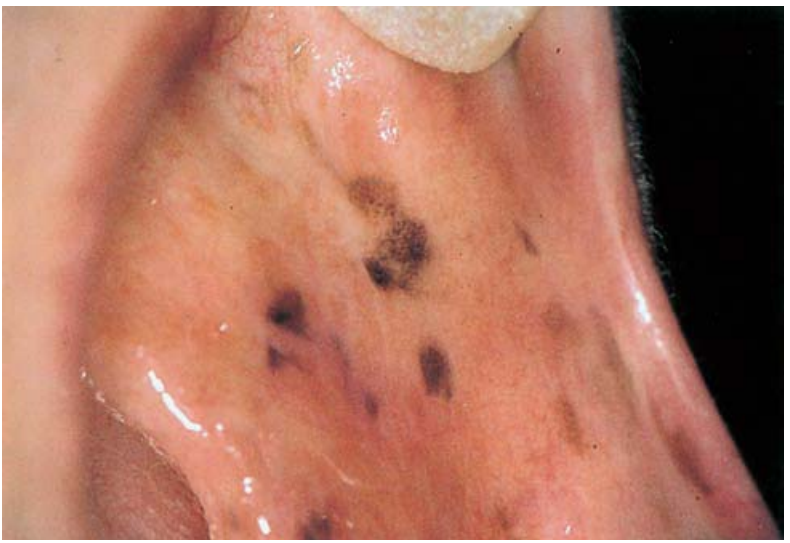


Fig. 98 Peutz–Jeghers syndrome: multiple pigmented spots on the buccal mucosa.

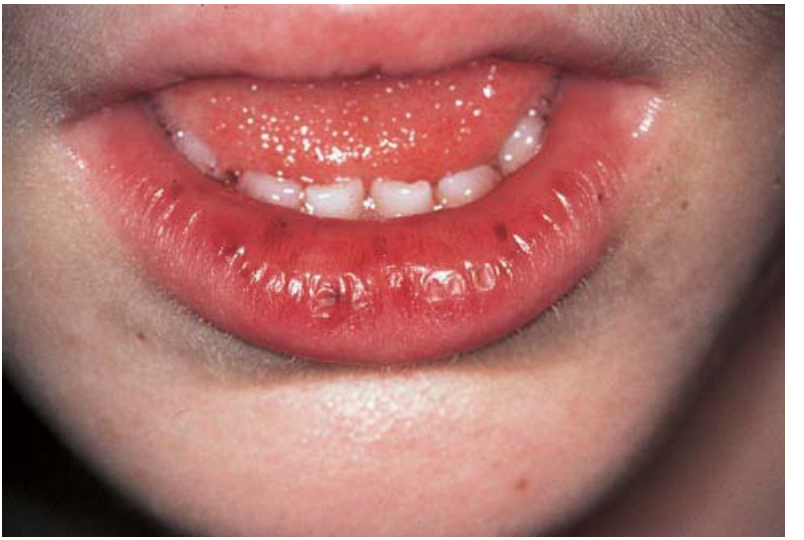


Fig. 99 Peutz–Jeghers syndrome: multiple round spots on the lower lip.

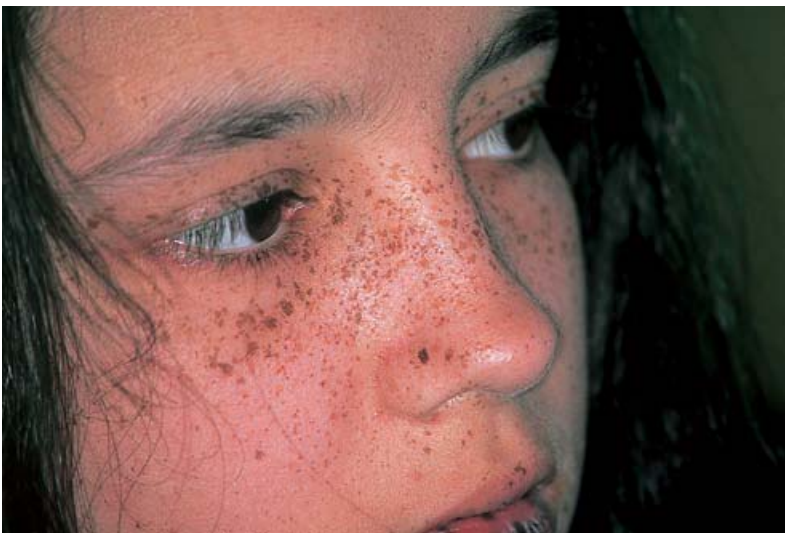
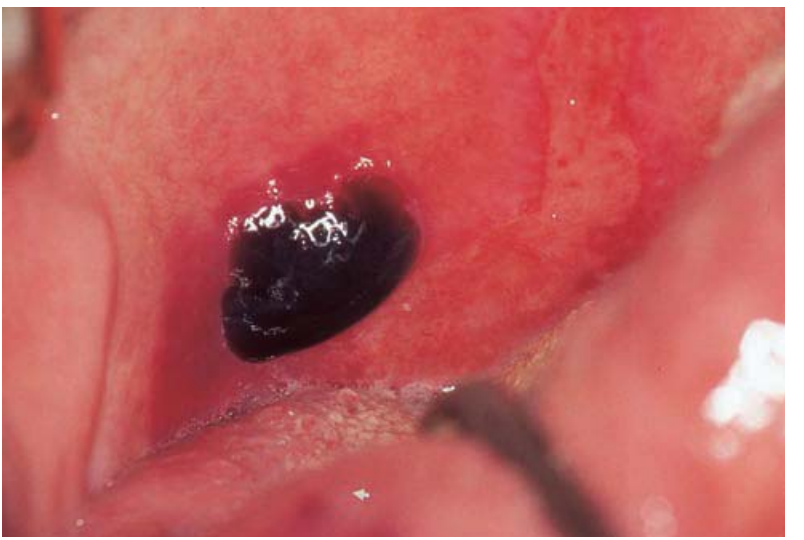


Fig. 100 Peutz-Jeghers syndrome, multiple pigmented spots on the skin.

4 Vesiculobullous Lesions

Vesiculobullous diseases are a distinct group of oral disorders characterized by the formation of vesicles or bullae. Clinicians must bear in mind that it is uncommon to see vesicles or bullae intraorally, as they soon rupture, leaving erosions or ulcers. This group includes viral diseases, autoimmune mucocutaneous diseases, diseases that probably have an immunologically mediated mechanism, and genetic diseases. The diagnosis of vesiculobullous diseases should be made on clinical, histopathological, and immunological grounds.

- Primary herpetic gingivostomatitis
- Secondary herpetic stomatitis
- Herpes zoster
- Herpangina
- Hand-foot-and-mouth disease
- Erythema multiforme
- Stevens–Johnson syndrome
- Toxic epidermal necrolysis
- Pemphigus
- Cicatricial pemphigoid
- Bullous pemphigoid
- Pemphigoid gestationis
- Linear IgA disease
- Dermatitis herpetiformis
- Bullous lichen planus
- Epidermolysis bullosa
- Epidermolysis bullosa acquisita
- Angina bullosa hemorrhagica



Primary Herpetic Gingivostomatitis

Definition Primary herpetic gingivostomatitis is a relatively common viral infection of the oral mucosa.

Etiology Usually herpes simplex virus type 1 (HSV-1), and rarely type 2 (HSV-2).

Clinical features It is usually seen between the ages of 6 months and 6 years. The onset of the disease is abrupt, and is clinically characterized by high fever, headache, malaise, anorexia, irritability, bilateral sensitive regional lymphadenopathy, and sore mouth lesions. The affected mucosa is red and edematous, with numerous coalescing vesicles, which rapidly rupture, leaving painful small, round, shallow ulcers covered by yellow fibrin (Figs. **101**, **102**). New lesions continue to develop during the first three to five days. The ulcers heal in 10–14 days. Both the movable and nonmovable oral mucosa may be affected. Gingival lesions are almost always present, resulting in enlargement and edematous and painful erosions. The diagnosis is usually made on clinical grounds.

Laboratory tests Smear, biopsy, serological tests.

Differential diagnosis Aphthous ulcers, hand-foot-and-mouth disease, herpangina, acute necrotizing ulcerative gingivitis, erythema multiforme, early pemphigus, desquamative gingivitis.

Treatment Symptomatic. In severe cases, systemic aciclovir or valaciclovir.

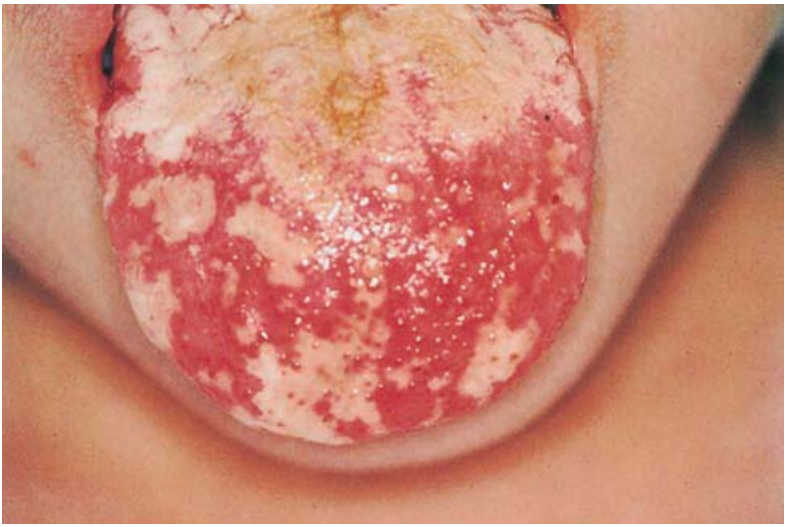


Fig. 101 Primary herpetic gingivostomatitis: multiple ulcers on the tongue.

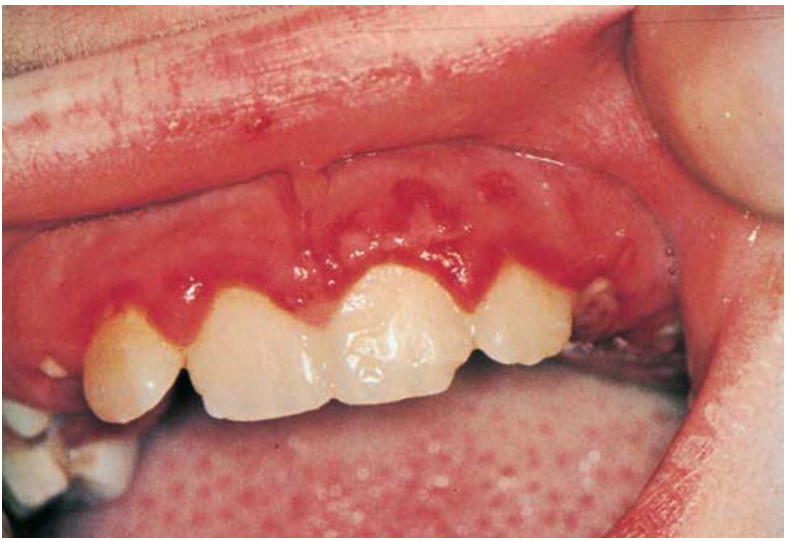


Fig. 102 Primary herpetic gingivostomatitis: erythema and multiple ulcers on the gingiva.

Secondary Herpetic Stomatitis

Definition and etiology Secondary or recurrent herpetic stomatitis is a relatively common oral and perioral disease that is due to reactivation of HSV-1. It is commonly precipitated by fever, trauma, cold, heat, sunlight, emotional stress, and HIV infection.

Clinical features The most common sites of recurrence for HSV-1 are the lips and perioral skin, the palate, and the attached gingiva. Clinically, the lesions present as multiple small vesicles arranged in clusters (Fig. **103**). The vesicles soon rupture, leaving small ulcers that heal spontaneously within 6–10 days. Prodromal symptoms are burning, itching, tingling, and erythema. Characteristically, fever, generalized regional lymphadenopathy, and constitutional symptoms are absent. The diagnosis is made on clinical grounds.

Differential diagnosis Aphthous ulcers, primary and secondary syphilis, streptococcal stomatitis, herpangina.

Treatment Symptomatic.

Herpes Zoster

Definition Herpes zoster, or shingles, is an acute self-limiting viral disease.

Etiology Reactivation of varicella-zoster virus. The most common predisposing factors for reactivation of the virus are AIDS, leukemia, lymphoma and other malignancies, radiation, immunosuppressive and cytotoxic drugs, and old age.

Clinical features The thoracic, cervical, trigeminal, and lumbosacral dermatomes are most commonly affected. Characteristically, one dermatome is usually affected. Pain and tenderness, usually associated with headache, pulpitis, malaise, and fever, are prodromal symptoms before the appearance of oral or skin lesions, or both. After two to four days, clusters of vesicles develop, and within two or three days evolve into pustules and ulcers, covered by crusts (Figs. **104**, **105**). The lesions persist for two to three weeks. The unilateral location of the lesions is a typical pattern of herpes zoster. Oral manifestations occur when the second and

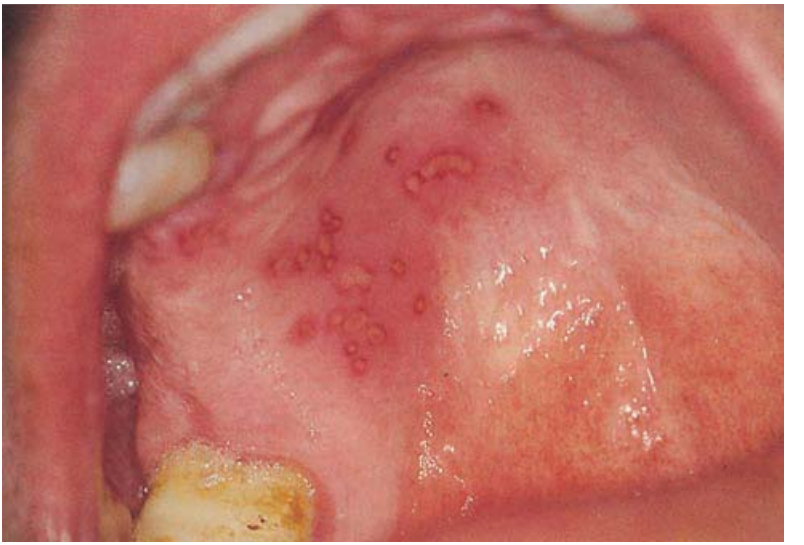


Fig. 103 Secondary herpetic stomatitis: small round ulcers on the palate.

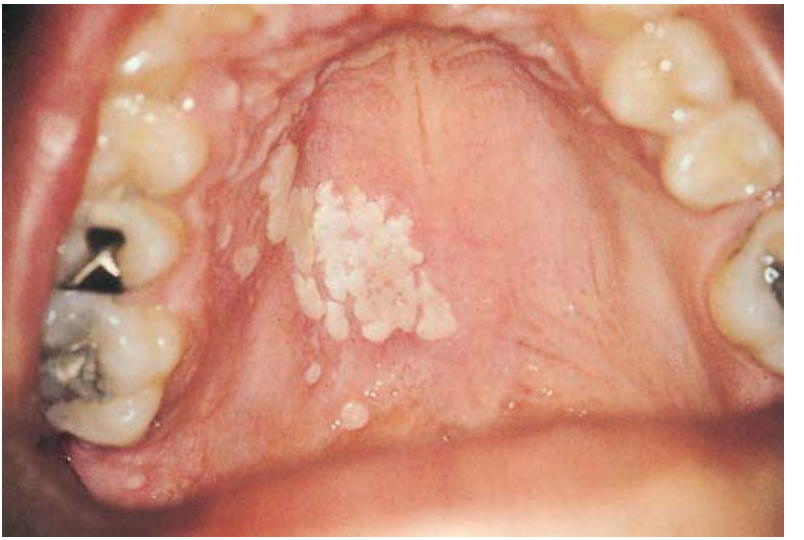


Fig. 104 Herpes zoster: clusters of vesicles on the palate.

third branches of the trigeminal nerve are involved. Postherpetic trigeminal neuralgia is a common complication, and rarely osteomyelitis, jawbone necrosis, and tooth loss are seen. The diagnosis is made on the basis of clinical criteria.

Differential diagnosis Herpes simplex, erythema multiforme.

Treatment Analgesics and sedatives to control the pain. Aciclovir, valaciclovir, and famciclovir as antiviral drugs may be helpful.

Herpangina

Definition and etiology Herpangina is an acute self-limiting viral infection, usually caused by coxsackievirus group A, types 1–6, 8, 10, and 22, and less commonly by other types.

Clinical features The disease presents with an acute onset of fever, sore throat, dysphagia, headache, and malaise, followed by diffuse erythema and vesicles. The vesicles are small and numerous, and rupture rapidly, leaving painful ulcers that heal within 7–10 days (Fig.**106**). Characteristically, the lesions appear on the soft palate and uvula, tonsillar pillars, and posterior pharyngeal wall. The disease has a peak incidence during summer and autumn, and frequently affects children and young adults. The diagnosis is exclusively based on clinical criteria.

Differential diagnosis Herpetiform ulcers, aphthous ulcers, primary herpes simplex infection, acute lymphonodular pharyngitis, erythema multiforme, FAPA syndrome, hand-foot-and-mouth disease.

Treatment Supportive.

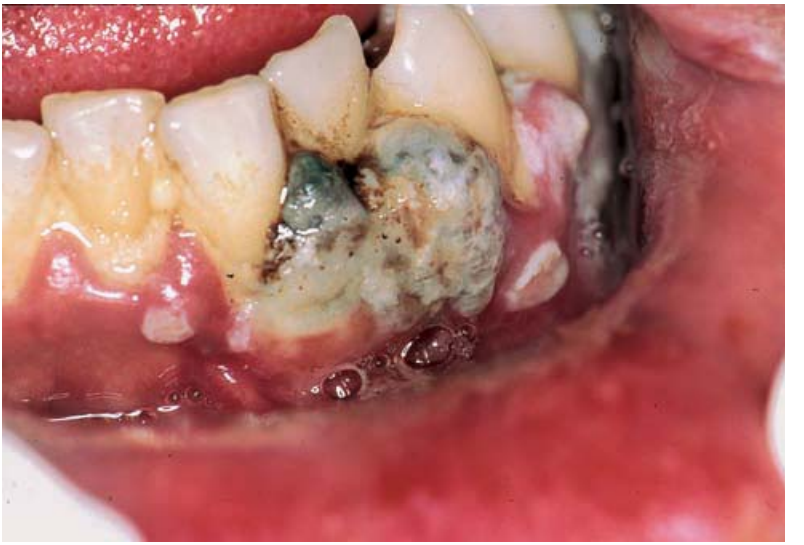


Fig. 105 Herpes zoster: vesicles and erosions on the lower gingiva

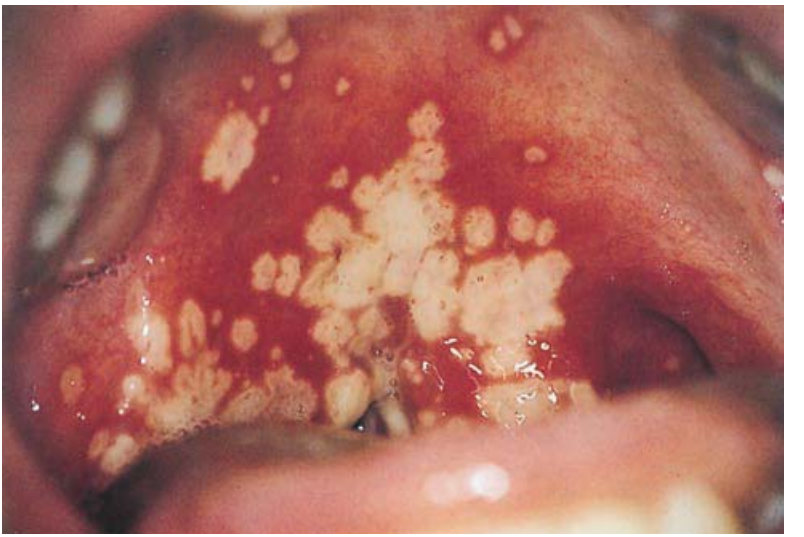


Fig. 106 Herpangina: numerous shallow ulcers on the soft palate.

Hand-Foot-and-Mouth Disease

Definition Hand-foot-and-mouth disease is an acute self-limiting contagious viral infection transmitted from one individual to another.

Etiology Coxsackievirus A16, and rarely other strains.

Clinical features The disease usually affects children and young adults, and often occurs in epidemics. Oral manifestations are always present, and are characterized by small vesicles (5–30 in number) that rapidly rupture, leaving painful, shallow ulcers (2–6 mm in diameter) surrounded by a red halo (Fig. **107**). The buccal mucosa, tongue, and labial mucosa are the most commonly affected sites. Skin lesions are not constant, and present as small vesicles with a narrow red halo. The lateral borders and the dorsal surfaces of the fingers and toes are the most common areas involved. Lesions may appear on the palms, soles, and buttocks. The disease lasts five to eight days. The diagnosis is made on the basis of clinical criteria.

Differential diagnosis Aphthous ulcers, herpes simplex infection, herpangina.

Treatment Supportive.

Erythema Multiforme

Definition Erythema multiforme is an acute or subacute self-limiting disease that involves the skin and mucous membranes.

Etiology The etiology is unclear. However, an immunologically mediated process triggered by herpes simplex or *Mycoplasma pneumoniae*, drugs, radiation, or malignancies, is probable.

Clinical features The disease more frequently affects young men between the ages of 20 and 30 years. The oral lesions present as coalescing small vesicles that rupture within two or three days, leaving irregular, painful erosions covered by a necrotic pseudomembrane (Fig. **108**). The lips, buccal mucosa, tongue, soft palate, and floor of the mouth are most commonly involved. The skin manifestations consist of erythematous, flat, round macules, papules, or plaques, usually in a symmetrical pat-

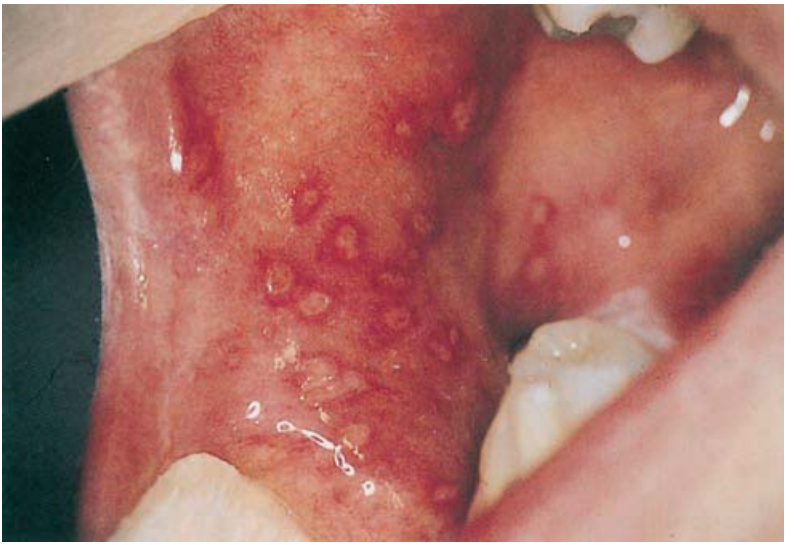


Fig. 107 Hand-foot-and-mouth disease: shallow ulcers on the buccal mucosa.

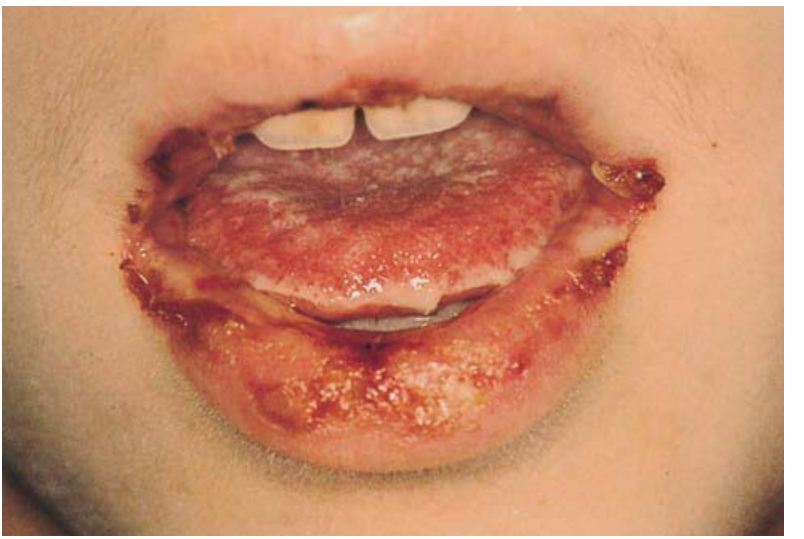


Fig. 108 Erythema multiforme: multiple erosions on the lips and tongue.

tern. The characteristic skin patterns are *target-* or *iris-like* lesions (Fig. **109**). Skin bullae may occasionally be seen. Conjunctivitis, balanitis, vulvitis, and prodromal symptoms such as headache, malaise, arthralgias, and fever, may also be present. Recurrences are common.

Laboratory tests Histopathological examination.

Differential diagnosis Primary herpetic gingivostomatitis, aphthous ulcers, erosive lichen planus, pemphigus vulgaris, pemphigoid.

Treatment Systemic steroids. Aciclovir may be helpful in cases of recurrence.

Stevens–Johnson Syndrome

Definition Stevens–Johnson syndrome, or erythema multiforme major, is a severe form of erythema multiforme that predominantly affects the mucous membranes.

Etiology Drugs usually trigger the disease.

Clinical features The oral lesions are always present, and are characterized by extensive vesicle formation, followed by painful erosions covered by grayish-white or hemorrhagic pseudomembranes (Fig. **110**). The lesions may extend to the pharynx, larynx, and esophagus. The ocular lesions consist of conjunctivitis, uveitis, symblepharon, or even panophthalmitis. The genital lesions are balanitis or vulvovaginitis, and scrotal erosions (Fig. **111**). The skin manifestations may vary from very light to severe. The diagnosis is mainly made on the basis of the clinical presentation.

Differential diagnosis Behçet disease, pemphigus, pemphigoid, primary herpes simplex.

Treatment Systemic steroids; antibiotics, if considered necessary in severe cases.

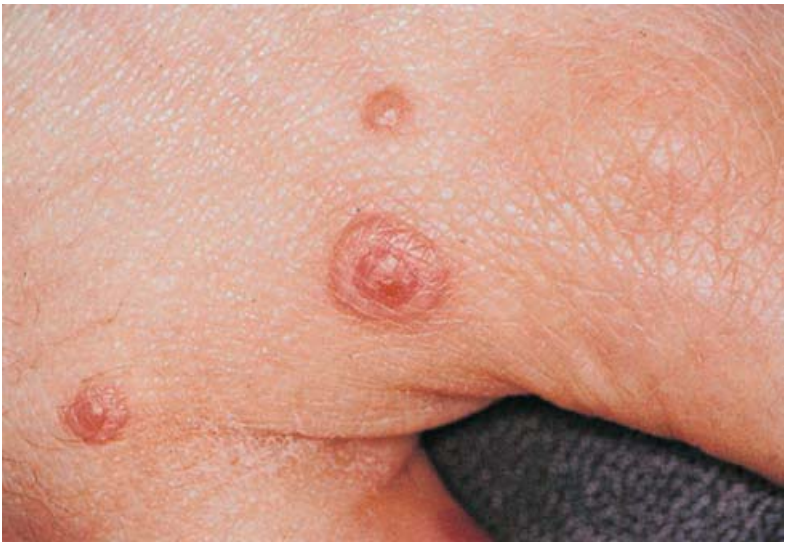


Fig. 109 Erythema multiforme: typical target- or iris-like lesions of the skin.

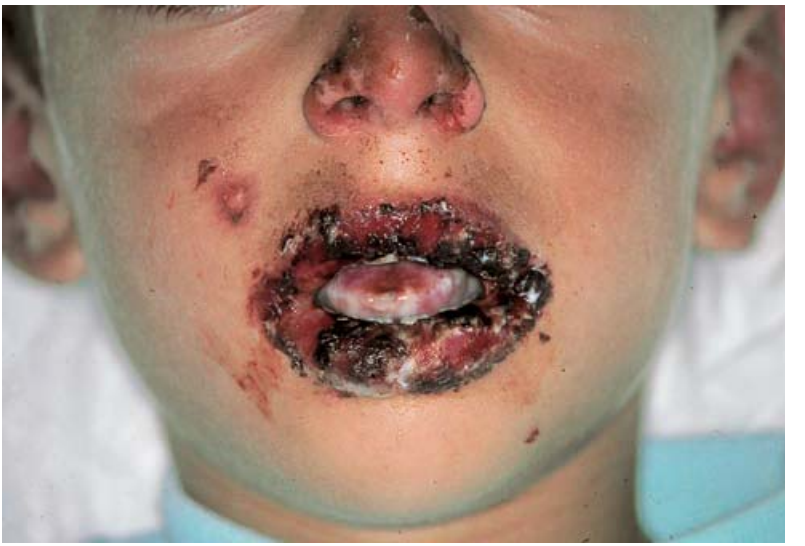


Fig. 110 Stevens–Johnson syndrome: severe erosions on the lips, tongue, and the nose in an 8-year-old boy.

Toxic Epidermal Necrolysis

Definition Toxic epidermal necrolysis, or Lyell disease, is a severe skin and mucous membrane disease with a severe prognosis.

Etiology Drugs almost always trigger the pathogenetic mechanism.

Clinical features The disease usually begins with low-grade fever, malaise, arthralgias, conjunctival burning sensation, skin tenderness, and erythema. After 24 hours, blisters appear, and the skin is lifted up so that the whole body surface appears scalded. Nikolsky's sign is positive. The oral manifestations consist of diffuse erythema, vesicles and painful erosions primarily on the lips and periorally, as well as on the buccal mucosa, tongue, and palate (Fig. **112**). Ocular, genital, and other mucous membrane lesions are common. The diagnosis is based on clinical criteria.

Differential diagnosis Stevens–Johnson syndrome, pemphigus vulgaris, severe and extensive burns.

Treatment Systemic steroids, antibiotics, fluids, and electrolytes.

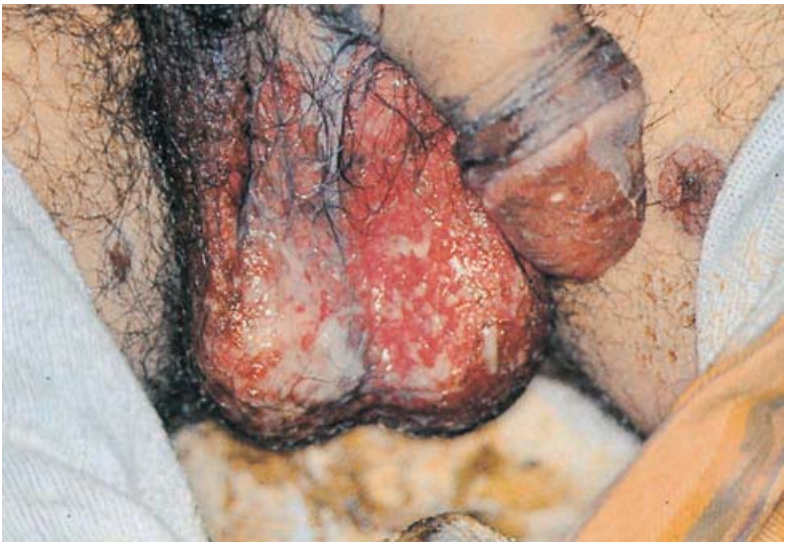


Fig. 111 Stevens–Johnson syndrome: genital lesions.

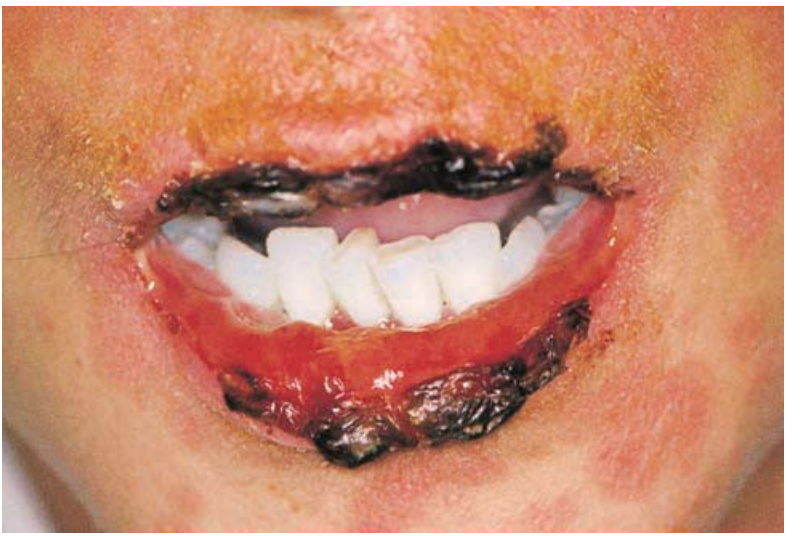


Fig. 112 Toxic epidermal necrolysis: severe erosions covered by hemorrhagic crusting on the lips.

Pemphigus

Definition Pemphigus is a severe chronic bullous autoimmune mucocutaneous disease.

Etiology Autoimmunity. Desmoglein 1 and 3 are the main target antigens.

Clinical features Four classical varieties of pemphigus are recognized: *vulgaris, vegetans, foliaceus*, and *erythematosus.* Recently, two additional forms of the disease have been described: *drug-induced pemphigus* and *paraneoplastic pemphigus,* which usually affect patients with lymphoreticular malignancies. Pemphigus vulgaris is the most common variant, representing 90–95% of cases. More than 70% of pemphigus vulgaris cases begin with oral involvement. Oral lesions are characterized by the formation of bullae, which rapidly rupture, leaving painful erosions with a tendency to extend peripherally (Figs. **113**, **114**). The buccal mucosa, labial mucosa, palate, tongue, floor of the mouth, and gingiva are often involved. The skin lesions present as flaccid bullae that rupture quickly, leaving persistent eroded areas (Fig. **115**). Nikolsky's sign is positive. Any skin area may be involved, although the intertriginous regions, umbilicus, trunk, and scalp are the most common sites affected. Lesions may develop on other mucosae (conjunctivae, nose, larynx, pharynx, genitals, anus) (Fig. **116**).

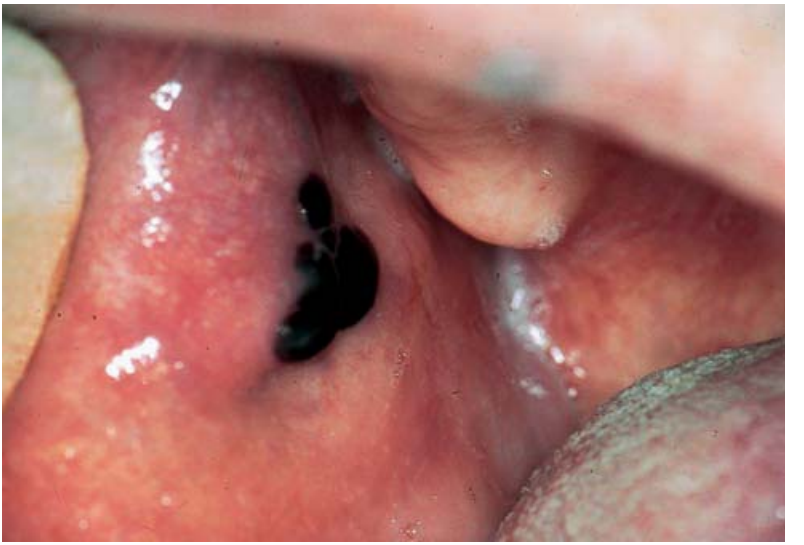


Fig. 113 Pemphigus vulgaris: hemorrhagic cluster of bullae on the buccal mucosa.

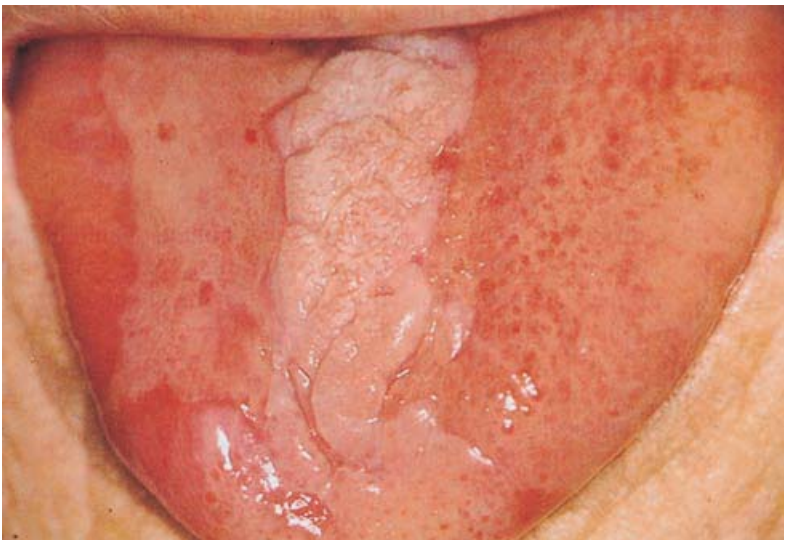


Fig. 114 Pemphigus vulgaris: erosions on the dorsum of the tongue.

Laboratory tests Histopathological and cytological examination, direct and indirect immunofluorescence.

Differential diagnosis Cicatricial pemphigoid, bullous pemphigoid, linear IgA disease, epidermolysis bullosa acquisita, toxic epidermal necrolysis, primary herpetic gingivostomatitis, erythema multiforme, erosive lichen planus, aphthous ulcers.

Treatment Systemic steroids. Ciclosporin, azathioprine, and mycophenolate mofetil may also be used, always in association with steroids. The prognosis has been improving steadily during the last two decades.

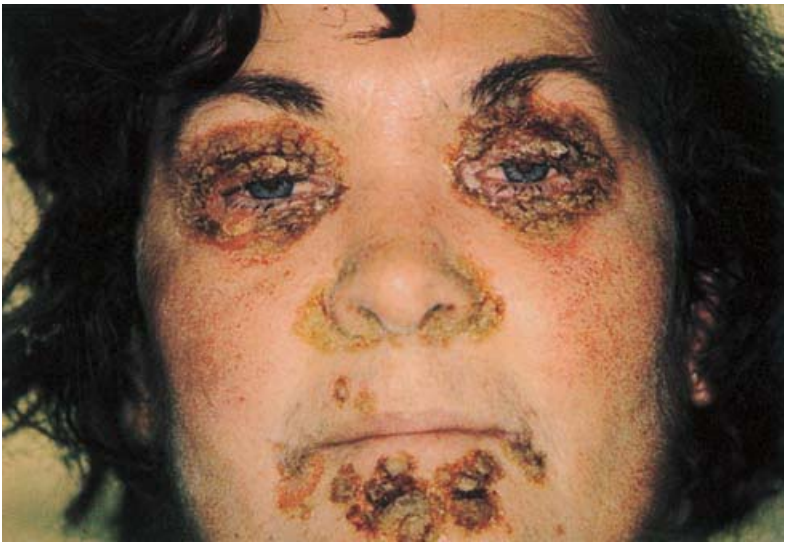


Fig. 115 Pemphigus vulgaris: severe lesions of the skin of the face.

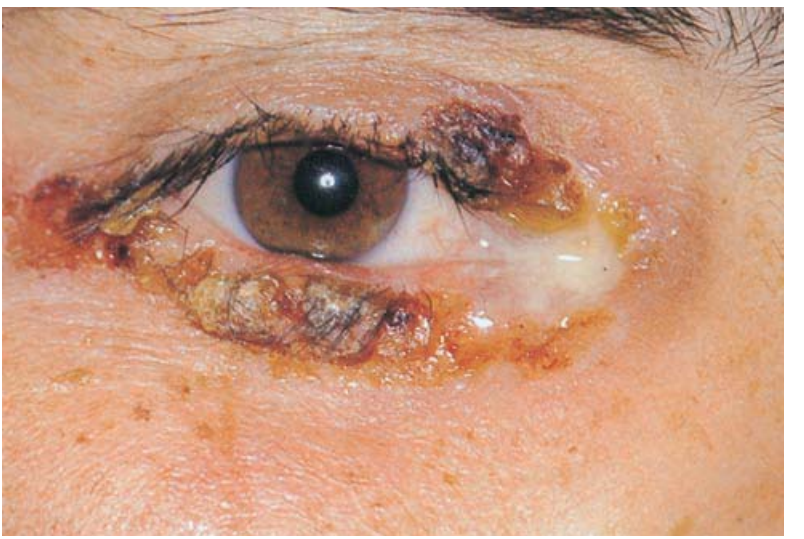


Fig. 116 Pemphigus vulgaris: ocular lesions.

Cicatricial Pemphigoid

Definition Cicatricial pemphigoid, or mucous membrane pemphigoid, is a chronic bullous mucocutaneous disease that primarily affects mucous membranes, and results in atrophy or scarring.

Etiology Autoimmunity. Bullous pemphigoid antigen (BP180), laminin 5, integrin B4, and type VII collagen are the main target antigens.

Clinical features The disease occurs more frequently in women than men (ratio 1.5 : 1), with a mean age at onset of 66 years. Oral manifestations are seen in almost all patients, but other mucosae and rarely the skin may be involved. The oral lesions are characterized by recurrent vesicles or bullae that rupture, leaving large, superficial painful ulcerations (Fig. **117**). Repeated recurrences may lead to epithelial atrophy or scarring. Usually, the lesions are limited to certain areas and they are rarely widespread. Gingival involvement is common, producing a specific clinical pattern of *desquamative gingivitis*. Ocular lesions consist of conjunctivitis, symblepharon, entropion, trichiasis, dryness, and corneal opacity, frequently leading to blindness (Fig. **118**). Less commonly, other mucosae and the skin may be involved.

Laboratory tests Histopathological examination, direct immunofluorescence.

Differential diagnosis Bullous pemphigoid, linear IgA disease, epidermolysis bullosa acquisita, pemphigus, erosive lichen planus, dermatitis herpetiformis, discoid lupus erythematosus, chronic ulcerative stomatitis.

Treatment Steroids and, rarely, immunosuppressive drugs.

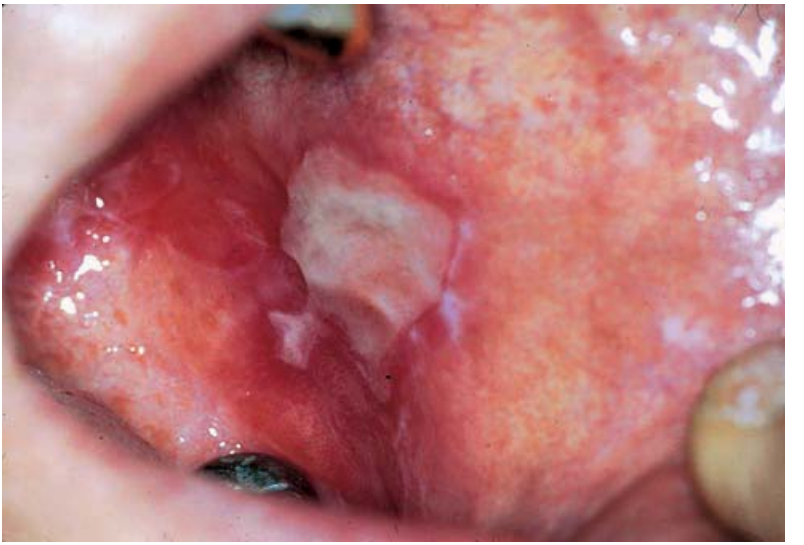


Fig. 117 Cicatricial pemphigoid: erosions on the buccosal mucosa.

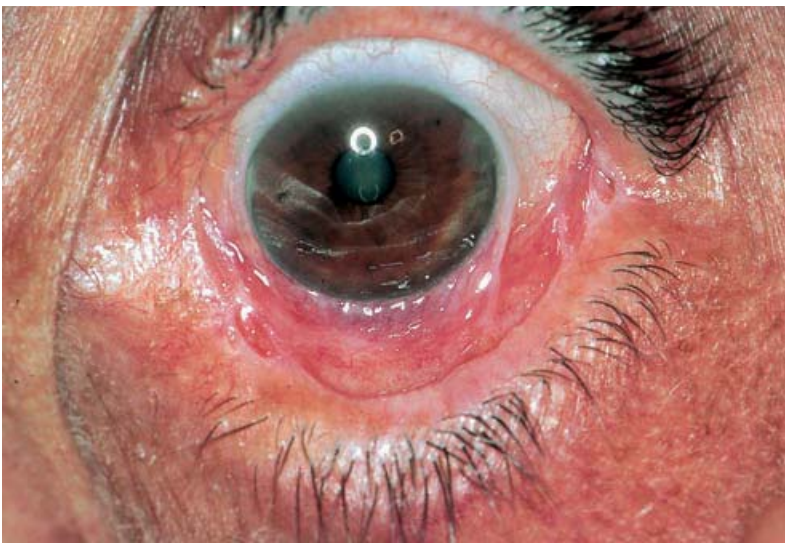


Fig. 118 Cicatricial pemphigoid: symblepharon and conjunctivitis.

Bullous Pemphigoid

Definition Bullous pemphigoid is a chronic mucocutaneous bullous disease that usually affects older individuals.

Etiology Autoimmunity. Bullous pemphigoid antigens (BP180, BP230) are the main target antigens.

Clinical features The disease affects women slightly more often than men (ratio 1.7 : 1), with a mean age of 65 years at onset. The oral mucosa is affected in about 20–40% of cases, usually after skin involvement. The oral lesions usually follow cutaneous manifestations and begin as bullae that soon rupture, leaving shallow ulcerations (Fig. **119**). Other mucous membranes may also be affected. Skin lesions are always present, and begin as a nonspecific generalized rash followed by large, tense bullae that rupture, leaving denuded areas without a tendency to extend peripherally (Fig. **120**). The trunk, arms, and legs are the sites of predilection. The prognosis is usually good.

Laboratory tests Histopathological examination, direct and indirect immunofluorescence.

Differential diagnosis Pemphigus, cicatricial pemphigoid, linear IgA disease, dermatitis herpetiformis, epidermolysis bullosa acquisita, pemphigoid gestationis.

Treatment Systemic steroids, immunosuppressive drugs, dapsone.

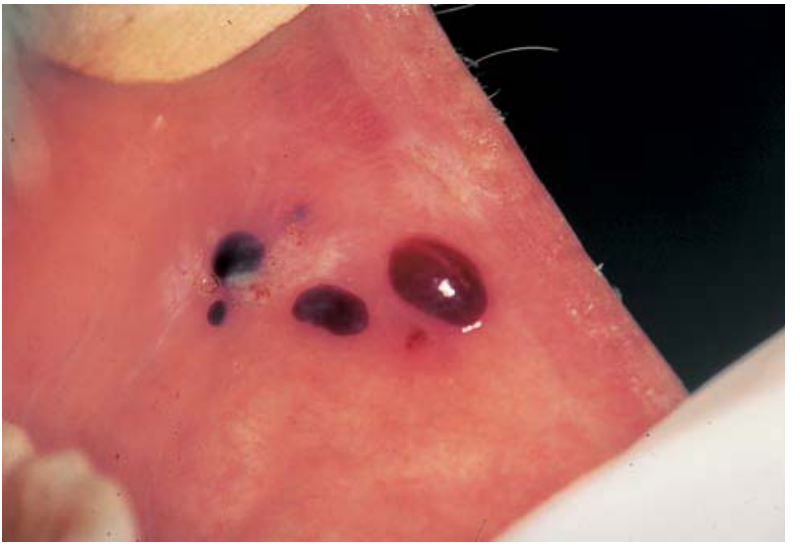


Fig. 119 Bullous pemphigoid: bullae on the buccal mucosa.

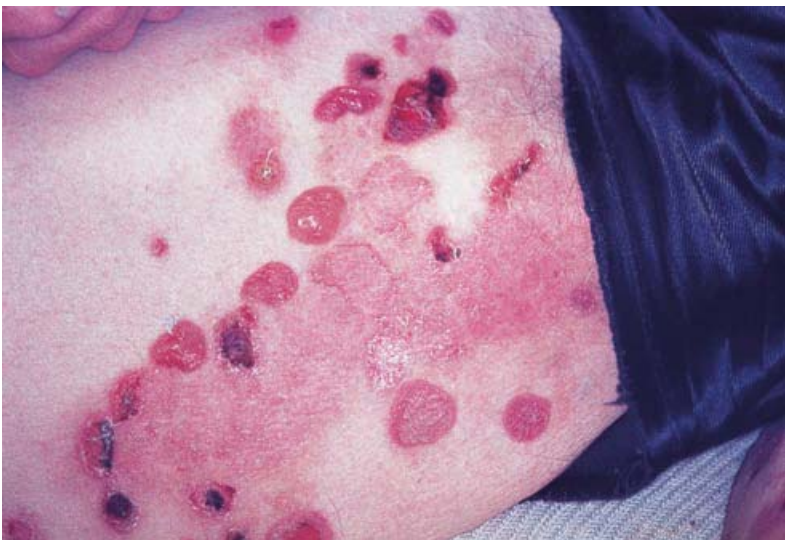


Fig. 120 Bullous pemphigoid: skin lesions.

Pemphigoid Gestationis

Definition Pemphigoid gestationis, or herpes gestationis, is a rare, acute subepidermal blistering disease occurring in the second or third trimester of pregnancy or in the early postpartum period.

Etiology Autoimmune. The autoimmune response is mainly directed to 180 kDa hemidesmosomal antigen (BP 180).

Clinical features Pemphigoid gestationis usually affects the skin and, less frequently, the mucous membranes. The skin manifestations present as pluritic, papulobullous eruptions and erythema (Fig. **121**). The bullae are numerous and often coalesce and soon rapture leaving painful ulcerations. The abdomen, chest, back, extremities, palms, and soles are the sites of predilection. The oral lesions are rare and present as multiple, usually hemorrhagic bullae that rupture quickly leaving painful ulcerations (Fig. **122**). The buccal mucosa, palate, tongue, and gingiva are the most frequently affected areas. The oral lesions usually follow the skin lesions. Other mucosae—e. g., conjunctival, vaginal, and anal—may rarely be affected. The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests Histopathological examination, direct and indirect immunofluorescence tests.

Differential diagnosis Bullous pemphigoid, cicatricial pemphigoid, linear IgA disease, dermatitis herpetiformis, epidermolysis bullosa acquisita, erythema multiforme, bullous systemic lupus erythematosus, drug eruptions.

Treatment Systemic corticosteroids, azathioprine, and plasmapheresis.

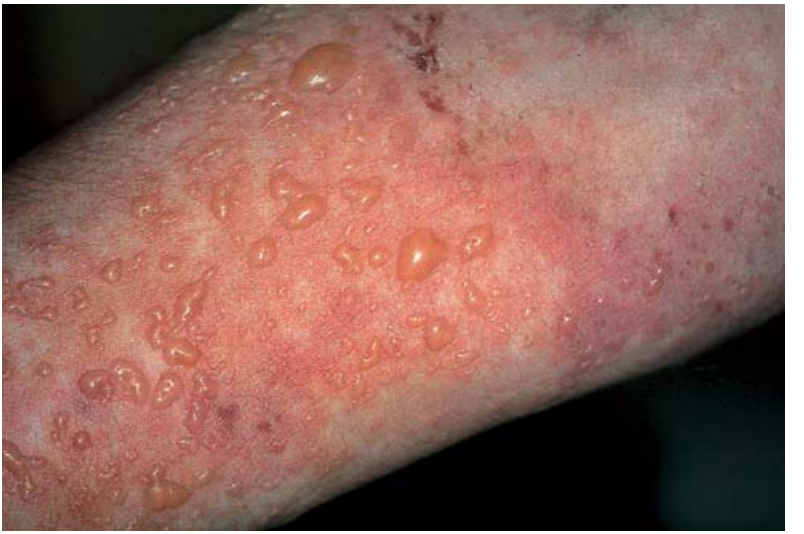


Fig. 121 Pemphigoid gestationis, multiple small bullae on the skin.

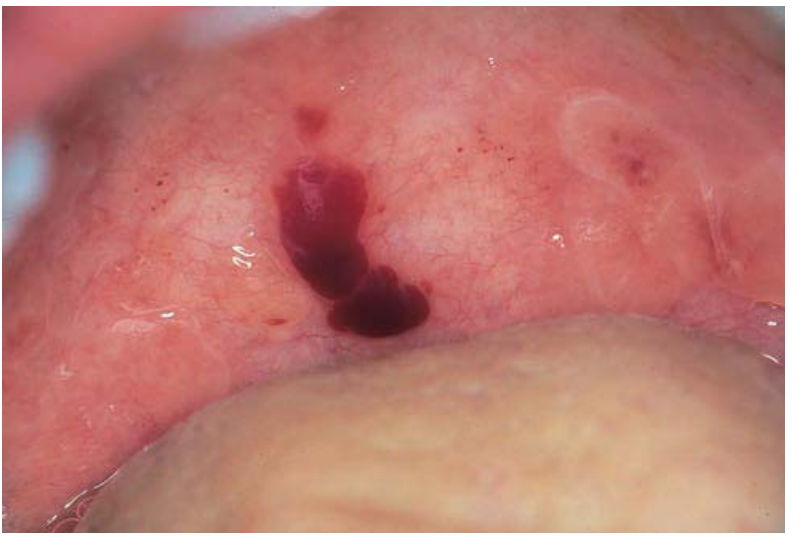


Fig. 122 Pemphigoid gestationis, hemorrhagic bullae on the soft palate.

Linear IgA Disease

Definition Linear immunoglobulin A (IgA) disease is a disorder that has recently been recognized in the spectrum of chronic bullous diseases, characterized by the linear deposition of IgA along the basement membrane zone.

Etiology Autoimmunity.

Clinical features The disease is more common in women than in men, and usually occurs between the ages of 40 and 50 years, although children may also be affected. Oral lesions occur in about 20–30% of cases, and are characterized by the formation of bullae that soon rupture, leaving superficial, nonspecific ulcerations (Figs. **123**, **124**). The skin lesions consist of bullae that rupture, forming ulcerations covered by crusts. Scarring conjunctivitis may also occur. The clinical features of the disease are similar to those seen in cicatricial pemphigoid.

Laboratory tests Histopathological examination, direct and indirect immunofluorescence.

Differential diagnosis Cicatricial pemphigoid, bullous pemphigoid, pemphigus, dermatitis herpetiformis, pemphigoid gestationis.

Treatment Dapsone and steroids.

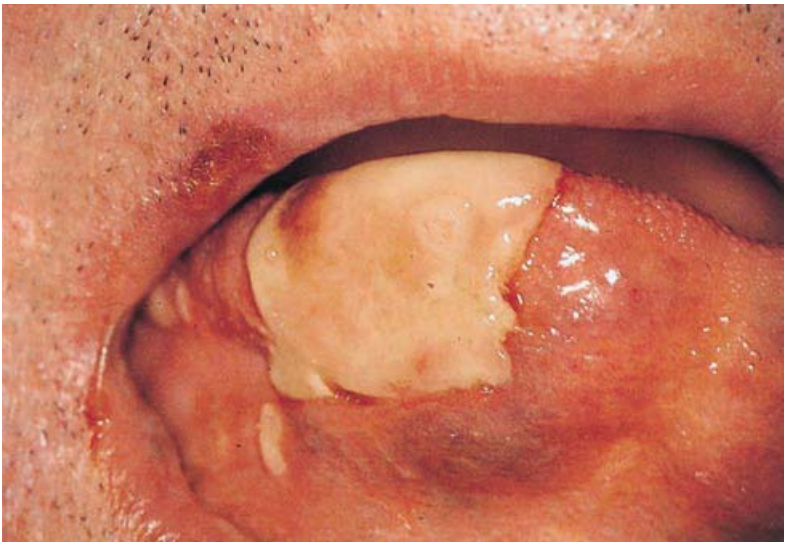


Fig. 123 Linear IgA disease: erosion on the tongue, covered by a whitish pseudomembrane.

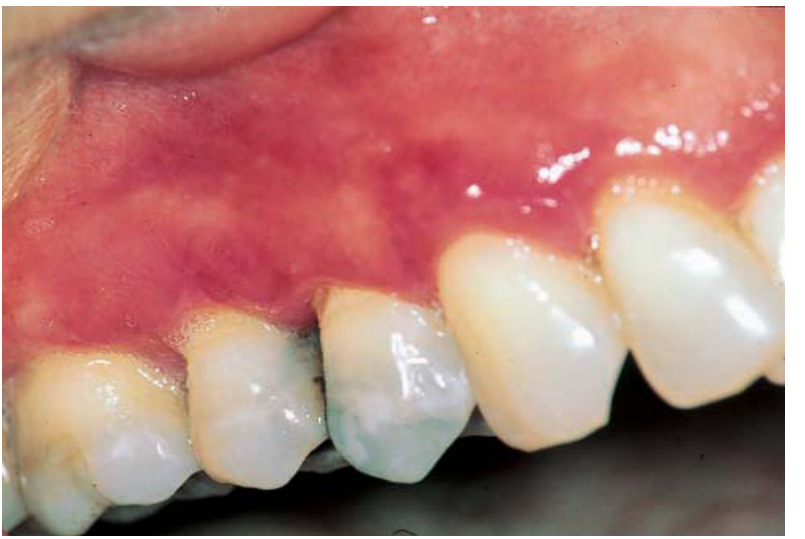


Fig. 124 Linear IgA disease: early gingival lesions.

Dermatitis Herpetiformis

Definition Dermatitis herpetiformis, or Duhring–Brocq disease, is a chronic recurrent cutaneous bullous disease, rarely with oral involvement.

Etiology Unclear. Immunological and genetic factors, as well as gluten sensitivity, may be involved in the pathogenesis.

Clinical features The disease is more common in men between the ages of 20 and 50 years. The oral mucosa is affected in 5–10% of cases. Oral manifestations follow the skin eruption, and present as maculopapular, erythematous, purpuric, and mainly vesicular lesions. The vesicles appear in a cyclic pattern, and rupture rapidly, leaving shallow, painful ulcerations (Fig. **125**). The tongue, buccal mucosa, and palate are more frequently involved. Cutaneous lesions are always present and appear as erythematous papules or plaques followed by severe burning and pruritus and small vesicles that group in a herpeslike pattern. The lesions exhibit exacerbations and remissions, and are commonly located symmetrically on the extensor surfaces.

Laboratory tests Histopathological examination, direct and indirect immunofluorescence.

Differential diagnosis Bullous pemphigoid, cicatricial pemphigoid, linear IgA disease, pemphigus, herpetiform ulcers.

Treatment Sulfones and sulfapyridines. A gluten-free diet may control the disease activity.

Bullous Lichen Planus

Definition Bullous lichen planus is a rare form of lichen planus (see p. 4).

Clinical features It is clinically characterized by the formation of bullae that soon rupture, leaving painful shallow ulcerations (Fig. **126**). The bullae usually arise on a background of papules or striae with the typical pattern of lichen planus.

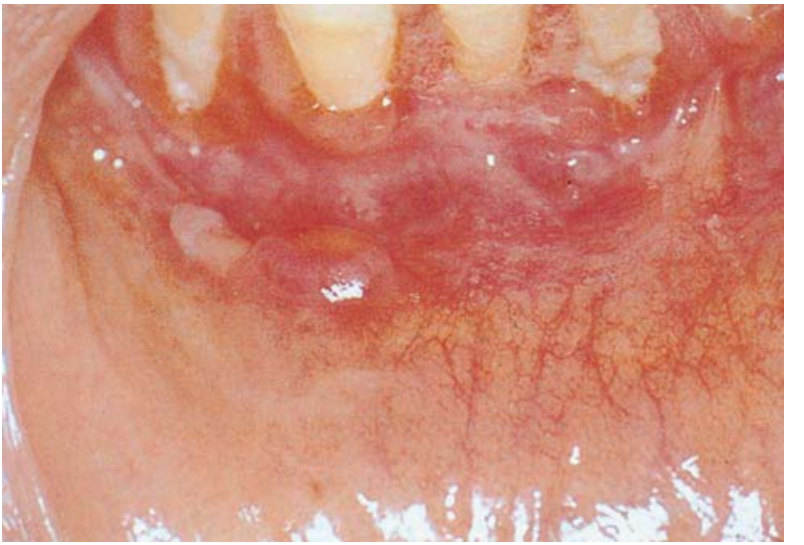


Fig. 125 Dermatitis herpetiformis: intact bulla on the lower lip mucosa and small erosions on the gingiva.

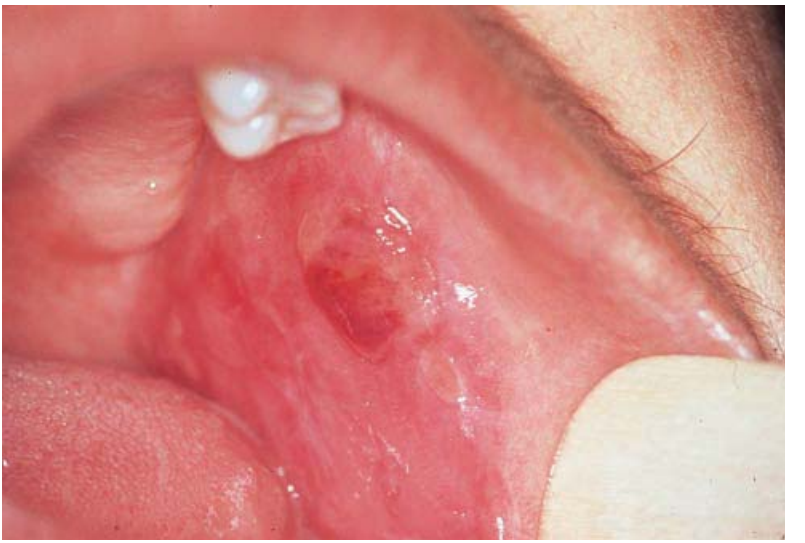


Fig. 126 Lichen planus of the buccal mucosa: bullous form.

Laboratory tests Histopathological examination, direct immunofluorescence.

Differential diagnosis Cicatricial pemphigoid, linear IgA disease, pemphigus, erythema multiforme, drug reactions.

Treatment Topical or systemic steroids in low doses, in severe cases.

Epidermolysis Bullosa

Definition Epidermolysis bullosa is a heterogeneous group of usually inherited mucocutaneous bullous disorders.

Etiology Genetic.

Clinical features Depending on the defective mechanism of cellular cohesion, three main inherited groups are recognized: *simplex, junctional,* and *dystrophic.* Each group includes several forms, depending on the inheritance pattern. The clinical spectrum and the degree of severity may range from mild to severe or fatal. The lesions appear at birth or early in infancy. Oral manifestations are more common in the junctional and dystrophic forms. Oral lesions present as bullae, usually in areas of friction, which rupture, leaving shallow ulcers, and later atrophy and scarring (Figs. **127**, **128**). Dysplastic teeth may be seen in the severe forms of the disease. Leukoplakia and squamous-cell carcinoma may develop on the scars. Skin lesions are characterized by the formation of bullae, followed by ulcerations and scarring, particularly in areas exposed to low-grade chronic trauma (Figs. **129**, **130**). Nail involvement, deformities of hands and feet, milia formation, and involvement of the larynx, pharynx, and esophagus are common in the recessive dystrophic type.

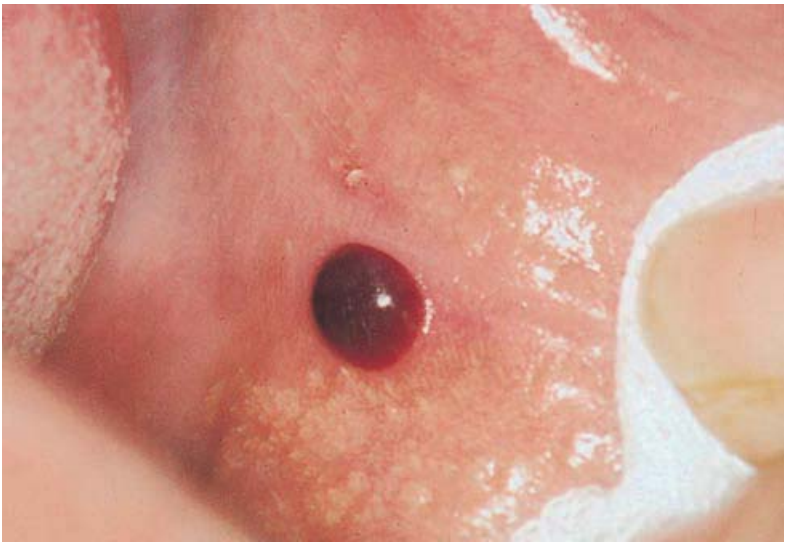


Fig. 127 Epidermolysis bullosa simplex: hemorrhagic bulla on the buccal mucosa.

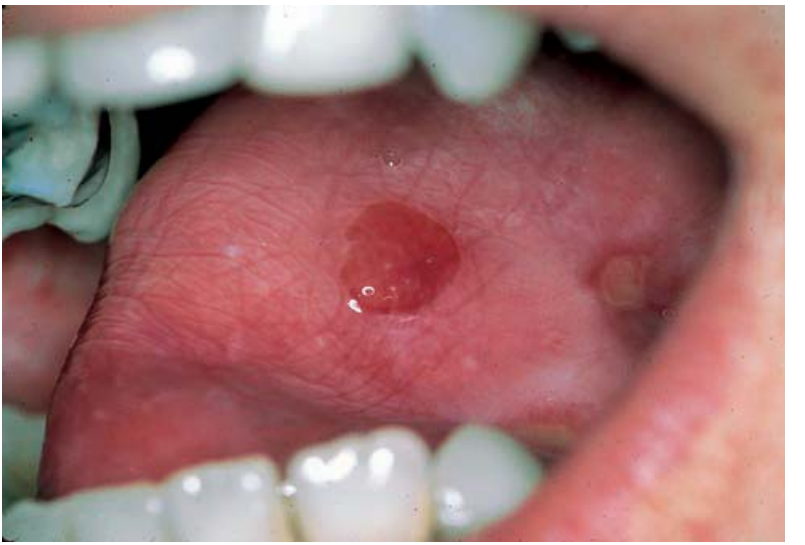


Fig. 128 Epidermolysis bullosa, recessive dystrophic form: bulla and scarring on the tongue.

Laboratory tests Histopathological and immunohistochemical examination.

Differential diagnosis Pemphigus, cicatricial and bullous pemphigoid, linear IgA disease, bullous dermatoses of childhood, epidermolysis bullosa acquisita.

Treatment Supportive. Systemic steroids in severe cases.

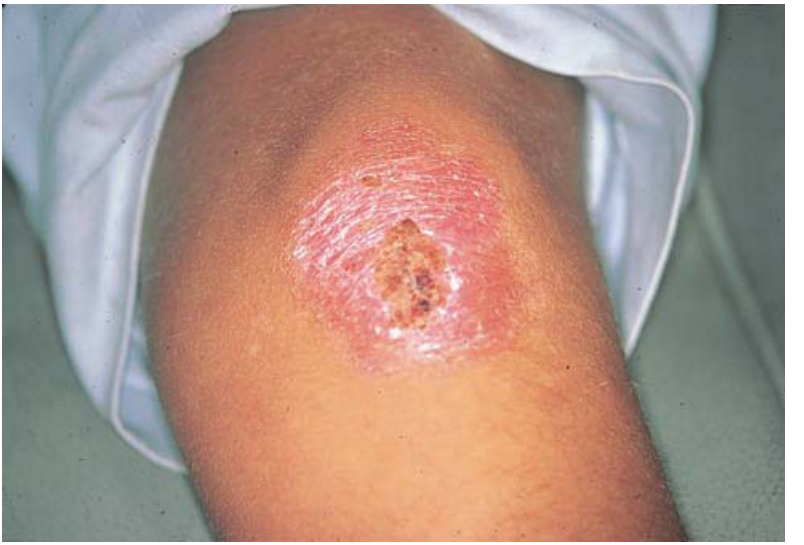


Fig. 129 Epidermolysis bullosa, skin scarring.

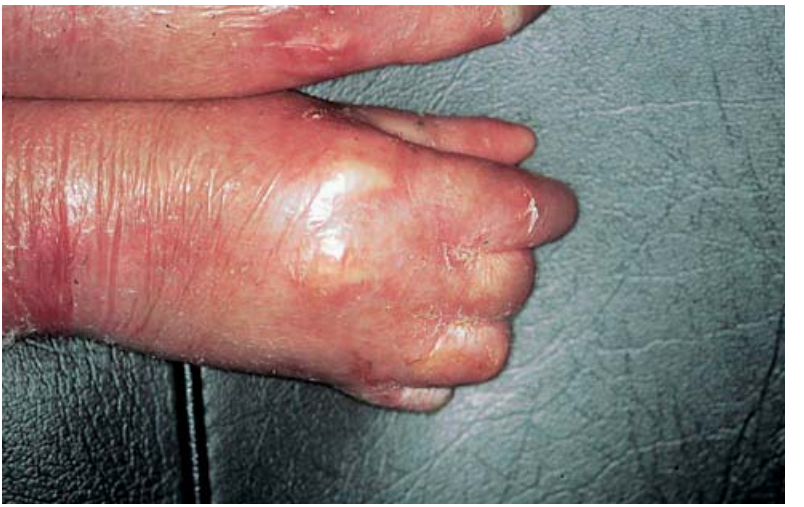


Fig. 130 Epidermolysis bullosa, dystrophic: severe scarring and dystrophy of the hands.

Epidermolysis Bullosa Acquisita

Definition Epidermolysis bullosa acquisita is a rare, noninherited, chronic mechanobullous disease involving the skin and mucous membranes.

Etiology Autoimmune. Type VII collagen has been identified as the main target antigen.

Clinical features The skin lesions present as hemorrhagic bullae and ulcerations usually at the sites of mechanical irritation. The lesions heal with scarring and milia (Fig. **131**). The dorsum of the hands and arms, feet, knees, and elbows are more frequently affected. Atrophic skin areas, hyperpigmentation, alopecia, and nail dystrophy may occur. The oral lesions are common (over 50%) and present as solitary or multiple bullae and painful ulcerations (Fig. **132**). Gingival involvement may present as *desquamative gingivitis* or as localized bullae that rupture, leaving painful ulcerations. Scarring on the oral mucosa may occur. There is no family history of blistering disease. The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests Histopathological examination, direct and indirect immunofluorescent tests.

Differential diagnosis Cicatricial pemphigoid, bullous pemphigoid, linear IgA disease, pemphigus, genetic epidermolysis bullosa, dermatitis herpetiformis, chronic ulcerative stomatitis, angina bullosa hemorrhagica, systemic lupus erythematosus, porphyria cutanea tarda.

Treatment. Systemic and/or topical corticosteroids, immunosuppressives, colchicine, immunoglobulin. Mechanical irritations should be avoided.

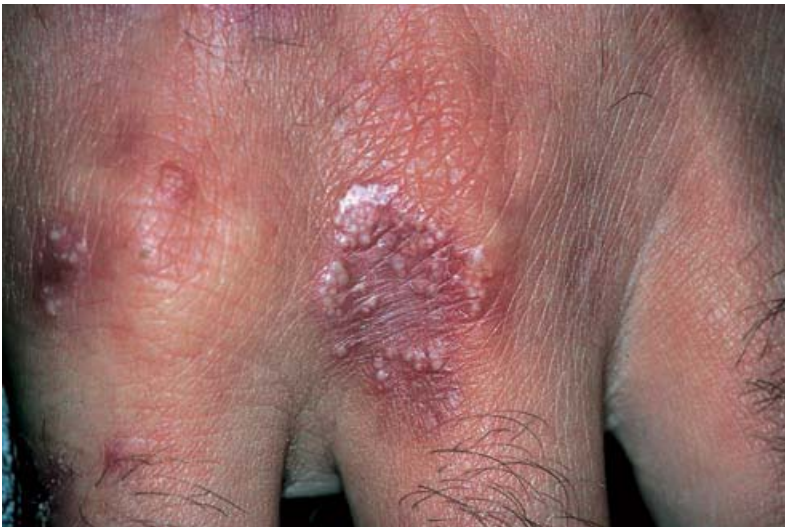


Fig. 131 Epidermolysis bullosa acquisita, milia and scarring of the skin.

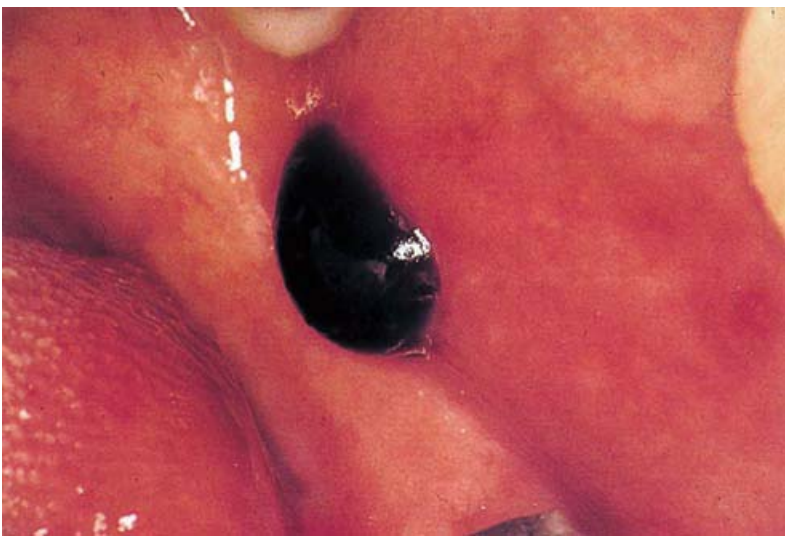


Fig. 132 Epidermolysis bullosa acquisita, hemorrhagic bulla on the buccal mucosa.

Angina Bullosa Hemorrhagica

Definition Angina bullosa hemorrhagica is a rare acute and benign blood blistering oral disorder.

Etiology The exact etiology is unknown. However, mild trauma and the chronic use of steroid inhalers seem to play an important role in the development of the lesions.

Clinical features Clinically, it appears as single or multiple hemorrhagic bullae that rupture spontaneously within hours or 1–2 days, leaving superficial ulcerations that heal without scarring in 5–10 days (Figs. **133**, **134**). The soft palate, buccal mucosa, and tongue are the sites of predilection. The disorder is more common in middle-aged women. The diagnosis is mainly based on the history and the clinical presentation. However, laboratory tests are sometimes necessary to rule out any other bullous diseases.

Laboratory tests Histopathological examination and immunofluorescent tests.

Differential diagnosis Epidermolysis bullosa acquisita, cicatricial pemphigoid, bullous pemphigoid, linear IgA disease, pemphigoid gestationis, pemphigus, bullous lichen planus, amyloidosis, blood dyscrasias.

Treatment Treatment is symptomatic.

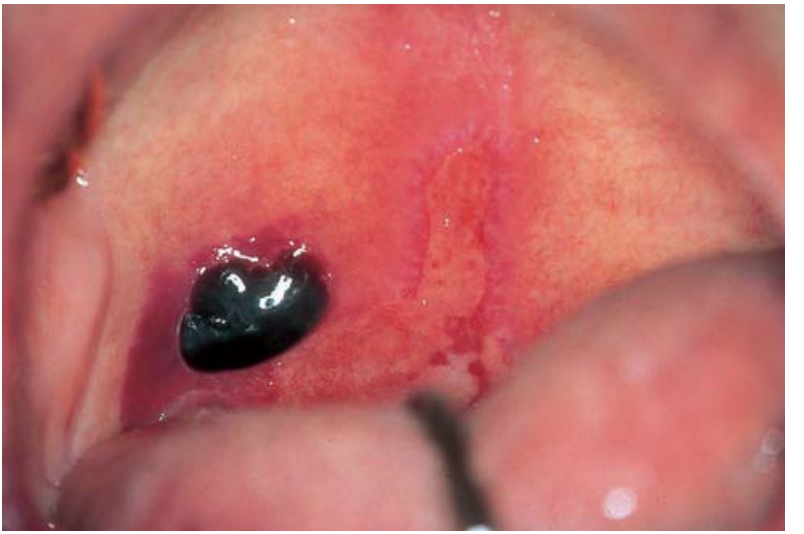


Fig. 133 Angina bullosa hemorrhagica, hemorrhagic bulla and ulcer on the soft palate.

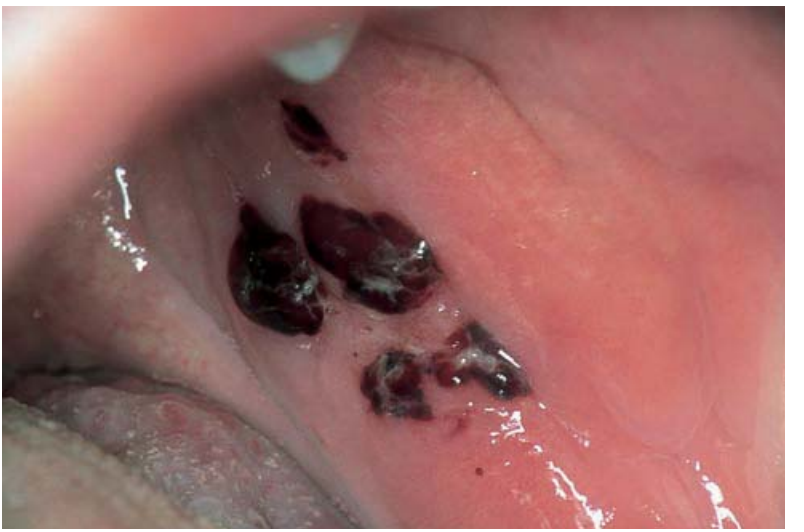
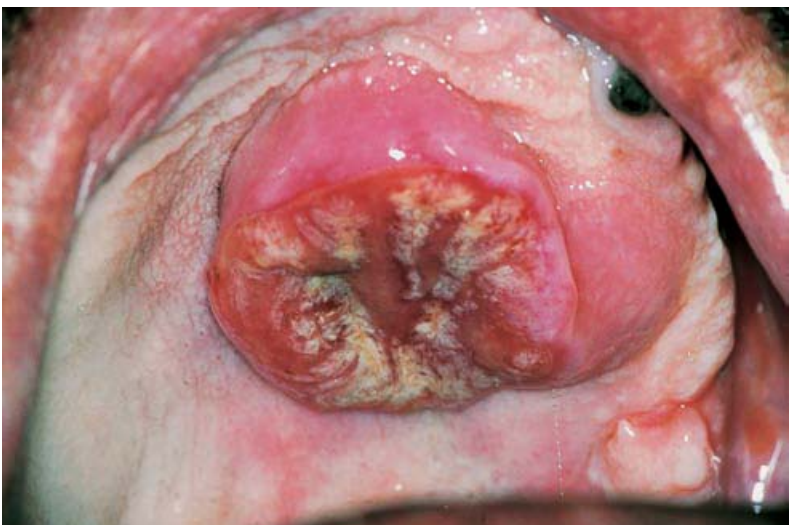


Fig. 134 Angina bullosa hemorrhagica, multiple hemorrhagic bullae on the buccal mucosa.

5 Ulcerative Lesions

Ulcerative lesions are a group of common oral mucosal disorders. The most common causes of these lesions are mechanical and reactive factors, infectious diseases, and neoplasms, as well as autoimmune and hematological disorders. The main clinical feature in all these conditions is an ulcer, which is defined as loss of all epithelial layers. In addition, the term "erosion" is used to defined a superficial loss of epithelium. However, at the clinical level, the terms "ulcer" and "erosion" are usually used interchangeably. In this chapter, only primary ulcerative lesions are discussed, and not lesions that arise secondarily from ruptured bullae.

- Traumatic ulcer
- Eosinophilic ulcer
- Necrotizing sialadenometaplasia
- Necrotizing ulcerative gingivitis
- Necrotizing ulcerative stomatitis
- Chronic ulcerative stomatitis
- Noma
- Syphilis
- Tuberculosis
- Systemic mycoses
- Recurrent aphthous ulcers
- Behçet disease
- Graft-versus-host disease
- Wegener granulomatosis
- Malignant granuloma



- Non-Hodgkin lymphoma
- Squamous-cell carcinoma
- Cyclic neutropenia
- Agranulocytosis
- Myelic aplasia
- Myelodysplastic syndrome
- Leukemias
- Langerhans cell histiocytosis
- Glycogen storage disease, type Ib
- FAPA syndrome
- Sweet syndrome
- Staphylococcal infection
- Congenital neutropenia
- Cytomegalovirus infection

Traumatic Ulcer

Definition and etiology Traumatic ulcers are common oral lesions, and can be caused by a sharp or broken tooth, rough fillings, dental instruments, biting, denture irritation, sharp foreign bodies, etc.

Clinical features They are clinically diverse, but usually appear as a single, painful ulcer with a smooth red or whitish-yellow surface and a thin erythematous halo (Figs. **135**, **136**, **137**). They are usually soft on palpation, and heal without scarring within 6–10 days, spontaneously or after removal of the cause. However, chronic traumatic ulcers may clinically mimic a carcinoma. The tongue, lip, and buccal mucosa are the sites of predilection. The diagnosis is based on the history and clinical features. However, if an ulcer persists over 10–12 days a biopsy must be taken to rule out cancer.

Laboratory tests Histopathological examination.

Differential diagnosis Squamous-cell carcinoma and other malignancies, eosinophilic ulcer, aphthous ulcer, Riga–Fede disease, syphilis, tuberculosis, systemic mycoses.

Treatment Removal of traumatic factors. Topical steroids may be used for a short time.

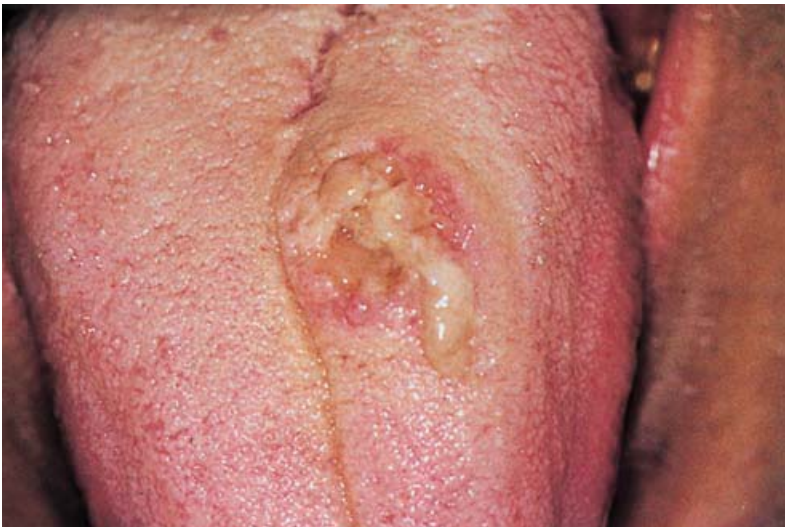


Fig. 135 Traumatic ulcer of the tongue.

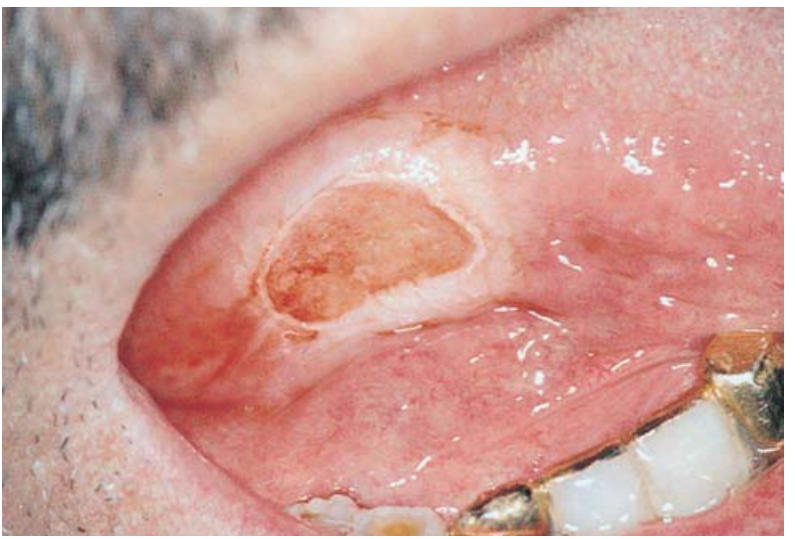


Fig. 136 Traumatic ulcer of the tongue.

Eosinophilic Ulcer

Definition Eosinophilic ulcer, or traumatic ulcerative granuloma with eosinophilia, is a rare, often self-limiting, benign lesion of the oral mucosa not related to Langerhans cell histiocytosis.

Etiology Traumatic injury is probably the cause.

Clinical features Clinically, the lesions appear as painful inflammatory ulcers with an irregular surface, a raised border, and covered with a whitish-yellow pseudomembrane (Fig. **138**). The ulcers may be single or multiple, and develop suddenly.

Laboratory tests Histopathological examination is always necessary for a final diagnosis.

Differential diagnosis Riga–Fede disease, major aphthous ulcers, traumatic ulcer, necrotizing sialadenometaplasia, Wegener granulomatosis, malignant granuloma, lymphoma, hematological disorders.

Treatment Spontaneous healing is common. A low dose of steroids for a short time is also helpful.

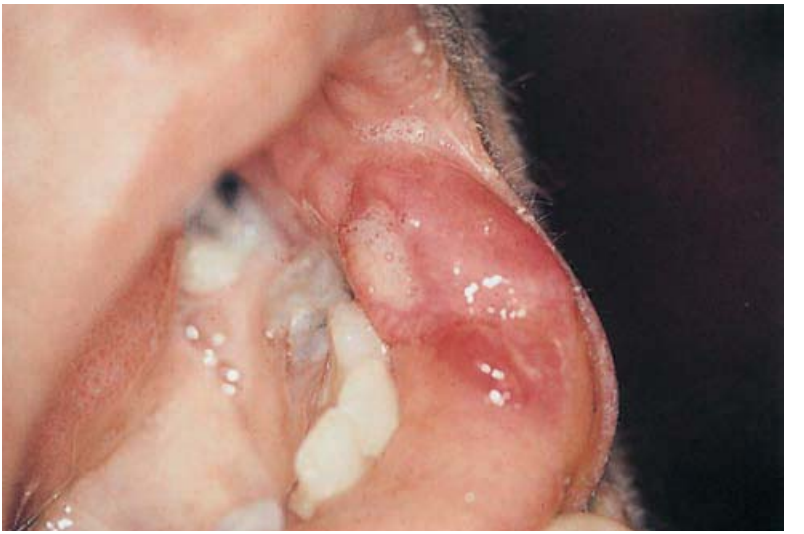


Fig. 137 Traumatic ulcer on the lower lip.

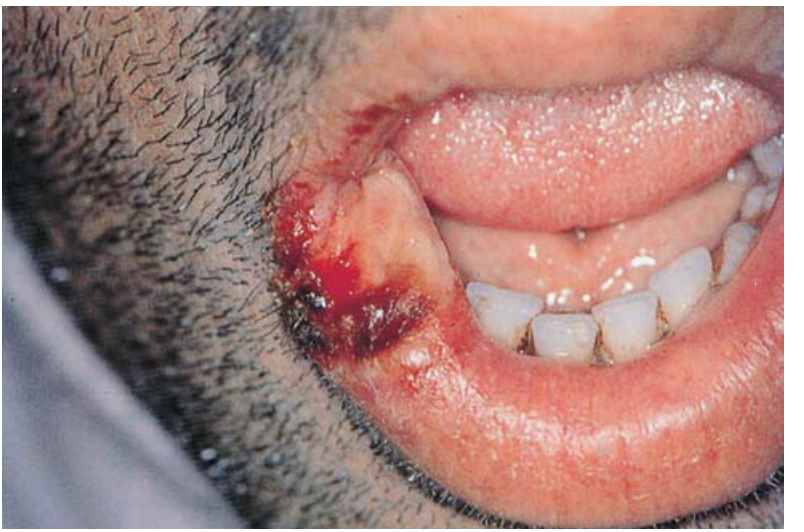


Fig. 138 Eosinophilic ulcer on the lower lip and the commissure.

Necrotizing Sialadenometaplasia

Definition Necrotizing sialadenometaplasia is an uncommon, usually self-limiting, benign inflammatory disorder of the salivary glands.

Etiology The cause is uncertain, although the hypothesis of ischemic necrosis after vascular infarction seems acceptable.

Clinical features The lesion has a sudden onset, and is clinically characterized by a nodular swelling that leads to a painful craterlike ulcer, 1–5 cm in diameter, with an irregular, ragged border (Figs. **139**, **140**). The lesion mimics a carcinoma, and is usually located on the posterior palate. Men are affected approximately twice as often as women.

Laboratory tests Histopathological examination.

Differential diagnosis Squamous-cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, traumatic ulcer, malignant granuloma.

Treatment The lesion usually heals spontaneously within 4–8 weeks.

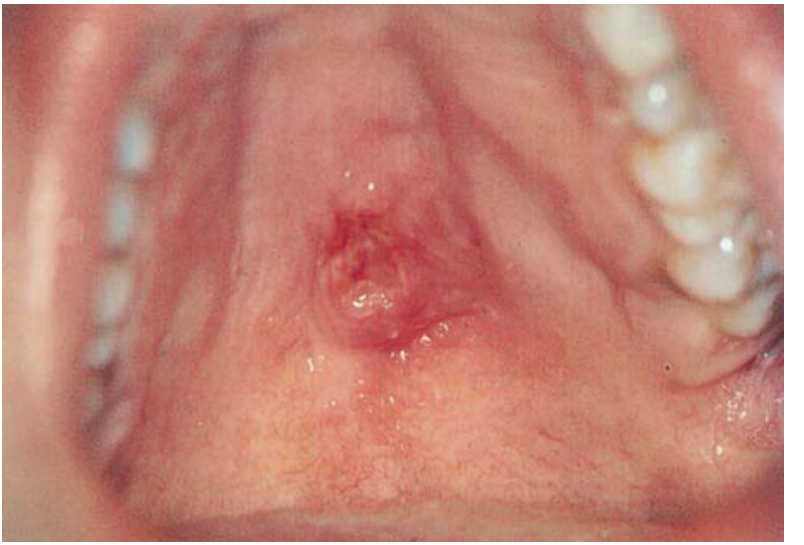


Fig. 139 Necrotizing sialadenometaplasia on the palate.

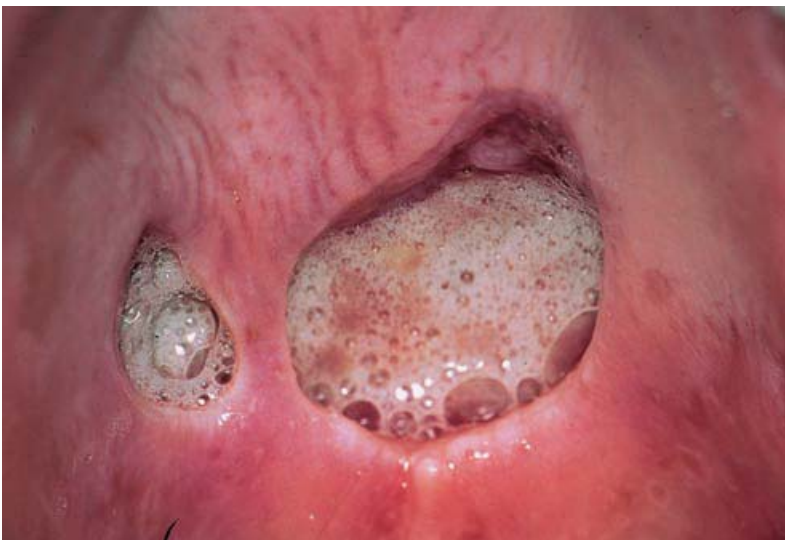


Fig. 140 Necrotizing sialadenometaplasia: two ulcers on the palate

Necrotizing Ulcerative Gingivitis

Definition Necrotizing ulcerative gingivitis is a relatively rare specific infectious gingival disease of young persons.

Etiology *Fusobacterium nucleatum*, *Treponema vincentii*, and probably other bacteria play an important role. Predisposing factors are emotional stress, smoking, poor oral hygiene, local trauma, and mainly HIV infection.

Clinical features The characteristic clinical feature is painful necrosis of the interdental papillae and the gingival margins, and the formation of craters covered with a gray pseudomembrane (Fig. **141**). Spontaneous gingival bleeding, halitosis, and intense salivation are common. Fever, malaise, and lymphadenopathy are less common. Rarely, the lesions may extend beyond the gingiva (*necrotizing ulcerative stomatitis*) (Fig. **142**). The diagnosis is made at the clinical level.

Differential diagnosis Herpetic gingivitis, desquamative gingivitis, agranulocytosis, leukemia, scurvy, noma.

Treatment Systemic metronidazole and oxygen-releasing agents topically are the best therapy in the acute phase, followed by a mechanical gingival treatment.

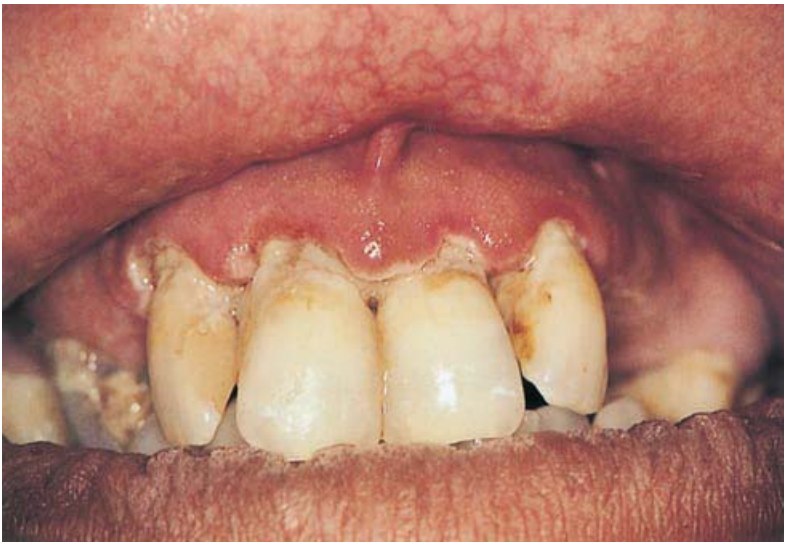


Fig. 141 Severe necrotizing gingivitis in a 32-year-old HIV-seropositive homosexual man.

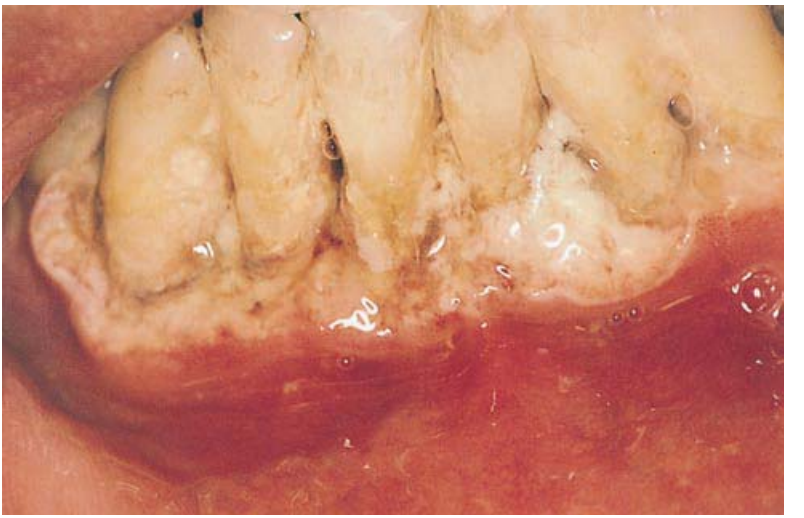


Fig. 142 Necrotizing gingivitis and stomatitis in a 30-year-old man with AIDS. Note the extensive soft-tissue necrosis beyond the gingiva.

Chronic Ulcerative Stomatitis

Definition Chronic ulcerative stomatitis is a rare oral disease with characteristic immunofluorescent pattern.

Etiology Autoimmune disease with specific antinuclear antibodies directed against the stratified epithelium.

Clinical features The disease involves, almost exclusively, the oral mucosa and has a chronic course with recurrences. The main target of the disease is the gingiva, where the lesions appear in the form of *desquamative gingivitis* or as localized painful erythema and ulcerations (Fig. **143**). Painful superficial ulcerations, usually associated with reticular white lesions identical to those seen in oral lichen planus, and discoid lupus erythematosus may also occur on the buccal mucosa and the tongue (Fig. **144**). The clinical diagnosis should be confirmed by laboratory examination.

Laboratory tests Histopathological examination, direct and indirect immunofluorescent tests.

Differential diagnosis Lichen planus, discoid lupus erythematosus, cicatricial pemphigoid, linear IgA disease, epidermolysis bullosa acquisita, pemphigus, idiopathic form of desquamative gingivitis.

Treatment Local or systemic corticosteroids, hydroxychloroquine.

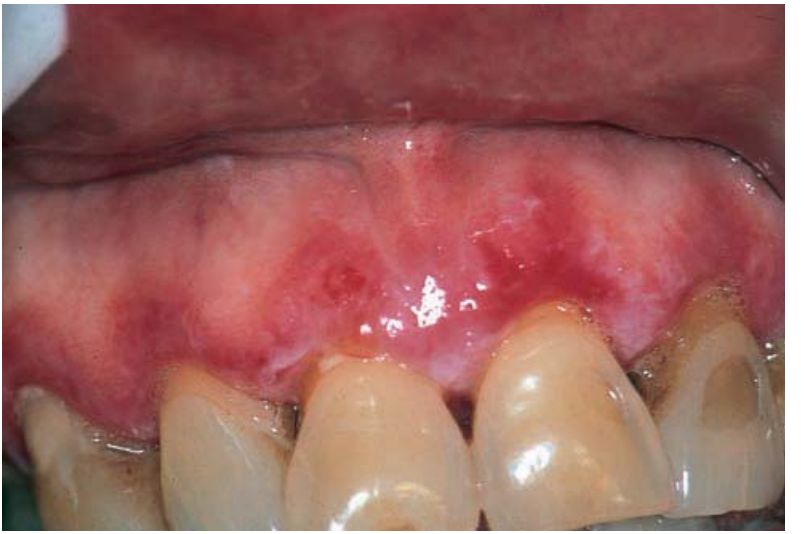


Fig. 143 Chronic ulcerative stomatitis, gingival lesions in the form of desquamative gingivitis.

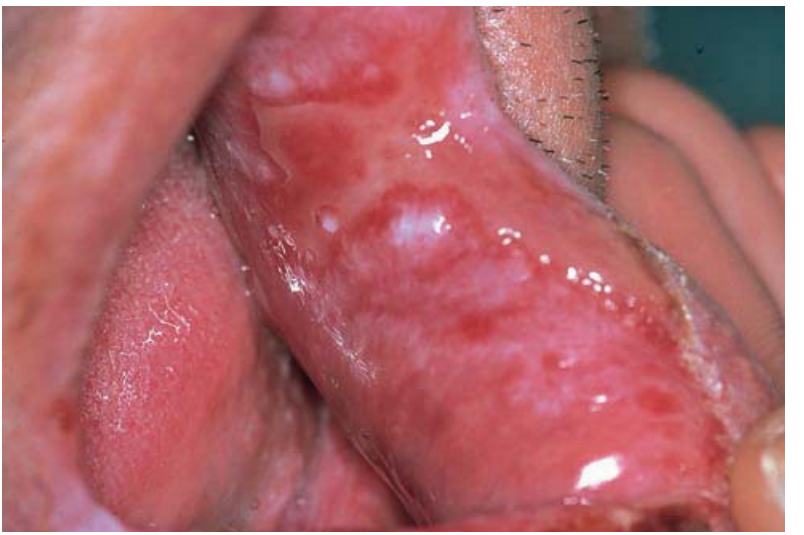


Fig. 144 Chronic ulcerative stomatitis, erosions on the buccal mucosa identical to lichen planus.

Noma

Definition Noma, or gangrenous stomatitis, is a rare rapidly progressive, opportunistic infection involving the oral tissues.

Etiology *Fusobacterium nucleatum*, *Prevotella intermedia*, *Borrelia vincentii*, *Streptococcus* species, and *Staphylococcus aureus* are the main pathogenic microorganisms. Predisposing factors are poor oral hygiene, severe protein malnutrition, severe diabetes mellitus, leukemias, and other malignancies and immune defects.

Clinical features Noma usually begins as necrotizing ulcerative gingivitis that quickly spreads to the adjacent soft tissue forming abnormal necrotizing ulcerations. The gangrenous necrosis progressively involves the buccae, the lips, and the adjacent bone, producing catastrophic lesions on the face (Figs. **145**, **146**). The ulcers are covered with whitish-yellow or brown fibrin and debris. Salivation, halitosis, fever, malaise, and regional lymphadenopathy are common. The diagnosis is usually based on the history and the clinical features.

Differential diagnosis Malignant granuloma, tuberculosis, agranulocytosis, leukemias.

Treatment Appropriate antibiotics, and conservative debridement of destructed tissues.

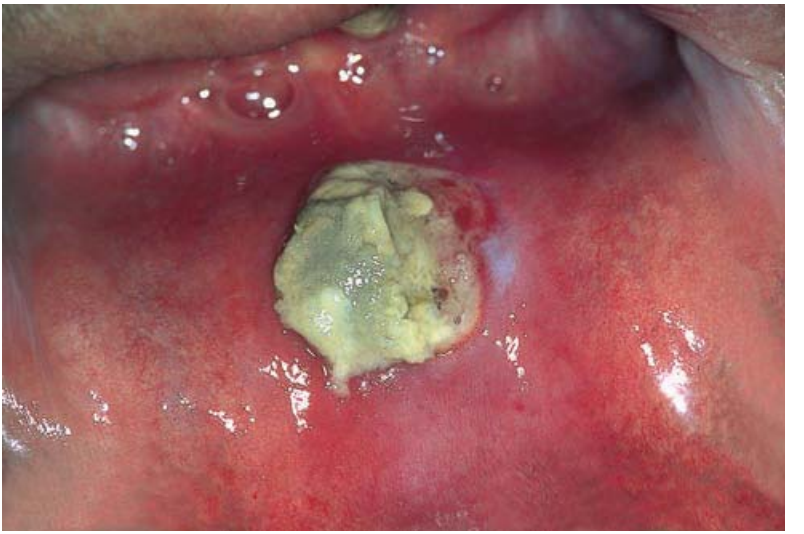


Fig. 145 Noma, early necrotic ulcer of the lower lip.

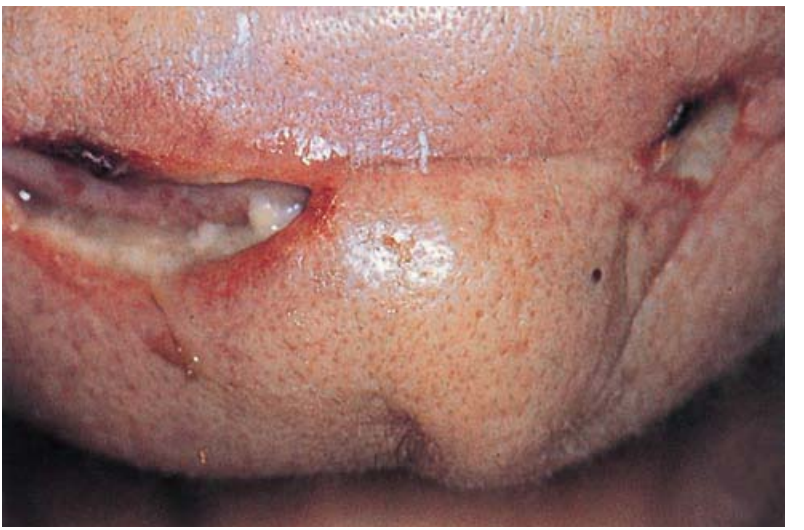


Fig. 146 Noma, destructive necrosis of oral and facial tissues.

Syphilis

Definition Syphilis is a relatively common sexually transmitted disease.

Etiology *Treponema pallidum*.
Clinical features Syphilis may be *acquired* (common) or *congenital* (rare). Acquired syphilis is classified as *primary*, *secondary* and *tertiary*.

The characteristic lesion in the primary stage is the chancre that appears at the site of inoculation, usually three weeks after the infection. Oral chancre appears in about 5–10% of cases, and clinically presents as a painless ulcer with a smooth surface, raised borders, and an indurated base (Figs. **147**, **148**). Regional lymphadenopathy is a constant finding.

The secondary stage begins 6–8 weeks after the appearance of the chancre, and lasts for 2–10 weeks. Oral lesions are mucous patches (common) (Fig. **149**), macular syphilids, and condylomata lata (rare) (Fig. **150**). Constitutional symptoms and signs (malaise, low-grade fever, headache, lacrimation, sore throat, weight loss, myalgias and multiple arthralgias, generalized lymphadenopathy) as well as cutaneous manifestations (macular syphilids, papular syphilids, condylomata lata, nail involvement, hair loss, atypical rash, etc.) are constant findings.

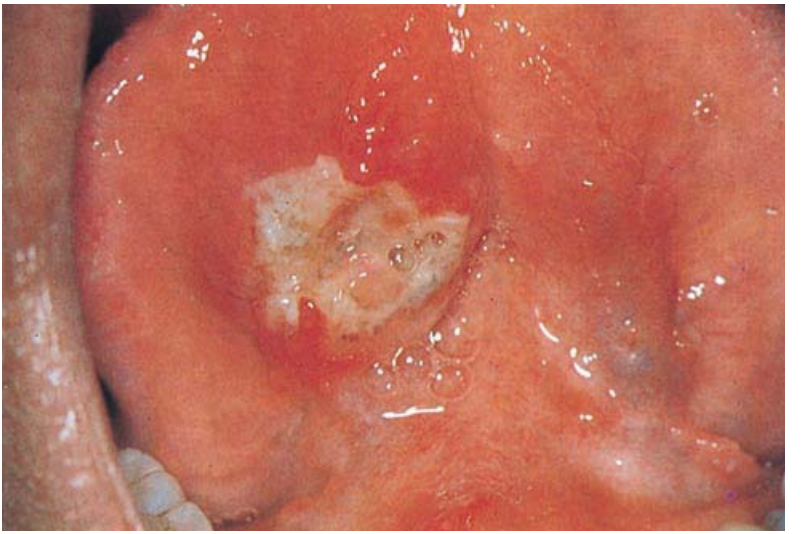


Fig. 147 Solitary chancre on the ventral surface of the tongue.

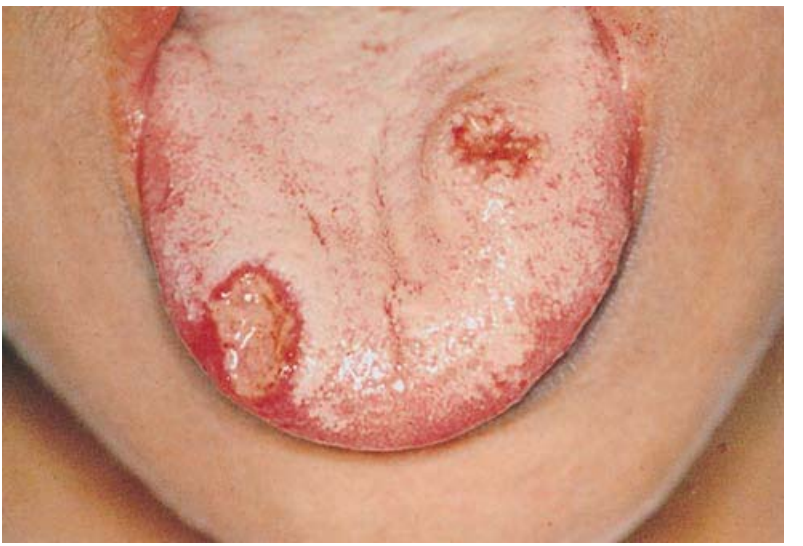


Fig. 148 Two chancres on the tongue.

Tertiary syphilis begins after a period of 4–7 years. Oral lesions are gumma, atrophic or luteic glossitis, and interstitial glossitis.

The most common oral lesions in congenital syphilis are a high-arched palate, short mandible, rhagades, Hutchinson's teeth, and Moon's or mulberry molars.

Laboratory tests Dark-field microscopic examination, and serological tests—Venereal Disease Research Laboratory (VDRL); fluorescent treponemal antibody, absorbed (FTA-ABS); *Treponema pallidum* immobilization (TPI); rapid plasma reagin (RPR).

Differential diagnosis Traumatic ulcer, aphthous ulcer, tuberculosis, herpes simplex, infectious mononucleosis, candidiasis, erythema multiforme, lichen planus.

Treatment Penicillin is the antibiotic of choice. Erythromycin or cephalosporins are good alternatives.

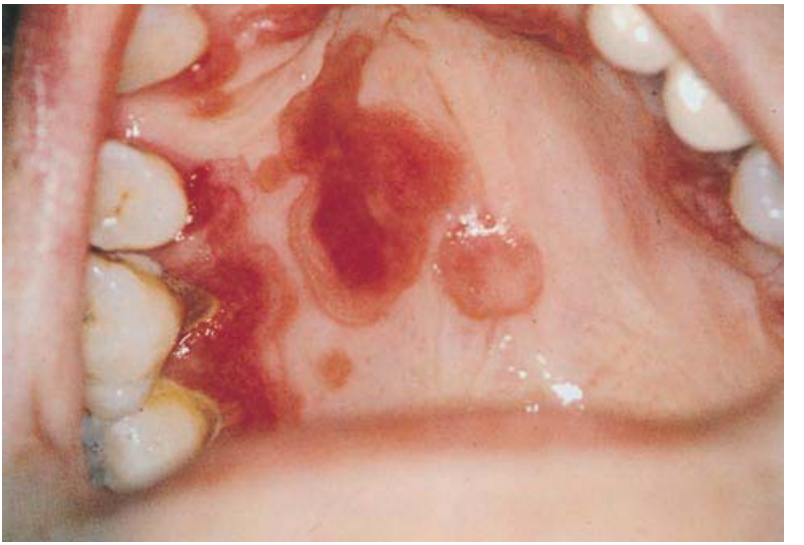


Fig. 149 Mucous patches on the palate and gingiva.

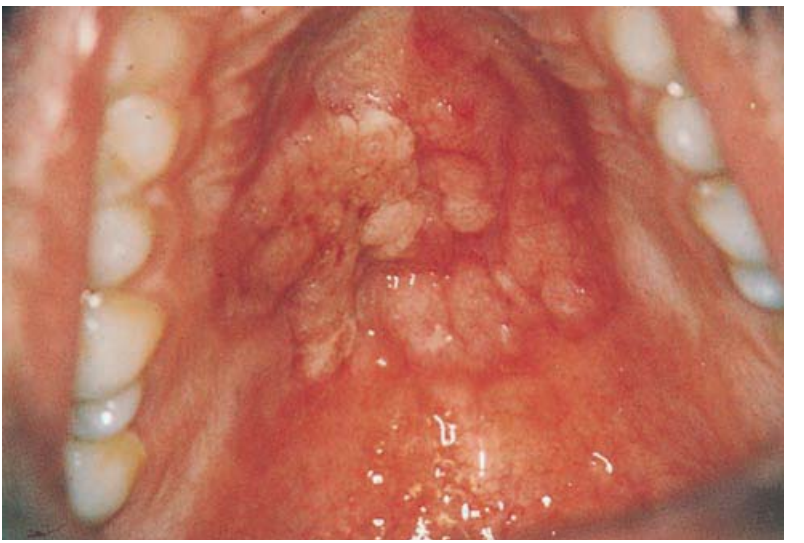


Fig. 150 Condylomata lata on the palate.

Tuberculosis

Definition Tuberculosis is a chronic, granulomatous, infectious disease that primarily affects the lungs.

Etiology *Mycobacterium tuberculosis*.

Clinical features The oral lesions are rare, and usually secondary to pulmonary tuberculosis. The tuberculous ulcer is the most common feature. Clinically, the ulcer is painless and irregular, with a thin undermined border and a vegetating surface, usually covered by a gray-yellowish exudate (Fig. **151**). The surrounding tissues are inflamed and indurated. The dorsum of the tongue is the most commonly affected site, followed by the lip, buccal mucosa, and palate. Osteomyelitis of the jaws, periapical granuloma, regional lymphadenopathy, and scrofula are less common oral manifestations.

Laboratory tests Sputum culture, histopathological examination, chest radiography.

Differential diagnosis Systemic mycoses, carcinomas, syphilis, eosinophilic ulcer, necrotizing sialadenometaplasia, Wegener granulomatosis, malignant granuloma, major aphthous ulcer.

Treatment Antituberculous drugs.

Systemic Mycoses

Definition Systemic mycoses are chronic fungal infections.

Classification and etiology The most common systemic mycoses are: histoplasmosis (*Histoplasma capsulatum*), blastomycosis (*Blastomyces dermatitidis*), cryptococcosis (*Cryptococcus neoformans*), paracoccidioidomycosis (*Paracoccidioides brasiliensis*), aspergillosis (*Aspergillus* species), mucormycosis (*Mucor*, *Rhizopus*). The most common predisposing conditions are HIV infection and immunocompromised status, neutropenia, leukemia, lymphoma, organ transplantation, diabetes, and cancer chemotherapy.

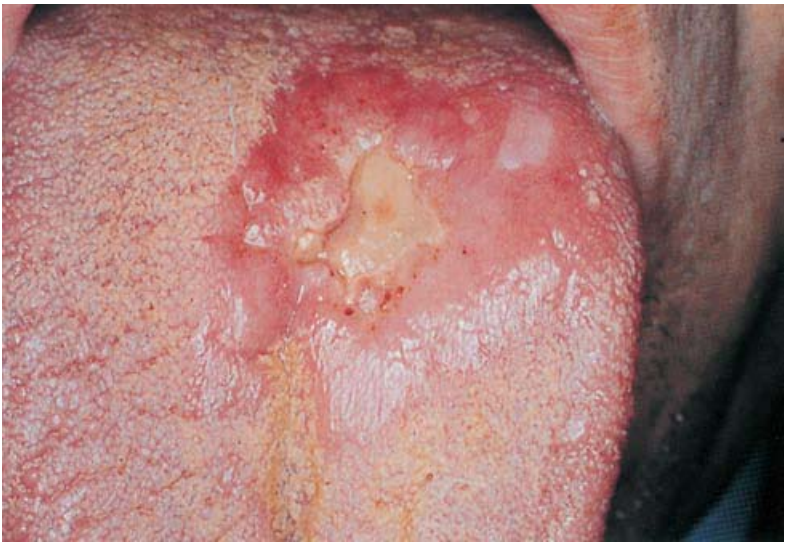


Fig. 151 Tuberculosis: typical ulcer on the dorsal surface of the tongue.

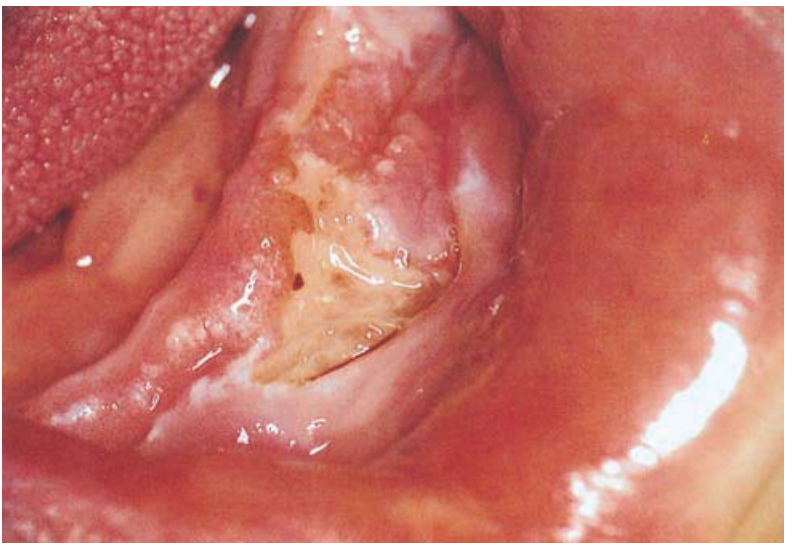


Fig. 152 Histoplasmosis: irregular ulcer on the alveolar mucosa.

Clinical features Oral lesions are relatively rare. However, over the past few years, there has been a dramatic increase in the oral lesions caused by some systemic mycoses. Clinically, oral lesions in almost all systemic mycoses are characterized by a chronic irregular and vegetating ulcer (Figs. **152**, **153**, **154**, **155**).

Laboratory tests Smear and histopathological examination.

Differential diagnosis Carcinoma, tuberculosis, malignant granuloma, syphilis, myelodysplastic syndrome, agranulocytosis.

Treatment Amphotericin B, itraconazole, ketoconazole, fluconazole.

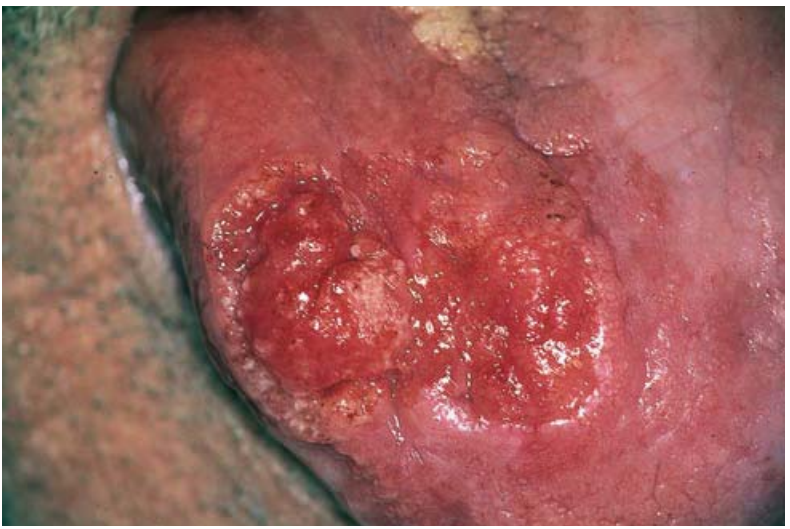


Fig. 153 Cryptococcosis, abnormal ulceration on the tongue.

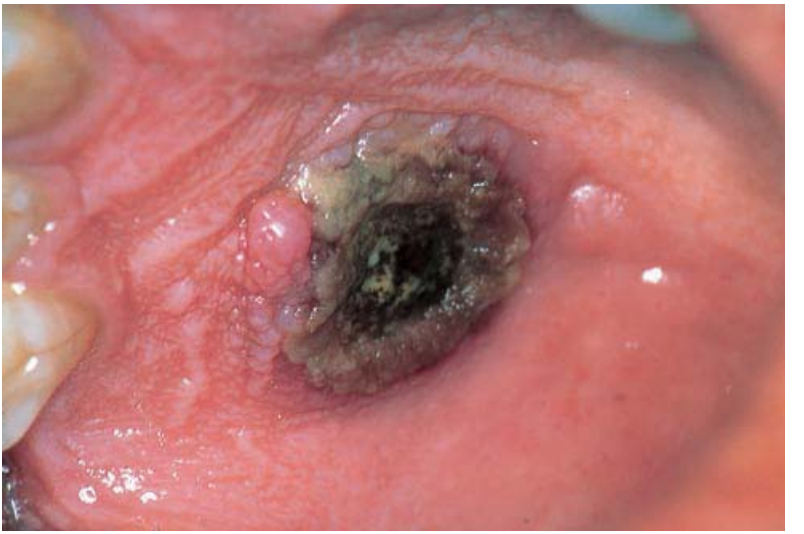


Fig. 154 Aspergillosis, black necrotic ulceration on the palate.

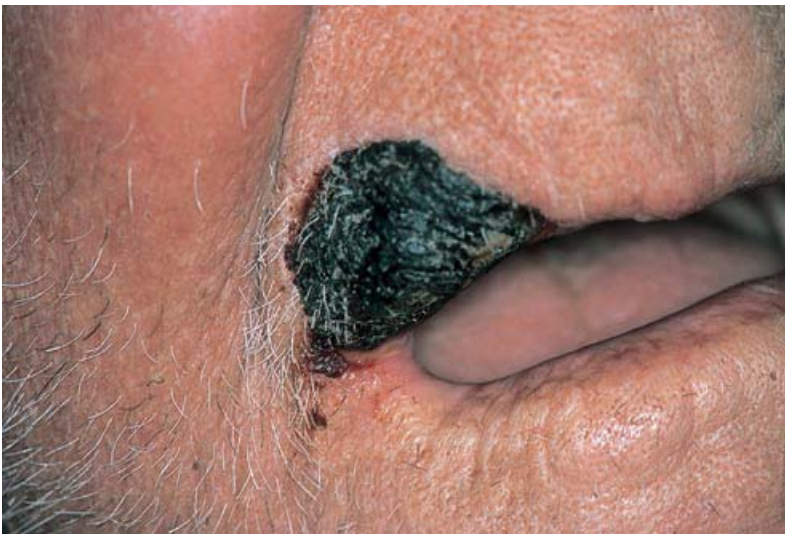


Fig. 155 Mucormycosis, black necrotic lesion on the upper lip.

Recurrent Aphthous Ulcers

Definition Recurrent aphthous ulcers are among the most common oral mucosal lesions, with a prevalence of 10–30% in the general population.

Etiology The cause remains unclear. Recent evidence supports the concept that cell-mediated immune responses play a primary role in the pathogenesis. Several predisposing factors have been reported, such as trauma, allergy, genetic predisposition, endocrine disturbances, emotional stress, hematological deficiencies, and AIDS.

Clinical features Three clinical variations have been recognized: *minor*, *major* and *herpetiform ulcers*. Minor aphthae are the most common form, and they present clinically as small, painful, round ulcers 3–6 mm in diameter, covered by a whitish-yellow membrane and surrounded by a thin red halo (Fig. **156**). The lesions may be single or multiple (two to six), and they heal without scarring in 7–12 days. The major form is characterized by deep painful ulcers, 1–2 cm in diameter, that persist for 3–6 weeks and may cause scarring (Figs. **157**, **158**). The number of lesions varies from one to five.

The herpetiform variation is characterized by small, painful, shallow ulcers, 1–2 mm in diameter, with a tendency to coalesce into larger irregular ulcers (Fig. **159**). Characteristically, the lesions are multiple (10–100), persist for one or two weeks, and heal without scarring.

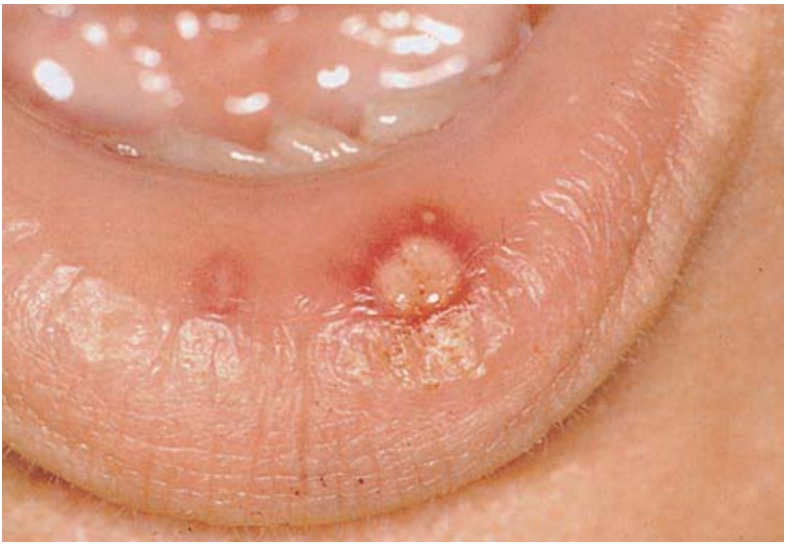


Fig. 156 Minor aphthous ulcer.

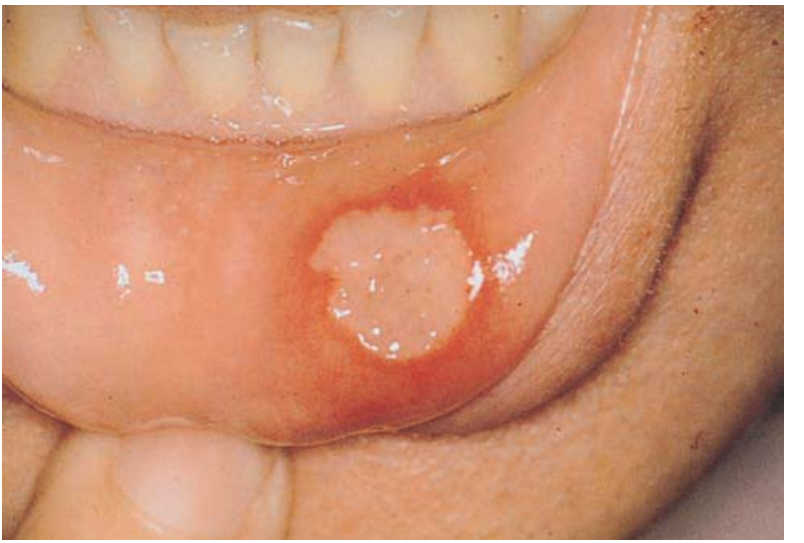


Fig. 157 Major aphthous ulcer on the lower lip.

The non-keratinized movable mucosa is most frequently affected in all three clinical variations of the disease. The diagnosis of aphthous ulcers is exclusively based on clinical criteria.

Differential diagnosis Herpes simplex, hand-foot-and mouth disease, chancre, Behçet disease, cyclic neutropenia, erythema multiforme, FAPA syndrome, Sweet syndrome.

Treatment Topical steroids. In severe cases, intralesional steroid injection or systemic steroids in low doses (10–20 mg prednisone) for four to eight days can reduce the symptoms dramatically.

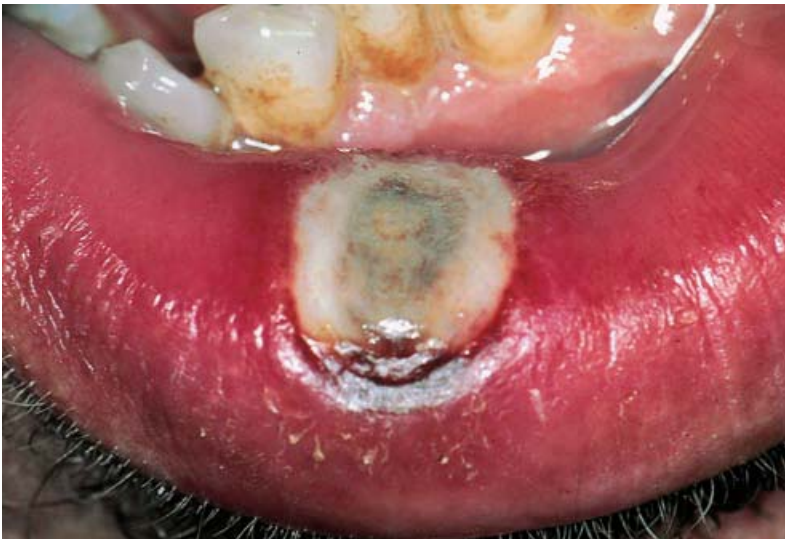


Fig. 158 Major aphthous ulcer, necrotic, on the lower lip

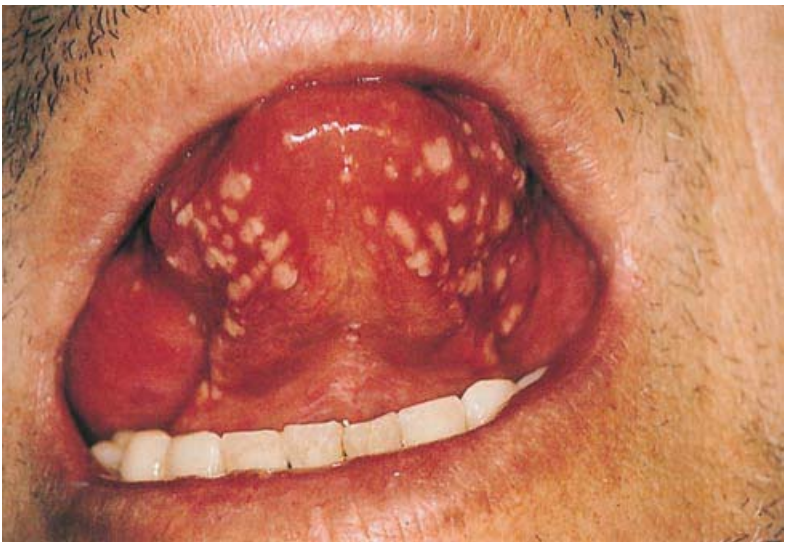


Fig. 159 Multiple herpetiform ulcers on the tongue.

Behçet Disease

Definition Behçet disease is a chronic multisystemic inflammatory disorder.

Etiology The exact cause is unclear, although an immunogenetic basis is suggested by the increased prevalence of HLA-Bw51, HLA-B5, HLA-B27, and HLA-B12 in affected patients. In addition, several immunological disorders have been recorded.

Clinical features It is more common in males (5–10 times), and the onset is usually in the 20–30 years age group. The major clinical diagnostic criteria for the disease are: (a) recurrent oral ulcerations (aphthae, Fig. **160**); (b) recurrent genital ulcerations (Figs. **161**, **162**); (c) ocular lesions (conjunctivitis, iritis with hypopyon, uveitis, retinal vasculitis, reduced visual acuity, Fig. **163**); (d) skin lesions (papules, pustules, folliculitis, erythema nodosum, ulcers, and rarely necrotic lesions); (e) positive pathergy test. Minor clinical features may also be present, e. g., arthritis, arthralgia, thrombophlebitis, vein thrombosis, arterial occlusion and aneurysms, central nervous system involvement, pulmonary, renal, and gastrointestinal manifestations. The diagnosis is mainly made on clinical grounds. For accurate diagnosis, recurrent oral ulcerations plus two of the other four major criteria must be present.

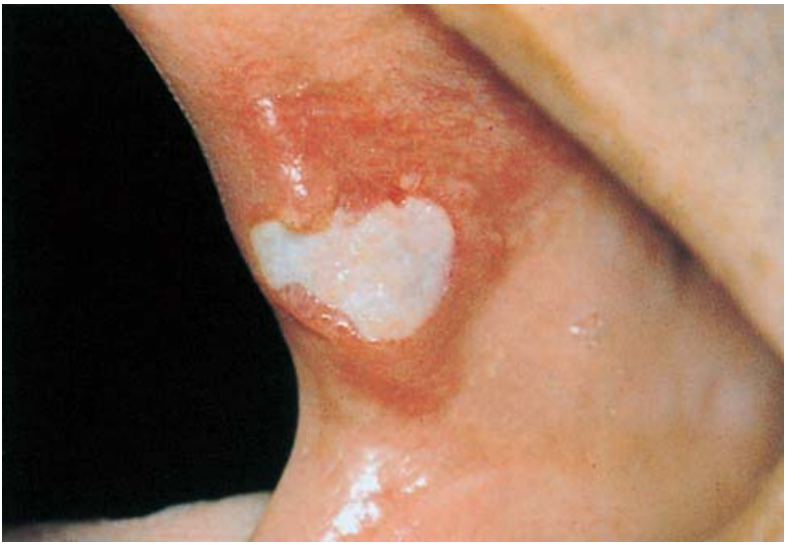


Fig. 160 Behçet disease: major aphthous ulcer on the buccal mucosa.

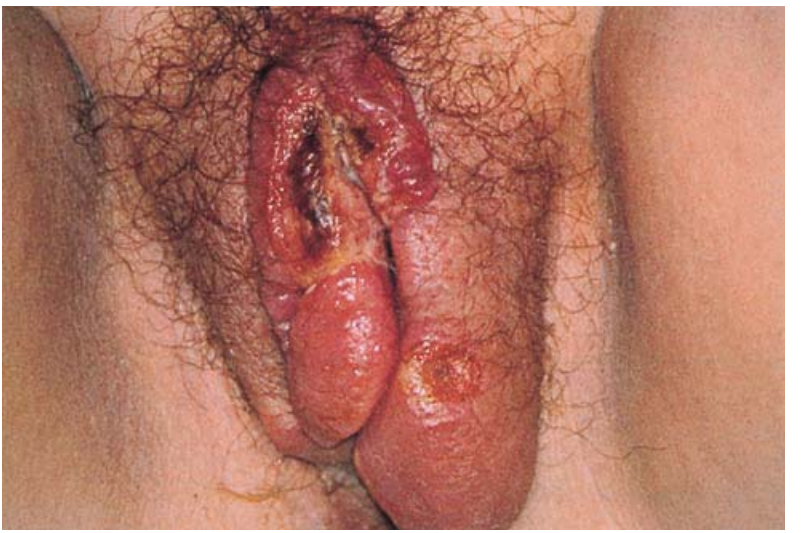


Fig. 161 Behçet disease: multiple ulcers on the labia majora.

Laboratory tests Laboratory findings are not diagnostic.

Differential diagnosis Recurrent aphthous ulcers, Reiter syndrome, ulcerative colitis, erythema multiforme, Stevens–Johnson syndrome, syphilis, Sweet syndrome.

Treatment Topical steroids in mild cases. Systemic steroids, ciclosporin and other immunosuppressive drugs, thalidomide, colchicine, dapsone in severe cases.

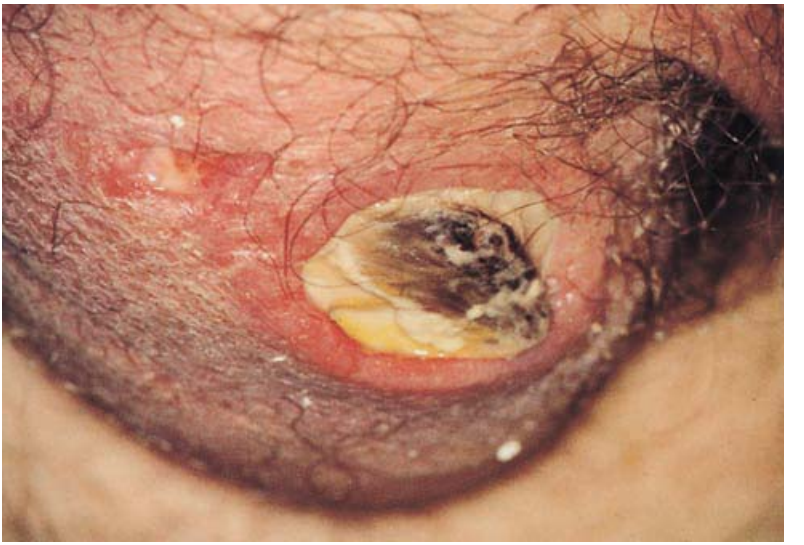


Fig. 162 Behçet syndrome: two ulcers on the scrotum.

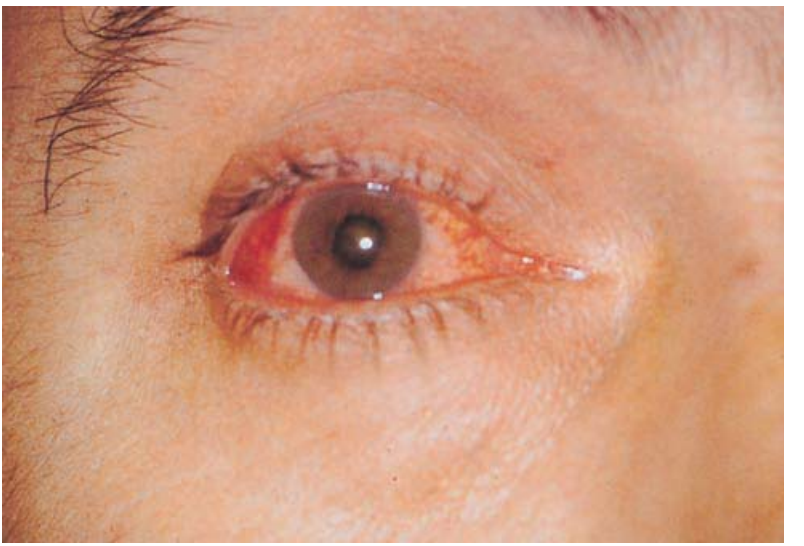


Fig. 163 Behçet syndrome: conjunctivitis and iritis.

Graft-Versus-Host Disease

Definition Graft-versus-host disease (GVHD) is a complex, multisystem immunological phenomenon, and one of the major complications in patients undergoing allogeneic bone-marrow or peripheral blood stem cell transplantation.

Etiology It is due to an immunological reaction of engrafted lymphoid cells, presumably T cells, against the host tissues.

Clinical features Two forms of the disease are recognized: *acute*, with skin, gastrointestinal tract, and hepatic manifestations, and *chronic*, which develops about 100 days after transplantation, and is characterized by liver dysfunction, pulmonary insufficiency, sclerodermatous skin changes, keratoconjunctivitis, gastrointestinal disorders, reduced production of tears and saliva, and oral lesions. Clinically, oral manifestations present as atypical diffuse ulcerations (Fig. **164**) and lichenoid lesions (Fig. **165**). Oral bleeding, xerostomia, and infections (viral, bacterial, mycoses) may occur. The diagnosis is mainly based on the history and clinical features.

Laboratory tests Histopathological examination of oral lesions, elevated sodium concentration in saliva.

Differential diagnosis Lichen planus, drug-induced stomatitis, chronic bullous diseases, Sjögren syndrome, systemic lupus erythematosus, scleroderma, radiation mucositis, neutropenia-associated mucositis.

Treatment Systemic steroids with or without immunosuppressives. Topical oral treatment (anesthetics, steroids, antiseptics, artificial saliva) may be helpful.

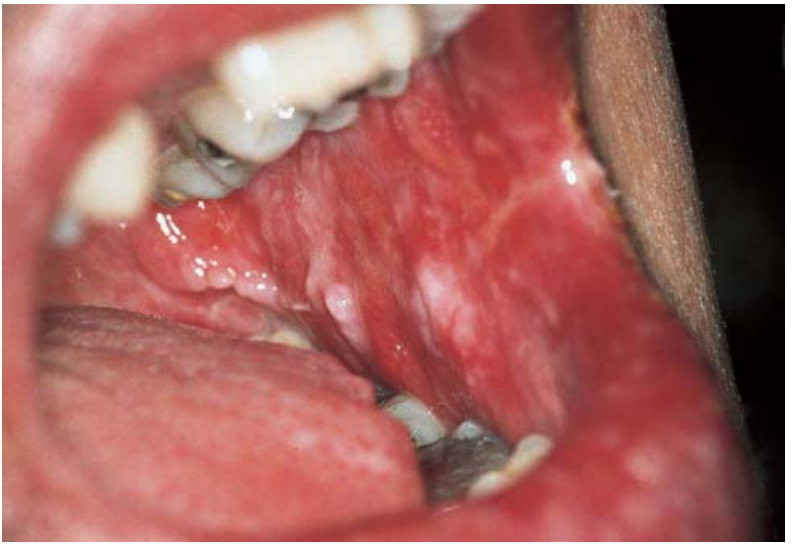


Fig. 164 Graft-versus-host disease: superficial ulceration on the buccal mucosa.

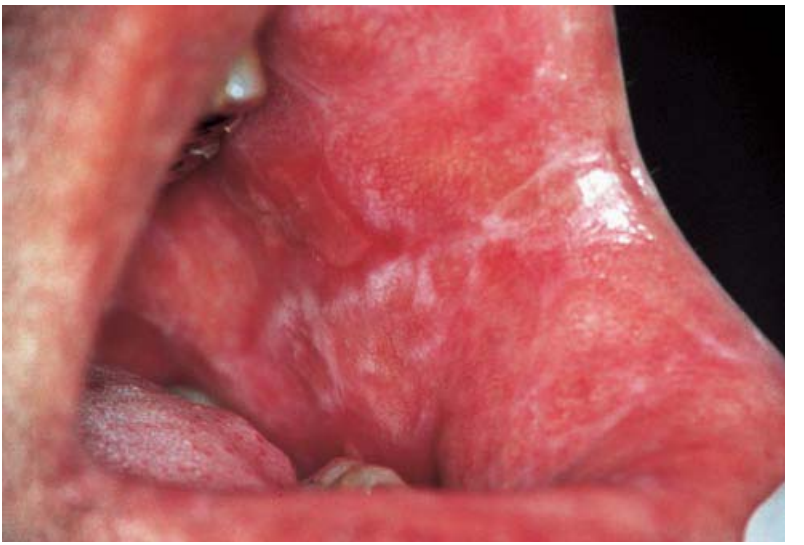


Fig. 165 Graft-versus-host disease: erosion and white lesions that resemble lichen planus on the buccal mucosa.

Wegener Granulomatosis

Definition and etiology Wegener granulomatosis is a rare chronic granulomatous disease with a probably immunological pathogenesis.

Clinical features The disease is characterized by necrotizing granulomatous lesions of the respiratory tract, generalized focal necrotizing vasculitis, and necrotizing glomerulitis. The oral lesions are fairly common, and present clinically as solitary or multiple irregular ulcers, surrounded by an inflammatory zone (Fig. **166**). The tongue, palate, buccal mucosa, and gingiva are the most commonly affected areas.

Laboratory tests Histopathological examination, detection of antineutrophil cytoplasm antibodies (ANCA) in the serum.

Differential diagnosis Malignant granuloma, tuberculosis, non-Hodgkin lymphoma, leukemia, systemic mycoses, squamous-cell carcinoma.

Treatment A combined regimen with steroids, azathioprine, and cyclophosphamide.

Malignant Granuloma

Definition Malignant granuloma, lethal midline granuloma, and nasal natural killer T-cell lymphoma represent a disease spectrum characterized by progressing ulcerations and necrosis that characteristically involves the midline structures of the palate and nasal cavity.

Etiology Unclear, although Epstein–Barr virus is frequently associated with the disease.

Clinical features Three varieties of the disease have been recognized: *inflammatory* or *idiopathic*; *neoplastic* or *polymorphic reticulosis*; and *lymphoma* with high-grade malignancy. Clinically, the condition is characterized by prodromal signs and symptoms (epistaxis, pain, nasal stuffiness and obstruction with a purulent discharge, foul-smelling secretions), and nonhealing ulceration and necrosis, usually of the nasal cavity and palate) (Fig. **167**). The ulcers deteriorate rapidly, causing destruction and perforation of soft and hard tissues, finally resulting in severe disfigurement (Fig. **168**). The prognosis is poor.

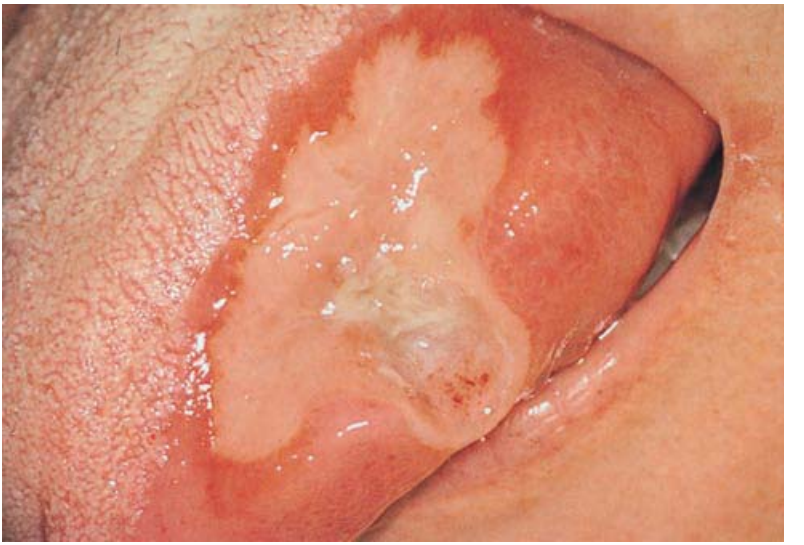


Fig. 166 Wegener granulomatosis: large ulcer surrounded by an erythematous zone on the tongue.

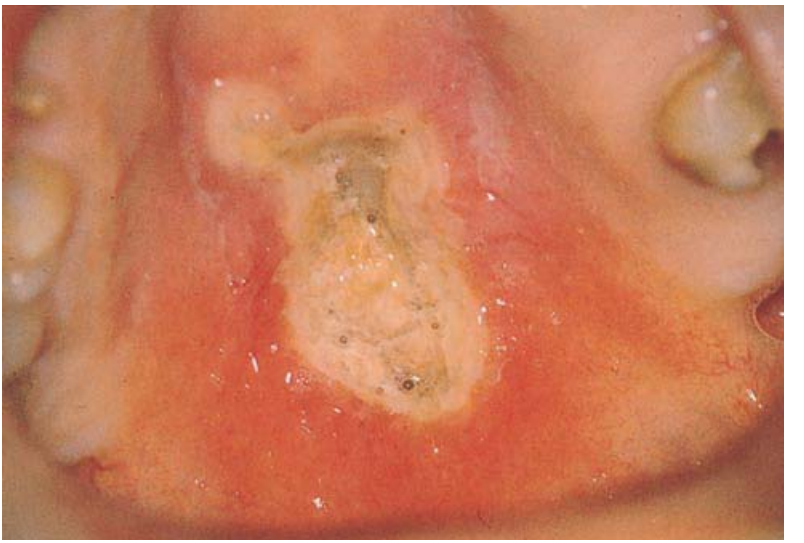


Fig. 167 Malignant granuloma: nonhealing ulcer and necrosis on the palate.

Laboratory tests Histopathological examination.

Differential diagnosis Wegener granulomatosis, systemic mycoses, non-Hodgkin lymphoma, malignancies, tuberculosis, necrotizing sialadenometaplasia.

Treatment Radiotherapy, chemotherapy.

Non-Hodgkin Lymphoma

Definition Non-Hodgkin lymphomas are a heterogeneous group of malignancies of the lymphoid cell lines. They usually originate from B-lymphocyte cell series, but T-lymphomas also occur.

Etiology Unclear. However, genetic and environmental factors (viruses, radiation) may play a role in the pathogenesis.

Clinical features The classification of non-Hodgkin lymphomas is based on histopathological, immunological, gene rearrangement, clinical, and therapeutic criteria. Both sexes are affected at any age. Lymph nodes are most commonly involved, but extranodal involvement may also occur. Oral lesions may be part of a disseminated disease, or the only sign. Clinically, oral lymphoma presents as a diffuse, painless swelling, which may or may not be ulcerated (Fig. **169**). The soft palate, the posterior part of the tongue, the gingiva, and the tonsillar area are most commonly affected.

Laboratory tests Histopathological and immunohistochemical examination.

Differential diagnosis Eosinophilic ulcer, necrotizing sialadenometaplasia, pseudolymphoma, Wegener granulomatosis, malignant granuloma, systemic mycoses, tuberculosis, squamous cell carcinoma.

Treatment Radiotherapy and chemotherapy.

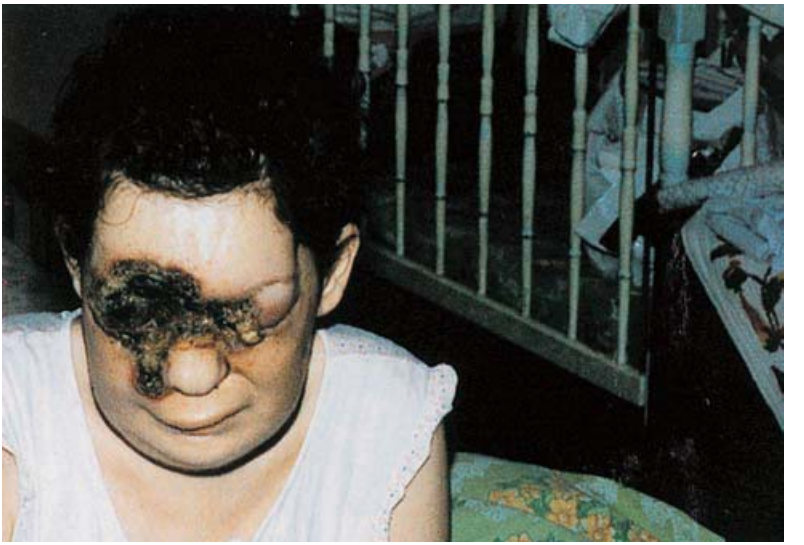


Fig. 168 Malignant granuloma: severe disfigurement of the face.

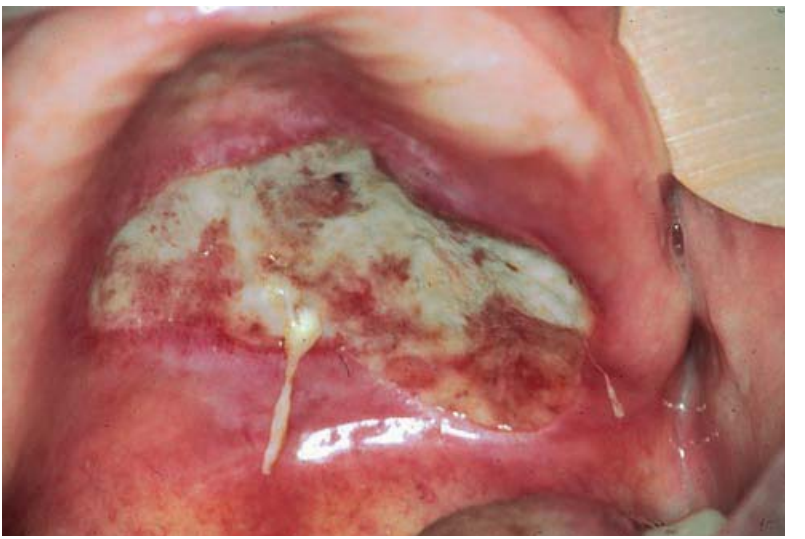


Fig. 169 Non-Hodgkin lymphoma: large ulcer on the soft palate.

Squamous-Cell Carcinoma

Definition Squamous-cell carcinoma represents about 90% of oral cancers, and accounts for 3–5% of all cancers.

Etiology The cause is multifactorial. The most important predisposing factors are tobacco smoke, alcohol, sun exposure, poor oral hygiene, dietary deficiencies, iron deficiency, liver cirrhosis, *Candida* infection, oncogenic viruses, oncogenes, and tumor-suppressor genes.

Clinical features Oral squamous-cell carcinoma occurs more frequently in men than in women (ratio 2 : 1), and usually in those over 40 years of age. It has a varied clinical presentation, and may mimic several diseases. Early carcinoma may appear as a white lesion, a red lesion, or both, or even as an exophytic mass. However, the most common clinical presentation is an erosion or an ulcer (Figs. **170**, **171**, **172**, **173**, **174**, **175**). Classically, a carcinomatous ulcer has an irregular papillary surface, elevated borders, and a hard base on palpation. The lesions are almost always chronic and indurated. The lateral border, the ventral surface of the tongue, and the lips are the most commonly affected areas,

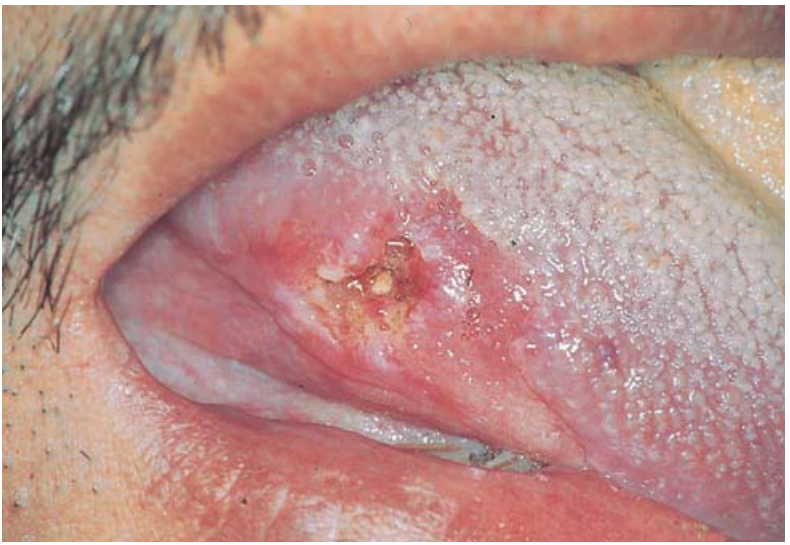


Fig. 170 Early squamous-cell carcinoma of the lateral border of the tongue.

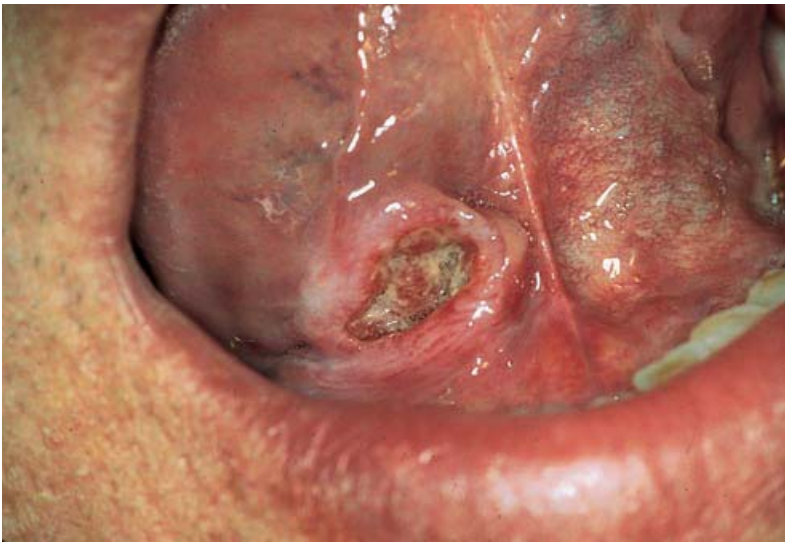


Fig. 171 Early squamous-cell carcinoma of the floor of the mouth.

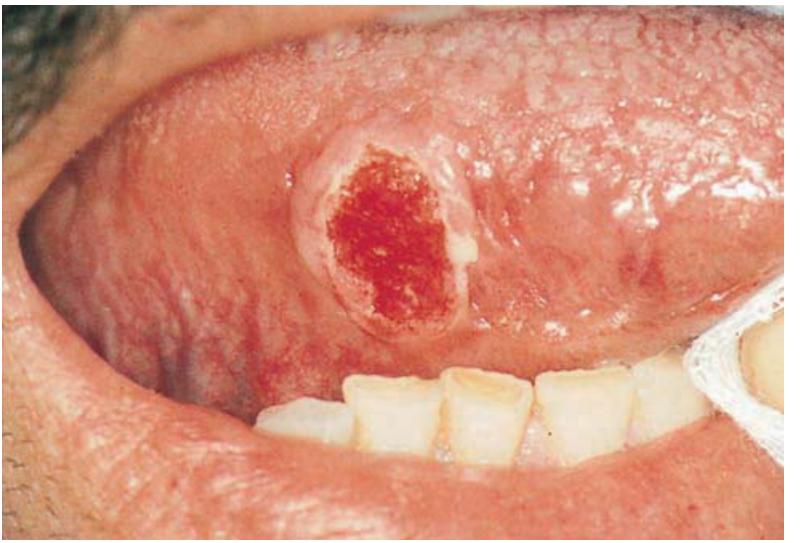


Fig. 172 Early squamous-cell carcinoma of the lateral border of the tongue.

followed by the floor of the mouth, the gingiva, the alveolar mucosa, the buccal mucosa, and the palate. The prognosis depends on the tumor stage and the histopathological pattern.

Laboratory tests Histopathological examination.

Differential diagnosis Traumatic ulcer, tuberculosis, systemic mycoses, syphilis, eosinophilic ulcer, necrotizing sialadenometaplasia, Wegener granulomatosis, malignant granuloma, minor salivary gland carcinomas.

Treatment Surgical excision, radiotherapy, or both, and chemotherapy.

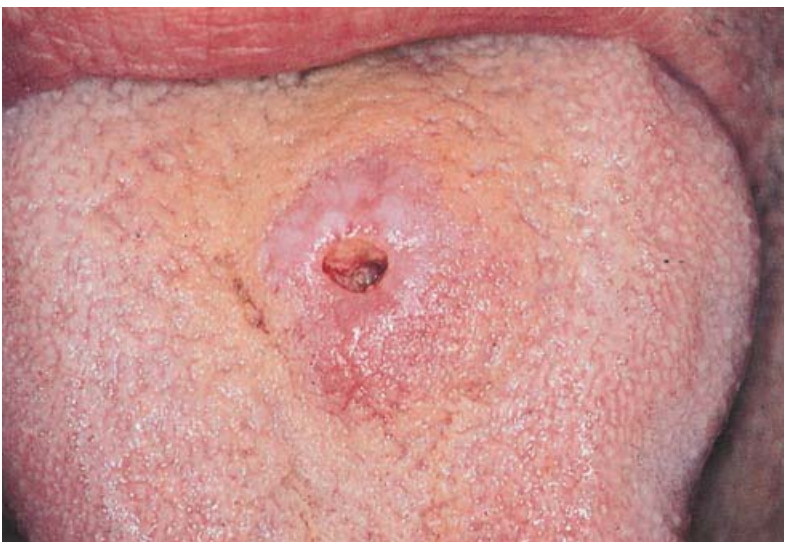


Fig. 173 Unusual location of squamous-cell carcinoma on the dorsum of the tongue.

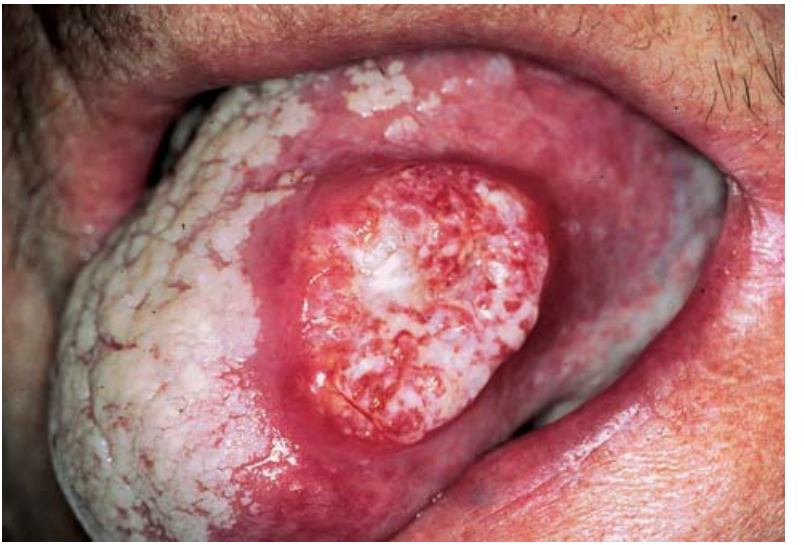


Fig. 174 Squamous-cell carcinoma presenting as exophytic ulcerated tumor of the lateral border of the tongue.

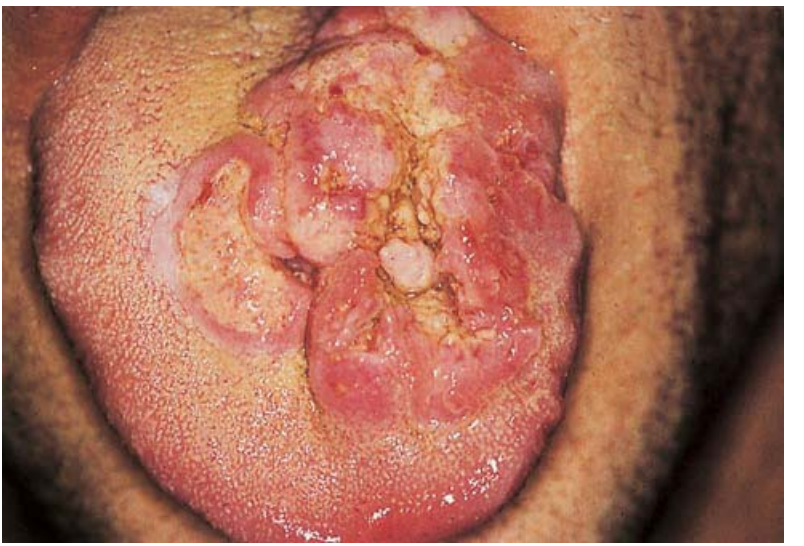


Fig. 175 Late squamous-cell carcinoma on the dorsum of the tongue.

Cyclic Neutropenia

Definition Cyclic neutropenia is a rare hematological disorder characterized by regular periodic reduction of the neutrophil leukocytes.

Etiology A hereditary autosomal dominant trait has been recorded in some cases.

Clinical features The disease is usually manifested in childhood, and the reduction of neutrophils occurs regularly in a 21-day cycle. Patients typically may complain of low-grade fever, headache, malaise, anorexia, arthralgias, cervical lymphadenopathy, gastrointestinal disorders, and skin and oral manifestations. Oral lesions present as a painful ulcer covered by a whitish membrane and surrounded by an erythematous halo (Fig. **176**). Localized gingivitis is also a common finding (Fig. **177**).

Laboratory tests Determination of neutrophils in the peripheral blood (usually two or three times per week for eight weeks).

Differential diagnosis Aphthous ulcers, congenital neutropenia, agranulocytosis, leukemia, syphilis.

Treatment Supportive care. Corticosteroids, granulocyte colony-stimulating factor (G-CSF) and splenectomy may be used.

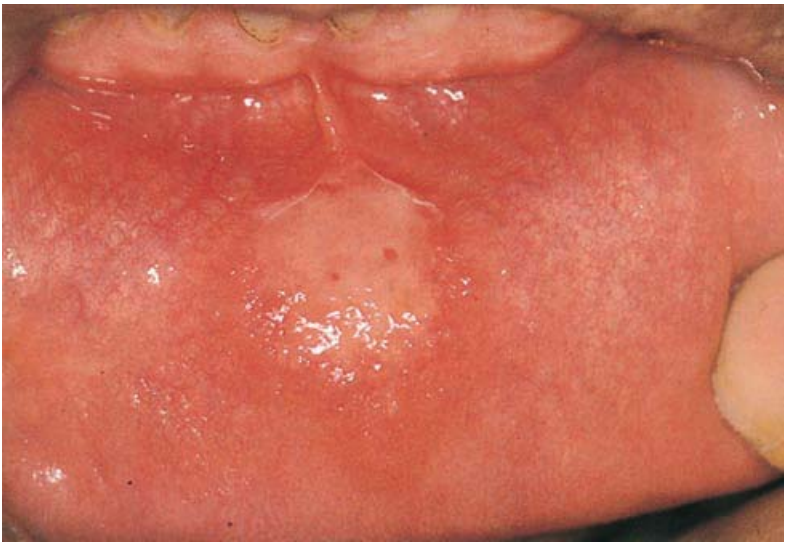


Fig. 176 Cyclic neutropenia: ulcer on the labial mucosa.

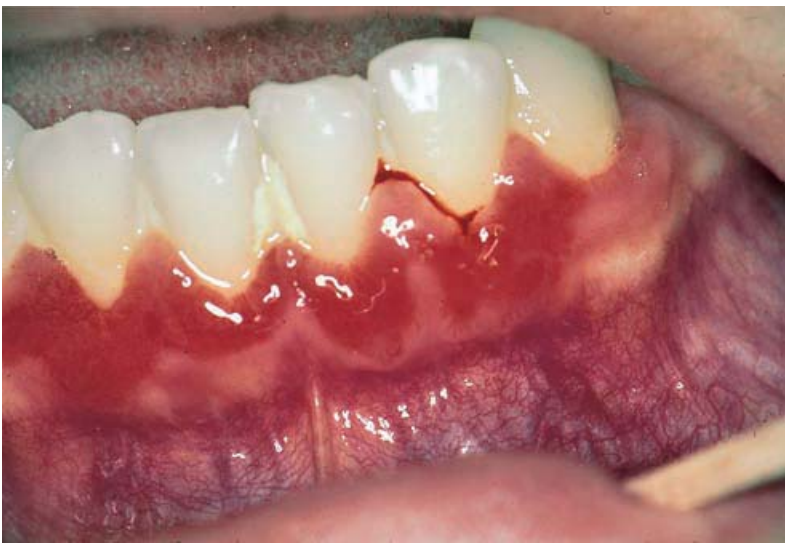


Fig. 177 Cyclic neutropenia: localized gingivitis.

Agranulocytosis

Definition Agranulocytosis is a hematological disorder characterized by a severe reduction of the granulocyte series, particularly neutrophils.

Etiology Drugs or infections are commonly the cause, although some cases are idiopathic.

Clinical features The disease has a sudden onset and is characterized by chills, fever, malaise, and sore throat. Bacterial infections often develop. Oral lesions are common early signs, and consist of multiple necrotic ulcers covered by a grayish-white or dark and dirty pseudomembrane without a red halo (Fig. **178**). The buccal mucosa, tongue, palate, and tonsillar area are the most common sites of involvement. Severe necrotizing gingivitis with periodontal tissue destruction is common (Fig. **179**). The systemic manifestations include sudden chills, fever, malaise, and sore throat. Within 12–24 hours, signs and symptoms of respiratory and/or gastrointestinal tract or other bacterial infections may develop. The risk of infections is usually related to the degree of neutropenia.

Laboratory tests White blood count and bone-marrow aspiration.

Differential diagnosis Cyclic neutropenia, necrotizing ulcerative gingivitis, myelic aplasia, acute leukemia, Wegener granulomatosis.

Treatment Antibiotics, white blood cell transfusions. Administration of granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) is also beneficial.

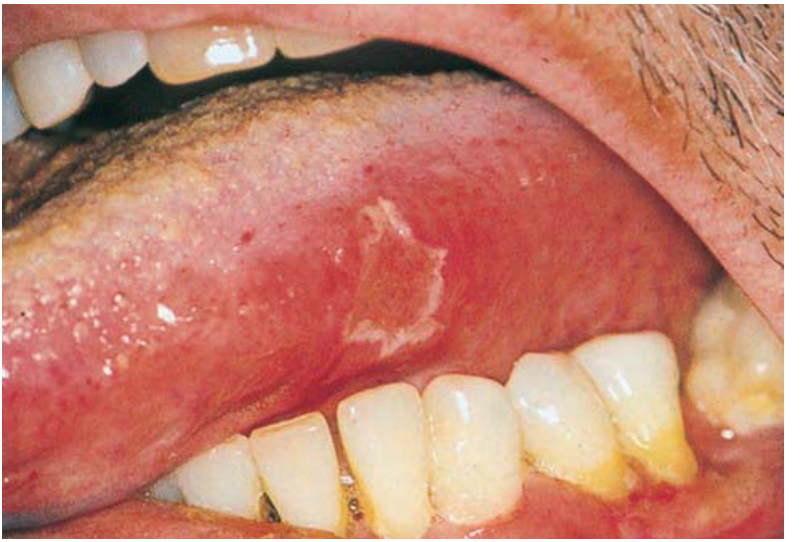


Fig. 178 Agranulocytosis: ulcer on the tongue.

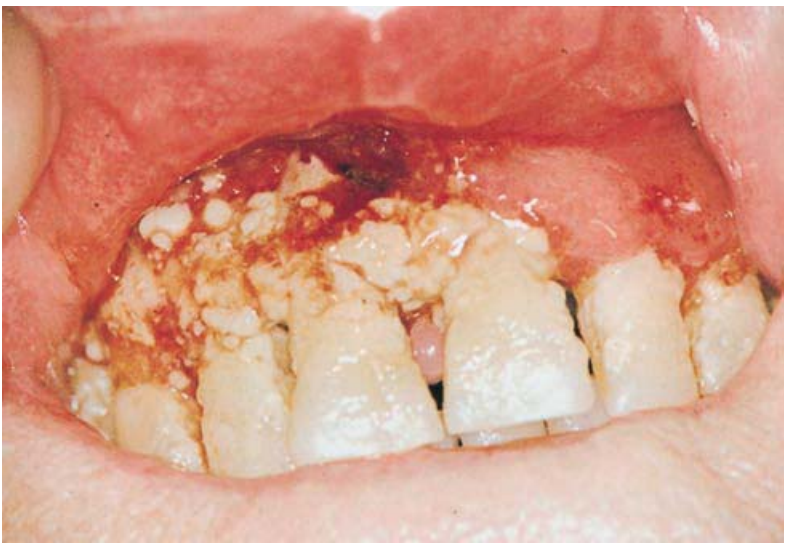


Fig. 179 Agranulocytosis: severe periodontal destruction.

Myelic Aplasia

Definition Myelic aplasia is a rare stem-cell disorder characterized by pancytopenia.

Etiology This is unknown, although some cases may be caused by drugs, radiation, infections, and immunological disorders.

Clinical features The onset of myelic aplasia is usually insidious, and the signs and symptoms are related to one or more hematological deficiencies. The oral manifestations are usually related to the degree of the coexisting neutropenia and thrombocytopenia. Gingival bleeding, oral mucosa petechiae, and ecchymoses are common. Necrotic ulcerations similar to those seen in agranulocytosis may be present (Figs. **180**, **181**, **182**).

Laboratory tests Blood cell counts, bone-marrow biopsy.

Differential diagnosis Agranulocytosis, cyclic neutropenia, leukemia, myelodysplastic syndrome, thrombocytopenic purpura, infectious mononucleosis.

Treatment Antibiotics, steroids, bone-marrow transplantation.

Myelodysplastic Syndrome

Definition Myelodysplastic syndrome is a heterogeneous group of refractory anemias, often associated with thrombocytopenia, neutropenia, and/or monocytosis.

Etiology Not clear.

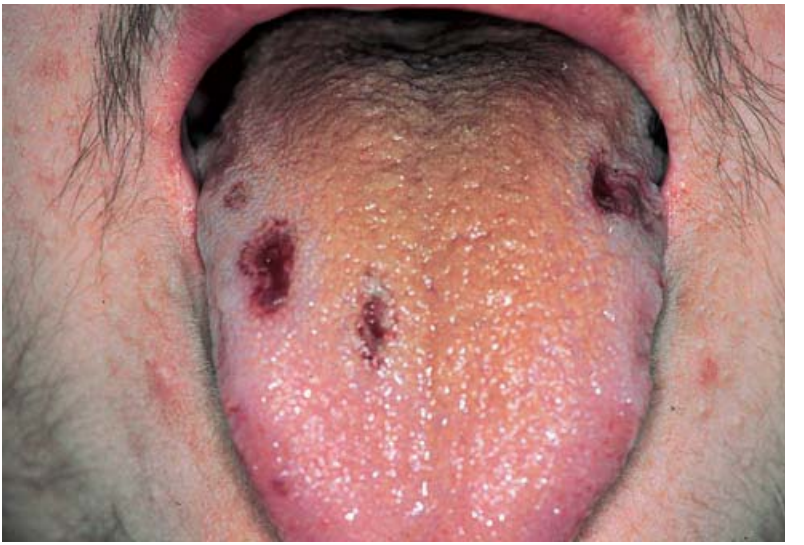


Fig. 180 Myelic aplasia: multiple necrotic ulcerations on the dorsum of the tongue.

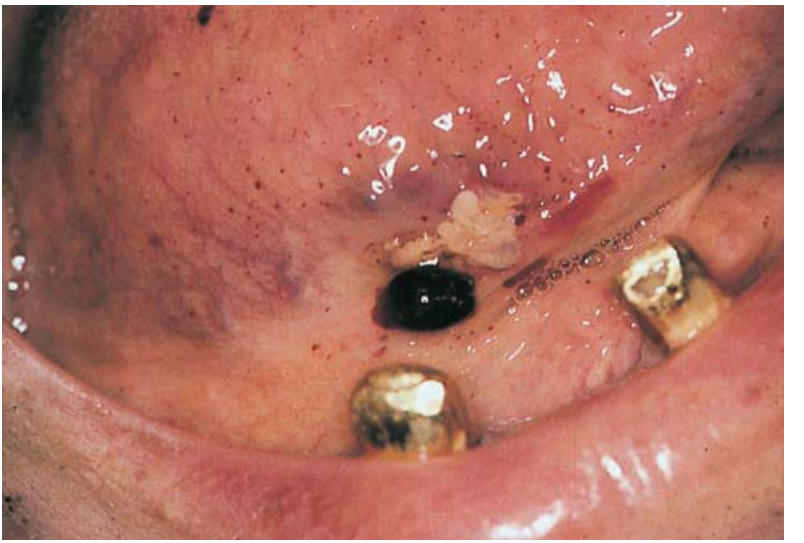


Fig. 181 Myelic aplasia: necrotic ulceration and ecchymoses on the tongue.

Clinical features Multiple bacterial infections and hemorrhage are the most common disorders. The oral manifestations consist of persistent and recurrent ulcerations (Fig. **183**), gingival hemorrhage, and less commonly periodontitis and candidiasis.

Laboratory tests Blood cell counts, bone-marrow aspiration, and biopsy.

Differential diagnosis Agranulocytosis, cyclic neutropenia, congenital neutropenia, myelic aplasia, leukemia, thrombocytopenia.

Treatment Antibiotics, steroids, and transfusions.

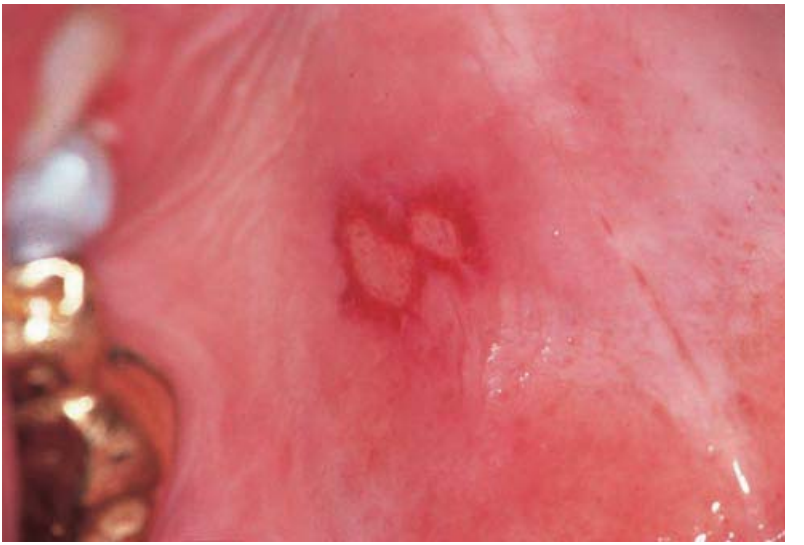


Fig. 182 Myelic aplasia: necrotic ulceration on the palate.

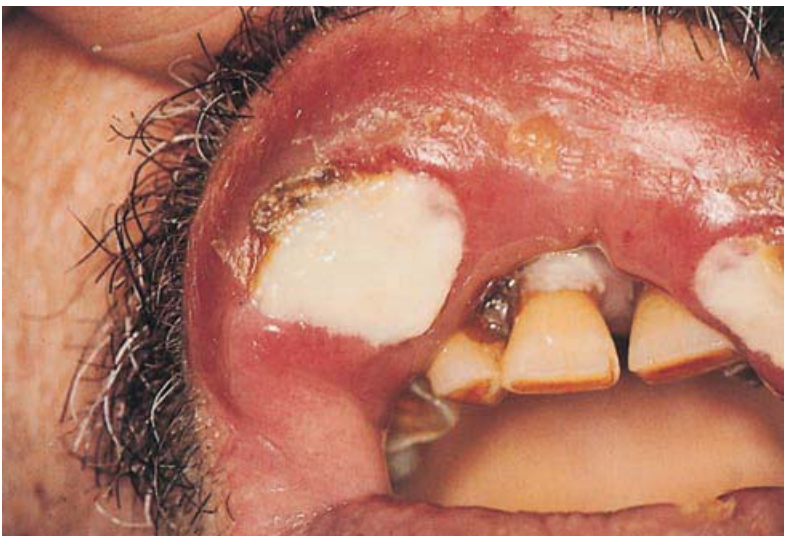


Fig. 183 Myelodysplastic syndrome: persistent ulcerations on the upper lip.

Leukemias

Definition Leukemias are a heterogeneous group of malignant disorders of the blood-forming tissues, characterized by defects in the maturation and proliferation of leukocytes.

Etiology These conditions are probably caused by a combination of genetic and environmental factors (viruses, chemicals, radiation).

Clinical features Leukemias are classified as *acute* and *chronic*, depending on the clinical course, and *myeloid* or *lymphocytic*, according to the histogenetic origin. The main clinical signs and symptoms of leukemias are weakness, fatigue, weight loss, fever, chills, headache, night sweats, skin and mucous membrane pallor, bleeding, infections, bone pain, lymphadenopathy, splenomegaly, hepatomegaly, and salivary gland enlargement. All forms of leukemia can have oral manifestations. The most common oral lesions are ulcerations (Figs. **184**, **185**), spontaneous gingival hemorrhage, petechiae, ecchymoses, tooth loosening, and delayed wound healing. Gingival enlargement is a characteristic pattern, frequently seen in patients with myelomonocytic leukemia (Figs. **186**, **187**). Candidiasis and herpetic infections are relatively common oral complications of leukemia.

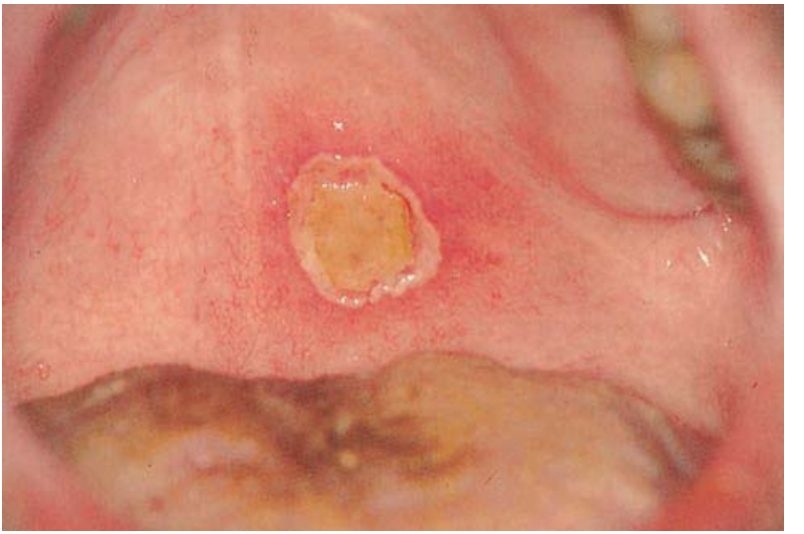


Fig. 184 Chronic lymphocytic leukemia: ulcer on the palate.

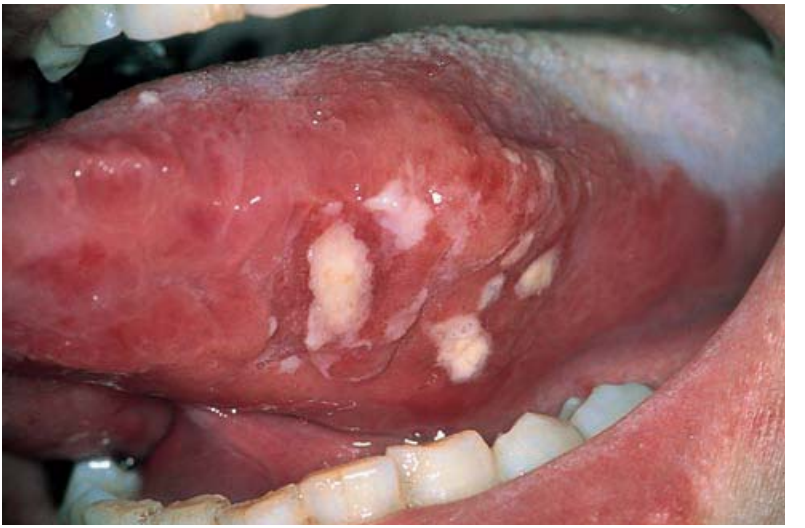


Fig. 185 Acute myelocytic leukemia, ulcers on the tongue.

Laboratory tests Peripheral blood counts, bone-marrow examination.

Differential diagnosis Agranulocytosis, cyclic neutropenia, myelic aplasia, thrombocytopenic purpura, acute necrotizing ulcerative gingivitis, idiopathic gingival fibromatosis, gingival overgrowth due to drugs (ciclosporin, phenytoin, calcium channel blocking agents).

Treatment Chemotherapy, bone-marrow transplantation, supportive therapy.

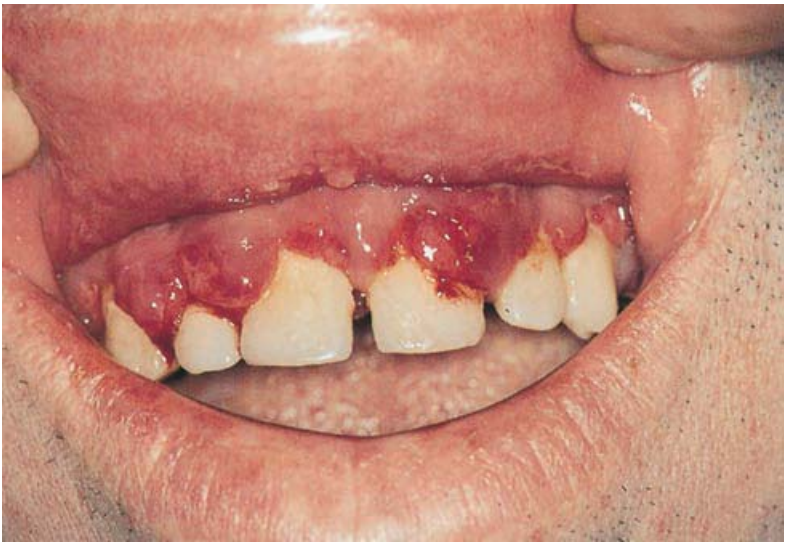


Fig. 186 Chronic lymphocytic leukemia: severe gingival enlargement and ulcerations.

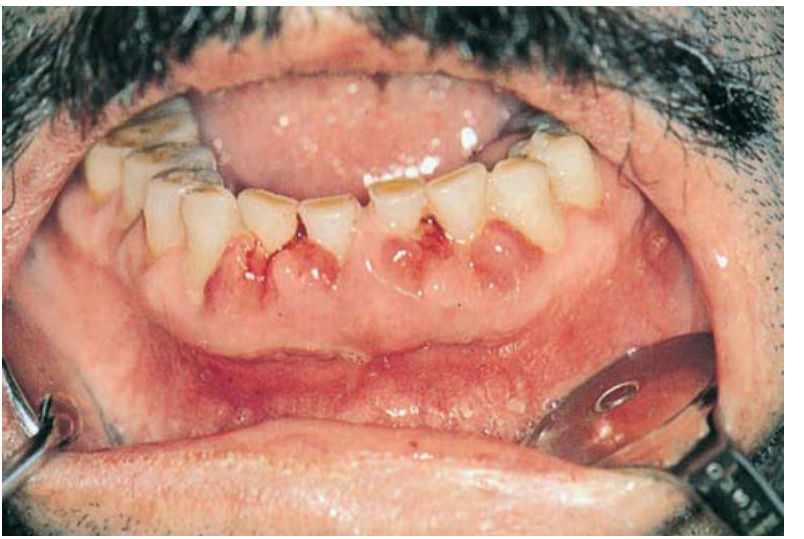


Fig. 187 Acute myelocytic leukemia: marked gingival enlargement and ulcerations.

Langerhans Cell Histiocytosis

Definition Langerhans cell histiocytosis, or histiocytosis-X, is a heterogeneous clonal proliferative disease of the Langerhans cells.

Etiology Unknown. A genetic predisposition in association with viral infection and immunological reaction are possibly involved in the pathogenesis of the disease.

Classification Four forms are recognized: (a) *Eosinophilic granuloma* (common and less severe), (b) *Hand–Schüller–Christian disease* (less common and more severe), (c) *Letterer–Siwe disease* (rare and severe), (d) *Hashimoto–Pritzker disease or congenital form* (rare and self-healing).

Clinical features Oral lesions may occur in all four forms but are more common in the first three forms. Eosinophilic granuloma is usually localized and appears as solitary or multiple ulceration on the gingiva and the palate usually associated with bone destruction and tooth loosening or loss (Fig. **188**). Hand–Schüller–Christian disease and Letterer–Siwe disease are disseminated forms and appear with multiple oral ulcerations, ecchymosis, edema, gingivitis and periodontitis, jaw bone involvement, and tooth loss (Fig. **189**). Skin rash, otitis media, lung, liver, bone and lymph nodes are commonly involved. The classic triad of Hand–Schüller–Christian consists of bone lesions, diabetes insipidus, and exophthalmos. The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests Histopathological examination, radiographs, and immunohistochemical examination.

Differential diagnosis Necrotizing ulcerative gingivitis and periodontitis, aggressive periodontitis, leukemia, multiple myeloma, squamous cell carcinoma.

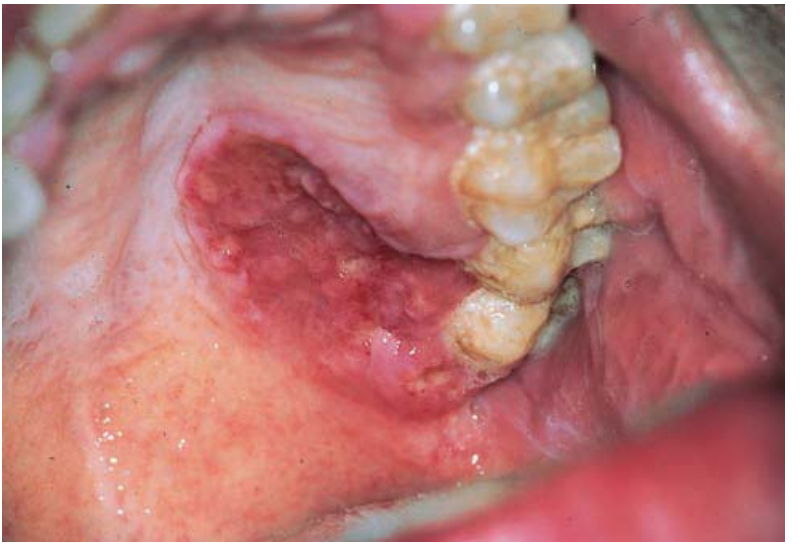


Fig. 188 Langerhans cell histiocytosis, ulcer on the palate.

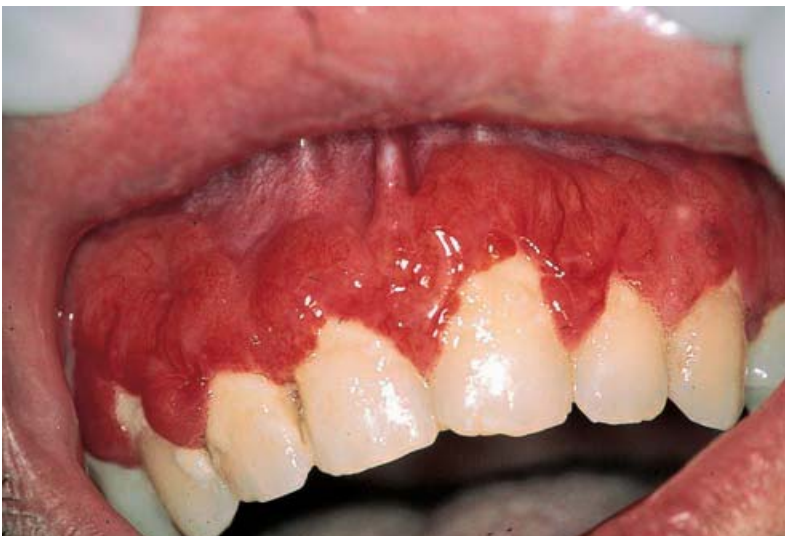


Fig. 189 Langerhans cell histiocytosis, gingival enlargement and periodontitis.

Glycogen Storage Disease, type Ib

Definition Glycogen storage diseases are a rare group of genetic disorders involving the metabolic pathways of glycogen.

Etiology Type Ib of the disease is transmitted by an autosomal recessive trait, and is caused by a defect in the microsomal translocate for glucose 6-phosphate.

Clinical features The main clinical features are hypoglycemia, hyperlipidemia, hepatomegaly, delayed physical development, short stature, "doll's face," neutropenia and neutrophil dysfunction, and recurrent infections. The oral lesions appear commonly and early, as gingivitis and periodontitis and recurrent ulcers (Fig. **190**). The ulcers present as painful discrete or multiple, deep, irregular, recurrent lesions a few millimeters to several centimeters in size, usually covered by whitish pseudomembranes. The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests Histological and biochemical examination, liver biopsy, and histopathological examination.

Differential diagnosis Congenital neutropenia, cyclic neutropenia, agranulocytosis, Chédiak–Higashi syndrome, acatalasia, hypophosphatasia.

Treatment High level of oral hygiene; topical oral antiseptics. The systemic treatment must be left to a pediatrician.

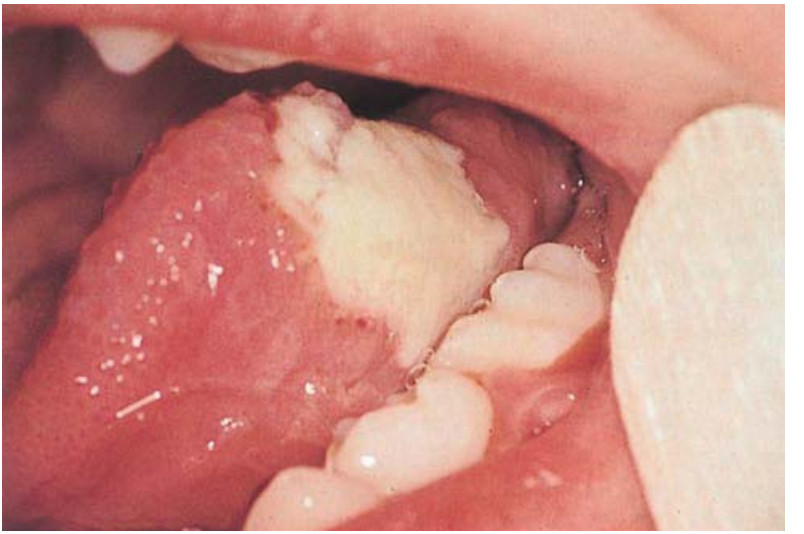


Fig. 190 Glycogen storage disease type Ib, large ulceration on the tongue.

FAPA Syndrome

Definition **FAPA** syndrome (periodic **F**ever, **A**phthous ulcer, **P**haryngitis, cervical **A**denitis) is an uncommon recurrent disease.

Etiology Unknown. However, an immune mechanism may be involved in the pathogenesis.

Clinical features Abruptly high fever (39–40°C), with chills and malaise, lasting for 4–6 days resolves spontaneously and recurs at intervals of 4–8 weeks. Aphthous ulcers in minor or major form are common (Fig. **191**). Pharyngitis, tonsillitis, and bilateral cervical adenitis are present. Headache, abdominal pain, and arthralgia may occur less frequently. Children below 10 years of age are more frequently affected. The diagnosis is made on the history and the clinical features.

Differential diagnosis Aphthous ulcer, cyclic neutropenia, Behçet disease, herpetic infection, leukemia.

Treatment Cimetidine, low doses of corticosteroids for 3–6 days, nonsteroidal anti-inflammatory agents.

Sweet Syndrome

Definition Sweet syndrome, or acute febrile neutrophilic dermatosis, is an uncommon acute dermatosis associated with systemic manifestations.

Etiology Unknown. However, a hypersensitivity reaction is possible. On the basis of possible etiology, five types of the disease are recognized (idiopathic, drug-induced, malignancy-associated, bowel disease-associated, and pregnancy-related).

Clinical features Fever (38–39°C), leukocytosis, arthralgias, myalgias, and ocular involvement are the most common manifestations. Renal, hepatic, pancreatic, and respiratory systems are less frequently involved. The skin is always affected. Nonpruritic, multiple, edematous and erythematous papules and plaques are common lesions. Vesiculobullous lesions may also occur (Fig. **192**). The head, neck, and the dorsa of the hands are more frequently affected. Oral lesions are rare and present as

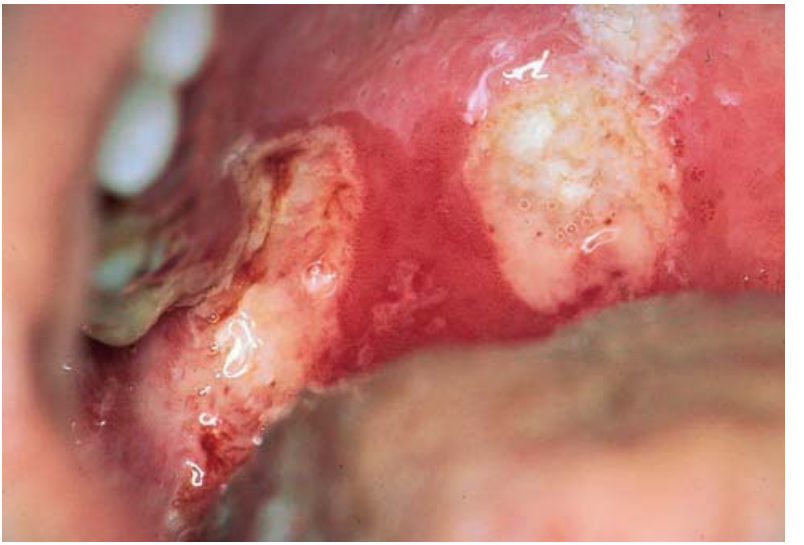


Fig. 191 FAPA syndrome, major aphthous ulcer on the soft palate.

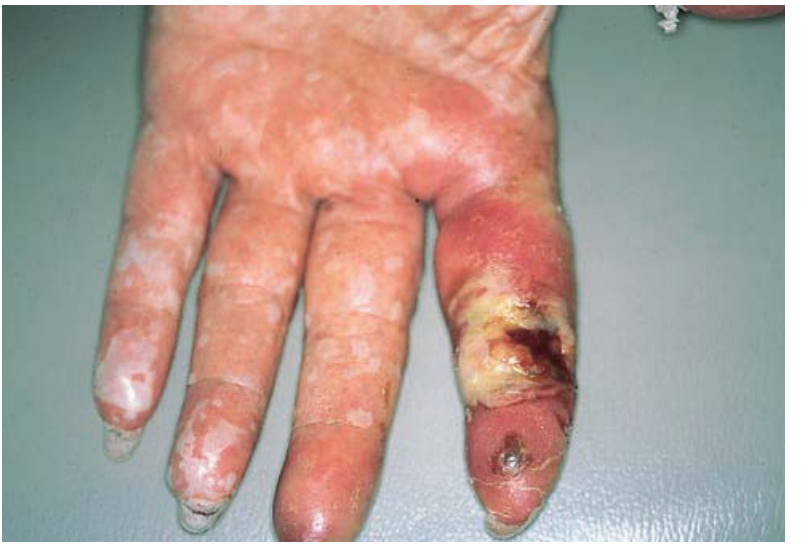


Fig. 192 Sweet syndrome: vesiculobullous lesions and edema of the fingers.

painful aphthous-like ulcers of varying size (Fig. **193**). The lip, tongue buccal mucosa, and palate are more frequently involved. The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests Histopathological examination of skin lesions, blood examination (leukocytosis with neutrophilia).

Differential diagnosis Aphthous ulcer, Behçet disease, FAPA syndrome, erythema multiforme, leukemia, systemic lupus erythematosus, Wegener granulomatosis.

Treatment Systemic corticosteroids, dapsone.

Staphylococcal Infection

Definition Staphylococcal infection is a rare infection of the oral mucosa.

Etiology *Staphylococcus aureus* and *Staphylococcus epidermides* are the most causative strains. Predisposing factors are trauma of the oral mucosa, poor oral hygiene, and systemic diseases such as diabetes mellitus, tuberculosis, immune deficiencies, and congenital neutropenia.

Clinical features Staphylococcal oral infection appears as a round or oval, abnormal, solitary ulcer with raised inflammatory border. The surface of the ulcer is covered by a whitish or yellow-white necrotic exudate (Fig. **194**). Low fever, malaise, headache, and regional lymphadenopathy may occur. The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests The definite diagnosis requires isolation of *Staphylococcus* species from smear and cultures.

Differential diagnosis Streptococcal infection, aphthous ulcer, mechanical trauma, chancre, tuberculous ulcer, cyclic neutropenia, myelodysplastic syndromes, Wegener granulomatosis.

Treatment Systemic antibiotics.

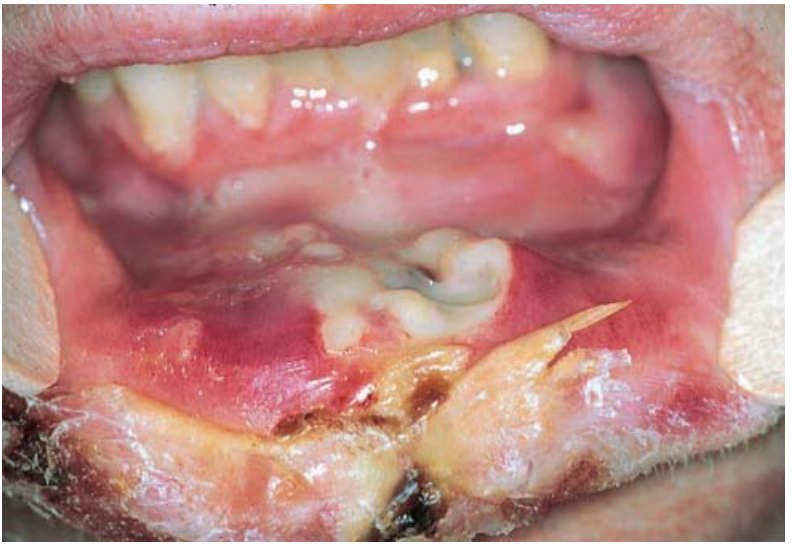


Fig. 193 Sweet syndrome, major aphthous-like ulcers on the lipmucosa.

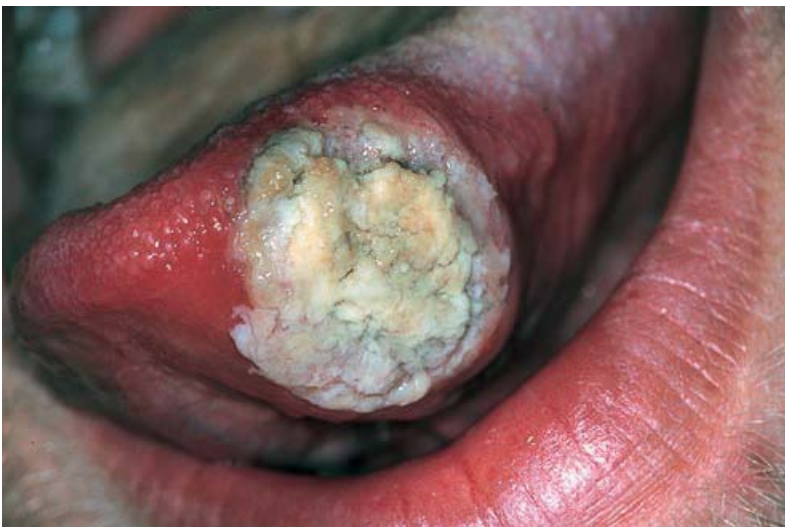


Fig. 194 Staphylococcal infection, necrotic ulcer of the tongue.

Congenital Neutropenia

Definition Congenital neutropenia is a rare hematological disorder characterized by a quantitative persistent decrease of neutrophils in the peripheral blood associated with life-threatening bacterial infections.

Etiology Genetic. Both autosomal dominant and recessive transmission have been reported, but some cases appear to be sporadic.

Clinical features The main clinical manifestations are recurrent infections, which are usually present at birth. The most common infections involve the respiratory and urinary tracts, middle ear, skin, and oral mucosa. Oral lesions are common and present as persistent and recurrent ulcerations, which may lead to scar formation (Fig.**195**). The ulcers characteristically lack an erythematous halo. Gingivitis and severe aggressive periodontitis, leading to tooth mobility, are common. Fever, malaise, fatigue, and lymphadenopathy are common symptoms. Affected children tend to improve with age and some undergo total remission in late childhood. The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests Complete blood count, radiographic examination.

Differential diagnosis Cyclic neutropenia, agranulocytosis, leukemia, glycogen storage disease type Ib, Chédiak–Higashi syndrome, hypophosphatasia, acatalasia, aggressive periodontitis.

Treatment A high level of oral hygiene, periodontal treatment, systemic antibiotics.

Cytomegalovirus Infection

Definition Oral infection with cytomegalovirus is a relatively rare disorder.

Etiology Cytomegalovirus (CMV, HHV-5), which is a member of the human herpesvirus family *Herpesviridae*. Predisposing conditions for CMV infection are HIV infection and immunocompromised transplantation. By the age of 70 years, 90–100% of the population are infected.

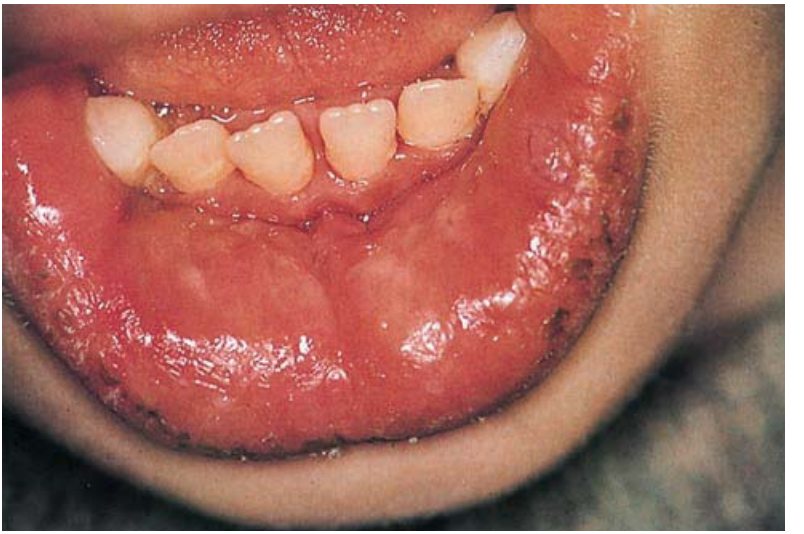


Fig. 195 Congenital neutropenia, lip mucosa ulceration and swelling, and periodontitis.

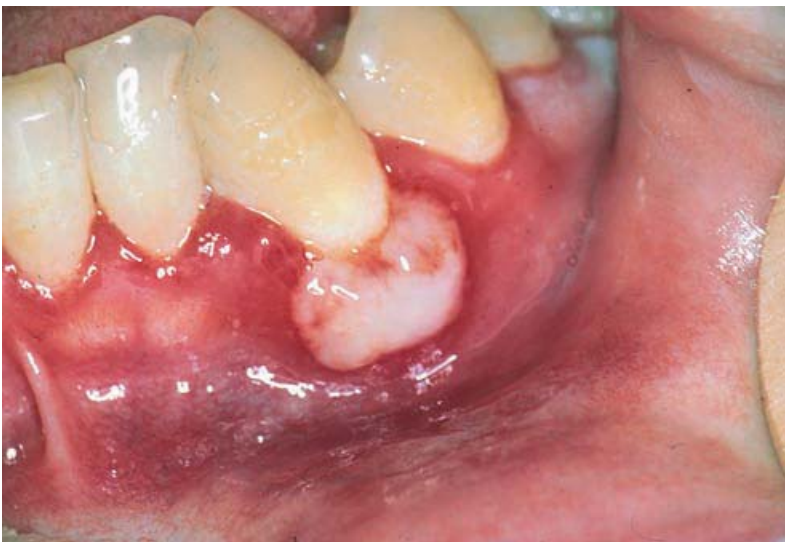


Fig. 196 Cytomegalovirus infection, ulcer on the gingiva.

Clinical features The great majority (over of 90%) of individuals with CMV infection are asymptomatic. Oral lesions due to CMV have been reported rarely, particularly in HIV-infected patients. Clinically, it presents as nonspecific painful ulcerations, usually on the gingiva and tongue (Fig. **196**). Enlargement of parotid and submandibular glands, leading to dry mouth, may occur. Fever, malaise, myalgias, headache, and liver dysfunction may be present. The clinical diagnosis of oral CMV infection should be confirmed by laboratory tests.

Laboratory tests Histopathological examination, immunochemistry, and molecular biology tests.

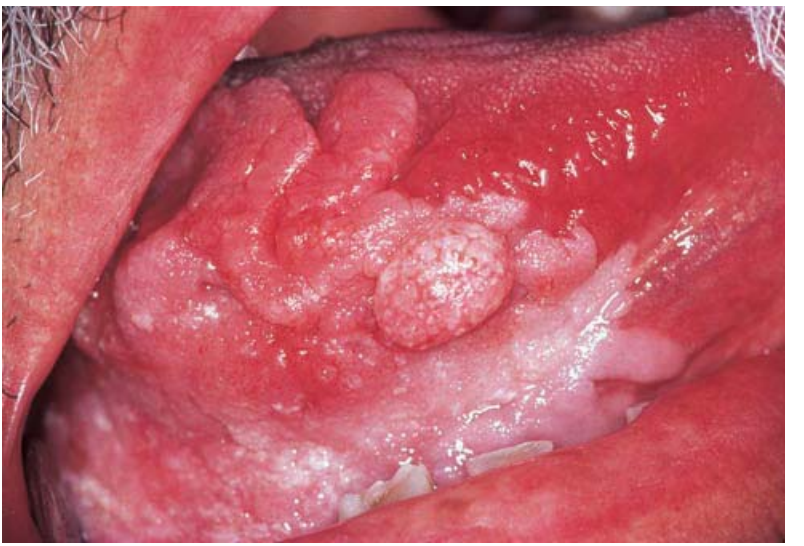
Differential diagnosis Aphthous ulcers, herpetic stomatitis, drug-related ulceration, mechanical trauma.

Treatment In most cases CMV infections resolve spontaneously. In persistent cases ganciclovir is the drug of choice.

6 Papillary Lesions

Papillary lesions of the oral mucosa are a small group, appearing clinically as exophytic growths with a verrucous or cauliflower-like surface. Reactive lesions, benign tumors, malignancies, and systemic diseases are included in this group. Etiologically, traumatic, viral, and neoplastic factors may cause these lesions. The diagnosis is based on clinical and histopathological criteria.

- Papilloma
- Condyloma acuminatum
- Verruca vulgaris
- Verruciform xanthoma
- Verrucous carcinoma
- Squamous-cell carcinoma
- Verrucous leukoplakia
- Focal epithelial hyperplasia
- Epulis fissuratum
- Crohn disease
- Acanthosis nigricans, malignant
- Familial acanthosis nigricans
- Darier disease



Papilloma

Papilloma is a common benign proliferation, originating from the stratified squamous epithelium (see also p. 34). Clinically, papilloma presents as a painless, exophytic, well-circumscribed and usually pedunculated lesion. Typically, it consists of numerous fingerlike projections, which give the lesion a "cauliflower" appearance (Fig. **197**). The tumor has a white or grayish color, and is usually between 0.5 cm and 1 cm in size. The tongue, gingiva, and soft palate are the sites of predilection (Figs. **198**, **199**). The differential diagnosis includes verruca vulgaris, condyloma acuminatum, early verrucous carcinoma, and verruciform xanthoma.

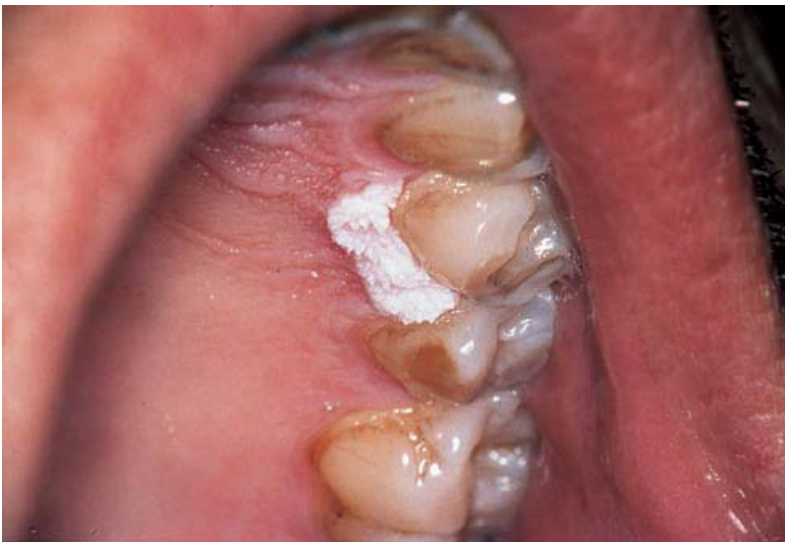


Fig. 197 Papilloma of the gingiva.

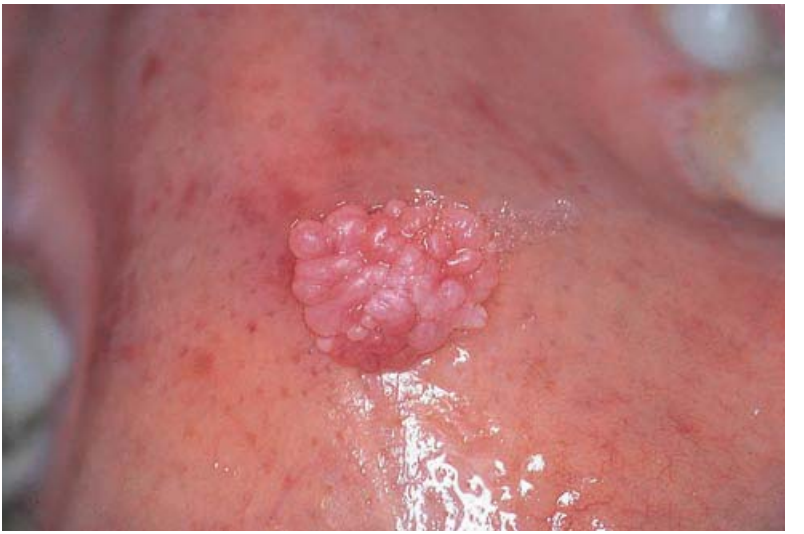


Fig. 198 Papilloma of the palate.

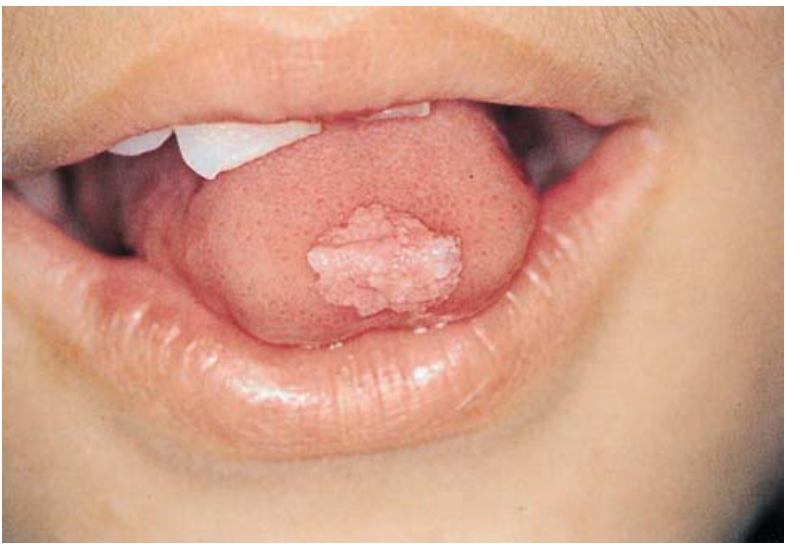


Fig. 199 Papilloma of the tongue.

Condyloma Acuminatum

Definition Condyloma acuminatum is a sexually transmitted benign lesion, mainly occurring in the anogenital region, and rarely in the mouth.

Etiology Human papillomavirus, types 6 and 11.

Clinical features Oral lesions appear as single, or more often multiple, small, sessile, well-demarcated, exophytic masses with a cauliflower-like surface (Fig. **200**). The lesions have a whitish or normal color, and usually recur; the average size is 0.5–1 cm. The labial mucosa, tongue, gingiva, buccal mucosa, and soft palate are the sites most frequently affected. Oral condyloma acuminatum occurs more frequently in HIV-infected patients (Fig. **201**). The anogenital lesions present as discrete or multiple, sessile or pedunculated, exophytic, small nodules with cauliflower-like appearance. The lesions may have whitish or brownish color and size that varies from 1–5 mm to several centimeters in diameter.

Laboratory tests Histopathological examination, in-situ hybridization, polymerase chain reaction (PCR).

Differential diagnosis Papilloma, verruca vulgaris, focal epithelial hyperplasia, verruciform xanthoma, sialadenoma papilliferum, focal dermal hypoplasia syndrome, early verrucous carcinoma, molluscum contagiosum.

Treatment Surgical excision, cryosurgery, CO2 laser, electrocautery, topical podophyllin.

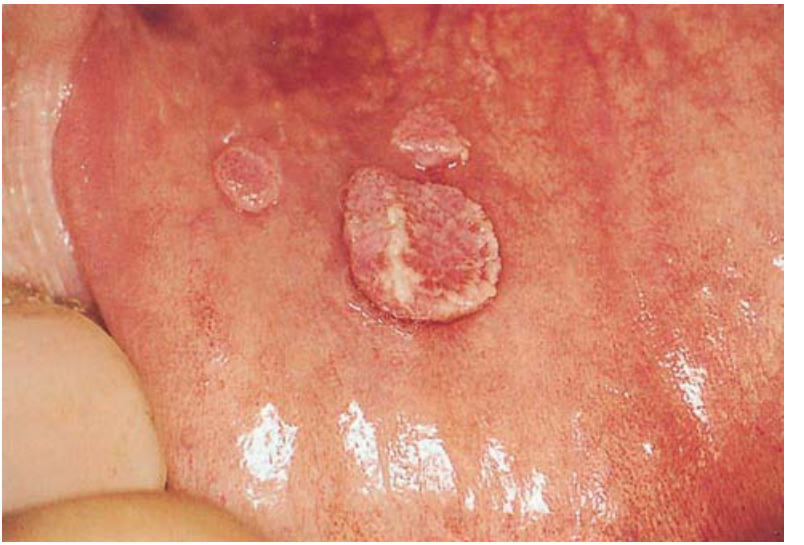


Fig. 200 Multiple condylomata acuminata on the lower lip mucosa.

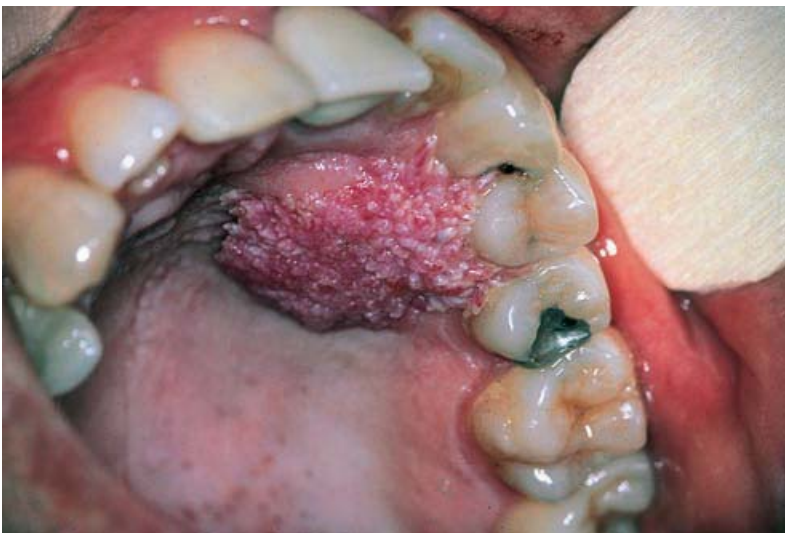


Fig. 201 Multiple condylomata acuminata of the gingiva.

Verruca Vulgaris

Definition Verruca vulgaris, or common wart, is a benign, mainly cutaneous lesion that may rarely appear in the oral mucosa.

Etiology Human papillomavirus (HPV-2, 4, and 40).

Clinical features Verruca vulgaris frequently develops on the hands of children. From the skin lesions, the virus can be autoinoculated into the oral mucosa, usually on the vermilion border and the lip mucosa, commissures, and tongue. Clinically, it appears as a painless, small, sessile, and well-defined exophytic growth with a cauliflower surface and whitish color (Figs. **202**, **203**, **204**). The lesions may be single or multiple.

Laboratory tests Histopathological examination.

Differential diagnosis Papilloma, condyloma acuminatum, verruciform xanthoma, focal epithelial hyperplasia.

Treatment Surgical excision, electrosurgery.

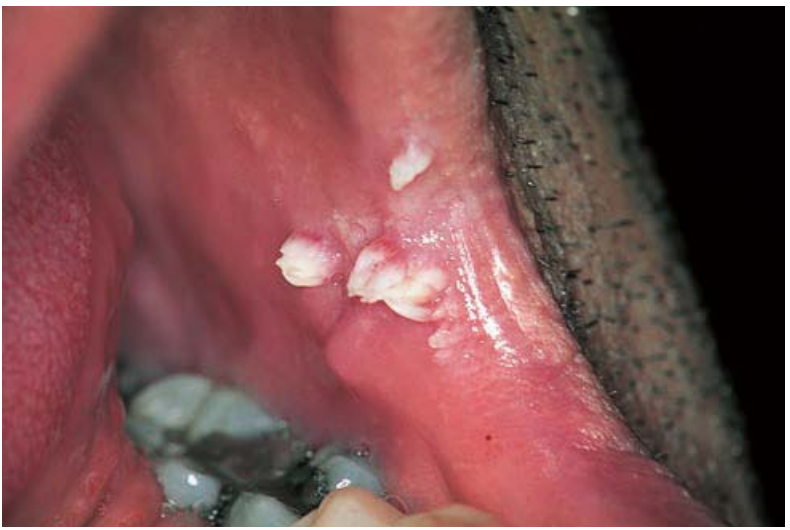


Fig. 202 Verruca vulgaris, multiple lesions on the buccal mucosa.

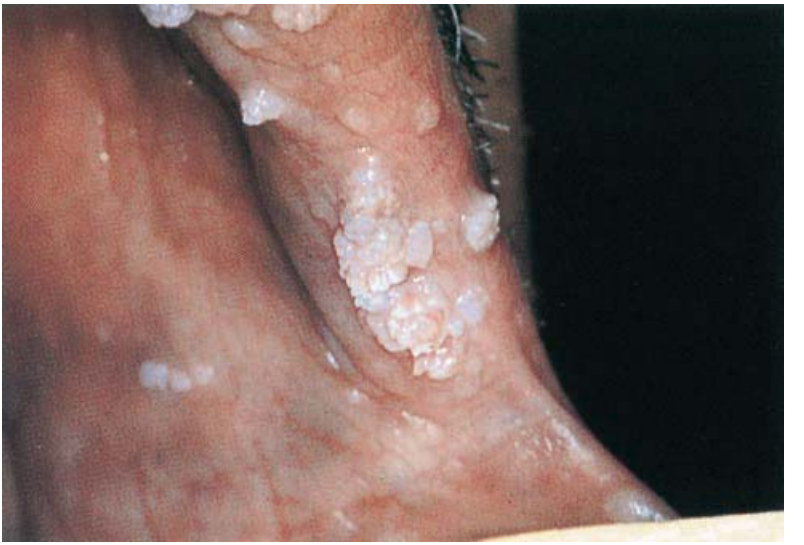


Fig. 203 Verruca vulgaris: multiple lesions on the lip mucosa.

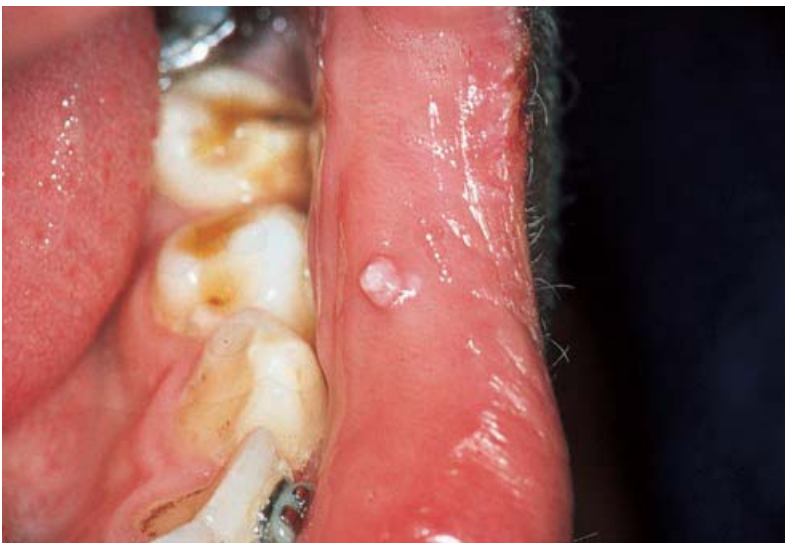


Fig. 204 Verruca vulgaris: solitary lesion on the lip mucosa.

Verruciform Xanthoma

Definition Verruciform xanthoma is a rare hyperplastic disorder of the oral mucosa.

Etiology Unknown. Presumably, it may represent a reaction to local trauma.

Clinical features The lesion is more common in women in the 50–70 year age group. Typically, it appears as a well-demarcated, painless, sessile, slightly elevated lesion. It has a cauliflower-like surface with a reddish-yellowish or normal color (Fig. **205**). The size ranges from 0.5 cm to 2 cm, and the gingiva and alveolar ridge, tongue, and palate are the most common locations.

Laboratory tests Histopathological examination.

Differential diagnosis Papilloma, verruca vulgaris, condyloma acuminatum, sialadenoma papilliferum, verrucous carcinoma.

Treatment Surgical excision.

Verrucous Carcinoma

Verrucous carcinoma (see also p. 36) is a low-grade variant of squamous-cell carcinoma. Typically, it presents as an exophytic, whitish mass with a papillary or verruciform surface (Fig. **206**). Along with the clinical features, biopsy and histopathological examination should be performed to rule out other papillary growths. Verrucous carcinoma is well-differentiated, slow-growing, rarely metastasizes, and has a good prognosis.

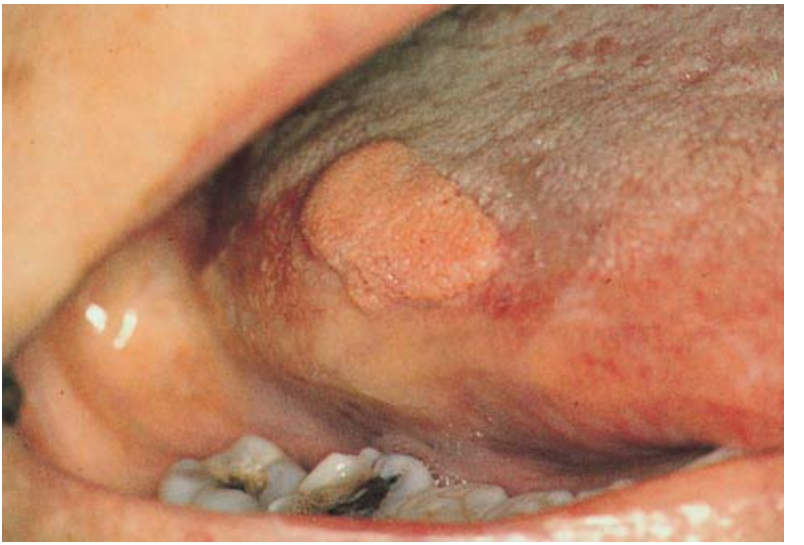


Fig. 205 Verruciform xanthoma of the tongue.

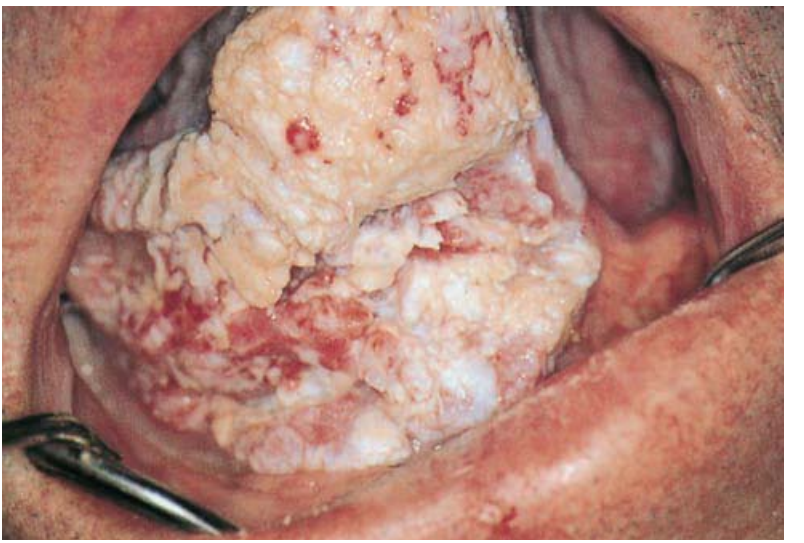


Fig. 206 Extensive verrucous carcinoma of the tongue.

Squamous-Cell Carcinoma

Squamous-cell carcinoma has a wide range of clinical presentations (see also pp. 172, 272). A common clinical feature is an exophytic mass. It has a papillary or verruciform surface and a red, whitish, or normal color (Fig. **207**). The surface is usually ulcerated, and the base of the lesion is indurated on palpation. The buccal mucosa, tongue, floor of the mouth, and gingiva are the most common regions affected by this clinical form of carcinoma.

Verrucous Leukoplakia

Verrucous leukoplakia is a rare clinical form of leukoplakia with a greater risk of malignant transformation (see also p. 2). Clinically, it presents as an irregular, white, exophytic plaque with a papillary surface (Figs. **208**, **209**) and a relative tendency to spread. Verrucous leukoplakia occurs more frequently in women (the female to male ratio is about 4 : 1). Biopsy and histopathological examination must always be performed. The treatment of choice is surgical excision. The lesions tend to recur.

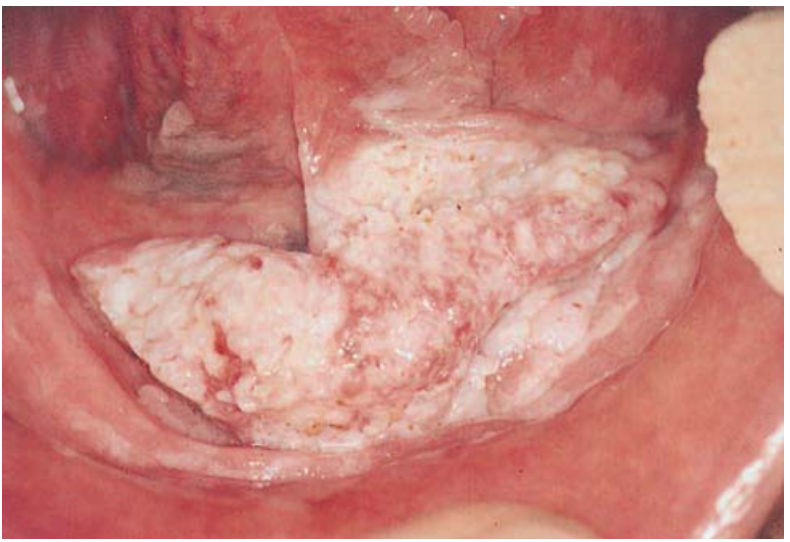


Fig. 207 Late squamous-cell carcinoma of the floor of the mouth.

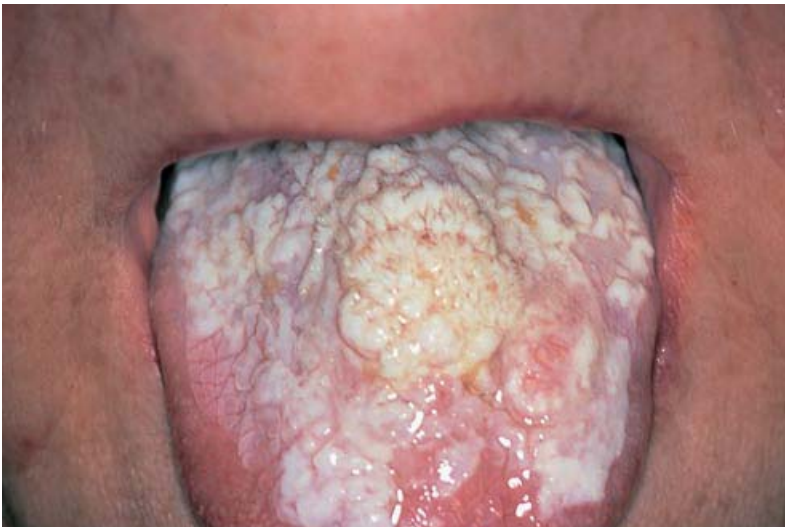


Fig. 208 Generalized proliferative verrucous leukoplakia on the dorsum of the tongue.

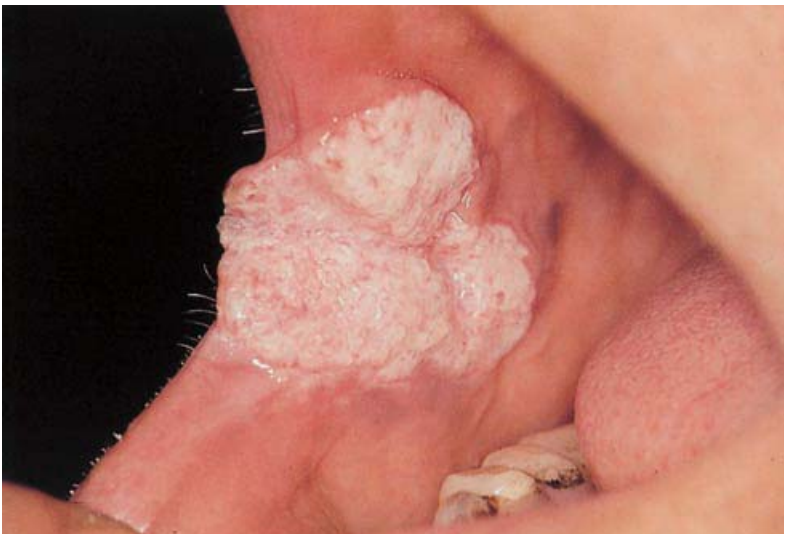


Fig. 209 Proliferative verrucous leukoplakia of the buccal mucosa.

Focal Epithelial Hyperplasia

Definition Focal epithelial hyperplasia, or Heck disease, is a benign hyperplastic lesion of the oral squamous epithelium.

Etiology Human papillomavirus (HPV-13 and 32). A genetic factor may also be involved.

Clinical features The disease frequently occurs among the Eskimos, North American Indians, South Africans, and, rarely, in other ethnic groups. Children are more often affected. The condition is characterized clinically by multiple painless, sessile, slightly elevated, soft nodules or plaques 1–10 mm in diameter (Figs. **210**, **211**, **212**). The lesions may occasionally have a slightly papillary surface, and they have a whitish or normal color. The buccal mucosa, lips, tongue, and gingiva are the sites more frequently involved.

Laboratory tests Histopathological examination, in-situ hybridization, polymerase chain reaction (PCR).

Differential diagnosis Multiple condylomata acuminata and verruca vulgaris, multiple papillomas, focal dermal hypoplasia syndrome, Cowden disease.

Treatment Conservative surgical excision only for aesthetic purposes. Spontaneous regression may occur.

Epulis Fissuratum

Definition Epulis fissuratum, or denture fibrous hyperplasia, is a relatively common hyperplasia of the fibrous connective tissue.

Etiology Poorly fitting partial or complete denture.

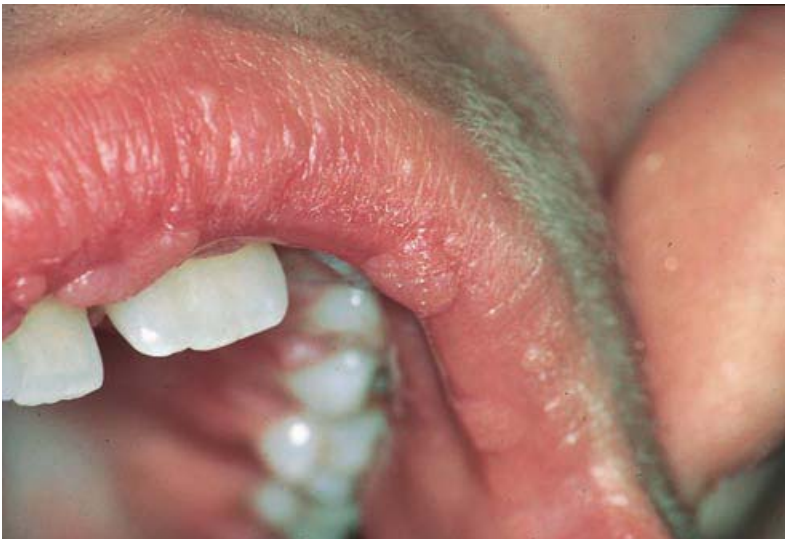


Fig. 210 Focal epithelial hyperplasia: multiple lesions on the upper lip.

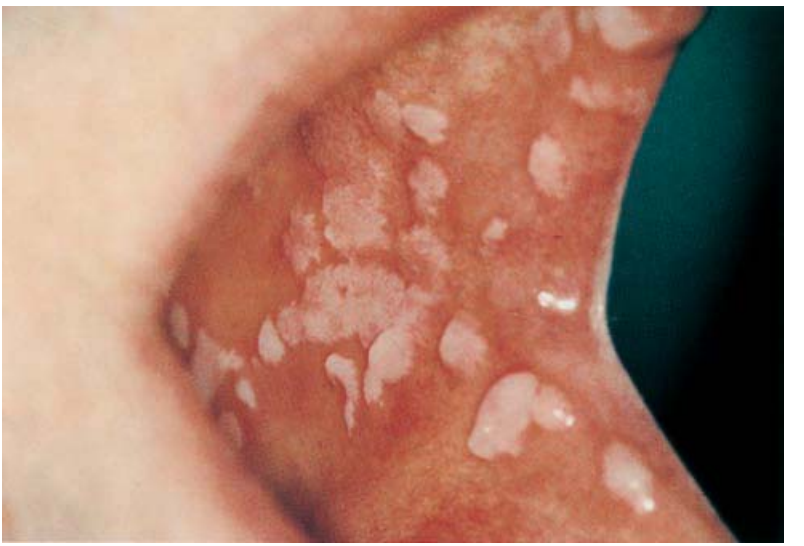


Fig. 211 Focal epithelial hyperplasia: multiple lesions on the buccal mucosa.

Clinical features The lesion presents as multiple or single inflamed and elongated papillary folds, usually in the mucolabial or mucobuccal grooves (Fig. **213**). The lesions are mobile, and usually ulcerated at the base of the folds. The diagnosis is usually made at the clinical level.

Laboratory test Histopathological examination.

Differential diagnosis Neurofibromatosis, fibroma, fibroepithelial polyp, squamous-cell carcinoma.

Treatment Surgical excision and construction of a new denture.

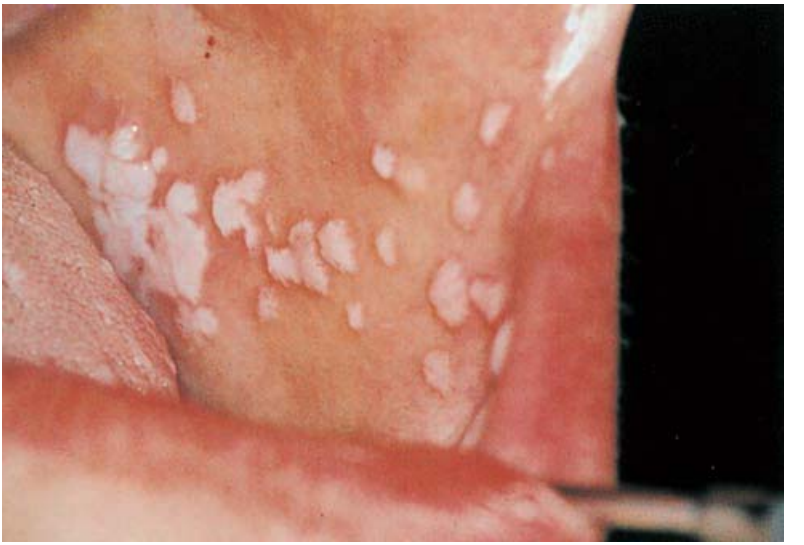


Fig. 212 Focal epithelial hyperplasia: multiple lesions on the buccal mucosa.

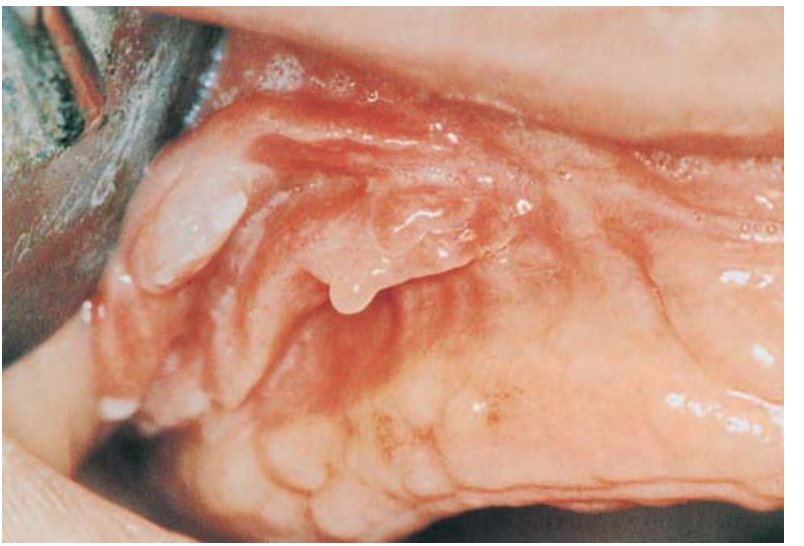


Fig. 213 Epulis fissuratum.

Crohn Disease

Definition Crohn disease or regional ileitis is a chronic inflammatory disease that primarily affects the ileum and other parts of the gastrointestinal tract.

Etiology Unknown; probably immunologically mediated.

Clinical features The disease usually affects young individuals, and presents clinically with abdominal pain, nausea, diarrhea, weight loss, low-grade fever, and rectal bleeding. Extra-abdominal involvement includes arthritis, spondylitis, uveitis, and oral manifestations. Oral lesions occur in 10–20% of patients and are characterized by nodular swelling, which may be ulcerated. Diffuse raised nodules resulting in a cobblestone appearance of the mucosa or mucosal tag lesions may occur (Fig. **214**). Granulomatous lip swelling, angular cheilitis, gingival swelling, and atypical ulcerations may be seen.

Laboratory tests Histopathological examination.

Differential diagnosis Orofacial granulomatosis, epulis fissuratum, pyogenic granuloma.

Treatment Topical steroids, systemic steroids, sulfasalazine.

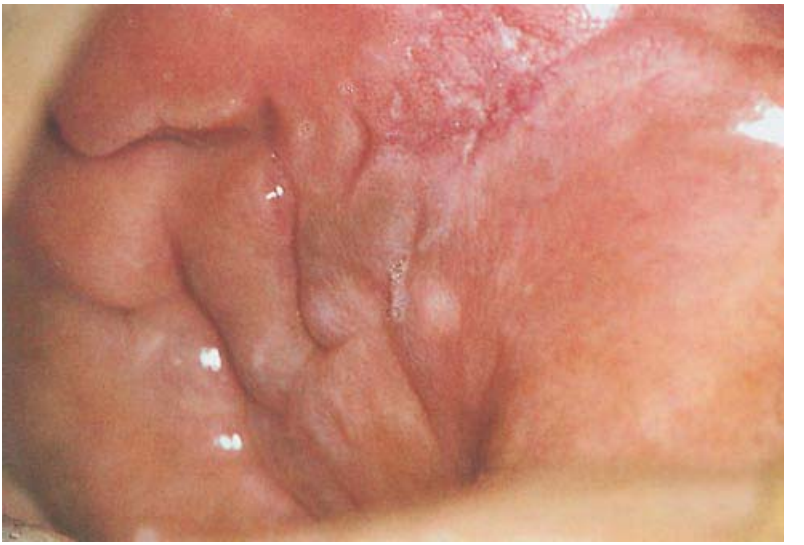


Fig. 214 Crohn disease: cobblestone appearance of the buccal mucosa.

Acanthosis Nigricans, Malignant

Definition Acanthosis nigricans is a rare disorder involving the skin and mucosae, characterized by papillary lesions and brownish alteration of the skin.

Etiology Unknown.

Clinical features The disorder is classified into two major types: the *benign* form (genetic or acquired) and the *malignant* form, which is associated with an internal malignancy, particularly adenocarcinoma. Oral manifestations are more common in the malignant form and are characterized by papillomatous growths that most often involve the lips, tongue, and gingiva (Fig. **215**). Hypertrophy and elongation of the filiform papillae may result in a shaggy appearance of the tongue. The skin manifestations present as small, velvety papillary lesions, tags, and dark pigmentation (Fig. **216**). The axillae, the genitofemoral area, the neck, and, less commonly, the palms of the hand and soles of the foot are the sites of predilection.

Laboratory tests Histopathological examination.

Differential diagnosis Benign acanthosis nigricans, pyostomatitis vegetans, focal epithelial hyperplasia, multiple papillomas, lipoid proteinosis, multiple verruca vulgaris, pemphigus vegetans.

Treatment Symptomatic. Treatment of the underlying malignancy may resolve the oral and skin lesions in the malignant form of the disease.

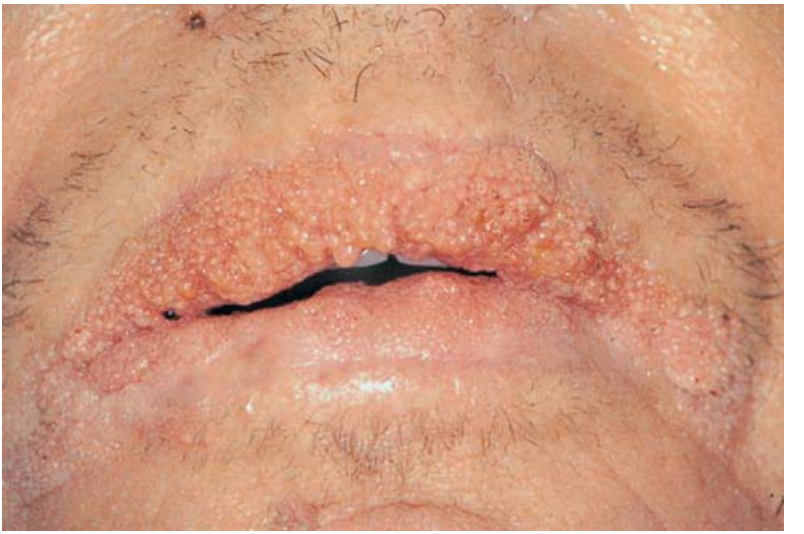


Fig. 215 Malignant acanthosis nigricans: verrucous and papillomatous lesions of the lips.

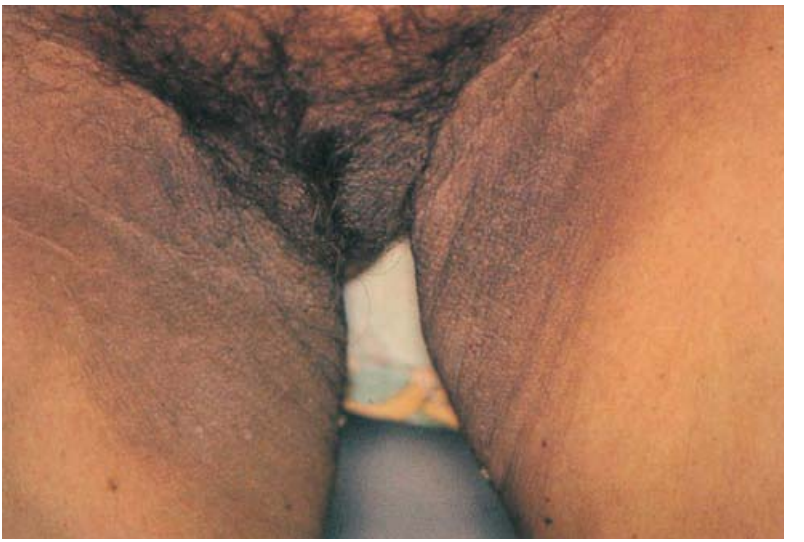


Fig. 216 Malignant acanthosis nigricans: marked pigmentation and papillary hyperplasia of the skin.

Familial Acanthosis Nigricans

Definition. Familial or genetic acanthosis nigricans is a rare benign mucocutaneous disorder, characterized by papillary lesions and skin discoloration.

Etiology. Genetic. It is inherited as an autosomal dominant trait.

Clinical features. The cutaneous lesions appear as multiple, painless small papillary growths (skin tags) and dark discoloration (Fig. **217**). The axillae, groin, neck, umbilicus, genitalia, and perianal area are more frequently affected. Oral lesions occur in 10–25% of the cases and present as multiple, small, painless, papillomatous growths with normal color (Fig. **218**). Hypertrophy and elongation of the filiform papillae result in a shaggy appearance of the tongue. The tongue, lips, gingiva, and palate are more frequently affected. The disorder usually begins during childhood or at puberty. The diagnosis is mainly based on the history and the clinical features. Biopsy and histopathological examination may also be helpful.

Differential diagnosis. Endocrine-related acanthosis nigricans, malignant acanthosis nigricans, Darier disease, Cowden disease.

Treatment. Good oral hygiene, electrosurgery, cryosurgery.

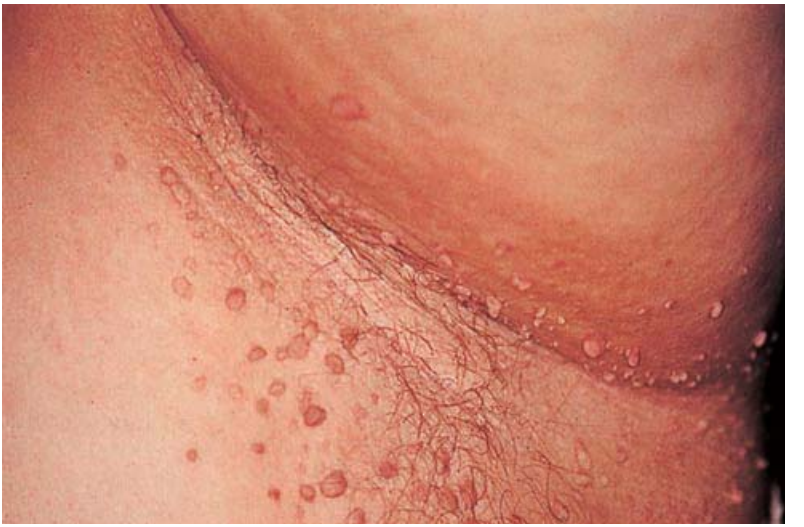


Fig. 217 Benign acanthosis nigricans, multiple skin tags.

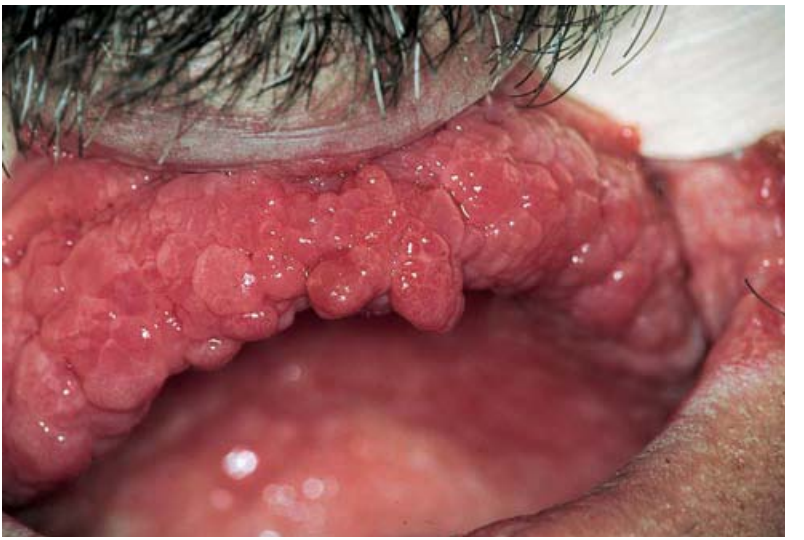


Fig. 218 Familial acanthosis nigricans

Darier Disease

Definition. Darier disease, or dyskeratosis follicularis, is a relatively rare mucocutaneous disease.

Etiology. Genetic. It is inherited as an autosomal dominant trait.

Clinical features. The disease affects mainly the skin and nails, but the mucosae may also be involved (oral mucosa, pharynx, genitalia, rectum). The skin lesions appear as multiple, painless, brownish-red papules that usually coalesce into plaques (Fig. **219**). The forehead, ears, scalp, chest, and back are more frequently affected. The nails exhibit subungual keratosis and longitudinal ridges and lines. Oral lesions occur in 20–40% of cases and appear as small multiple whitish confluent papules, which may become hypertrophic, assuming a cobblestone or papillary pattern (Fig. **220**). The palate, gingiva, buccal mucosa, and tongue are more frequently affected. The oral lesions develop after the cutaneous ones. The clinical diagnosis should be confirmed by a biopsy and histopathological examination.

Differential diagnosis. Familial acanthosis nigricans, familial benign pemphigus, papillary hyperplasia of the palate, Cowden disease.

Treatment. Good oral hygiene, systemic aromatic retinoids.

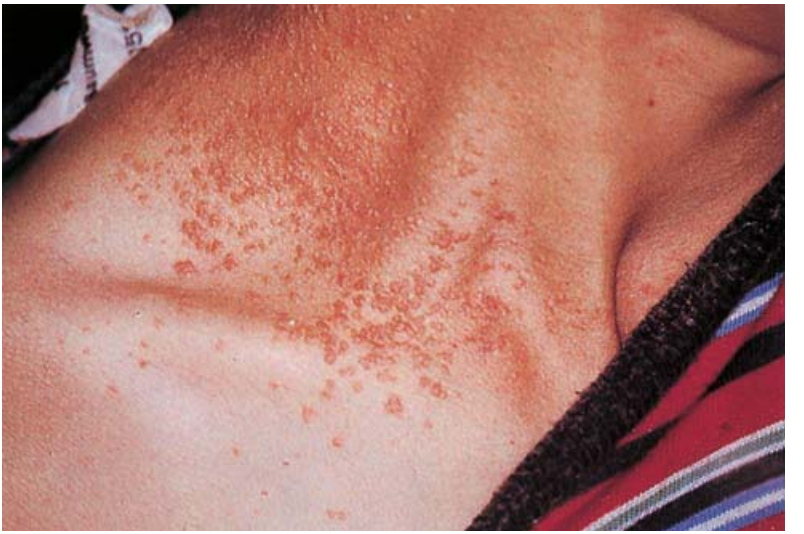


Fig. 219 Darier disease, multiple skin papules.

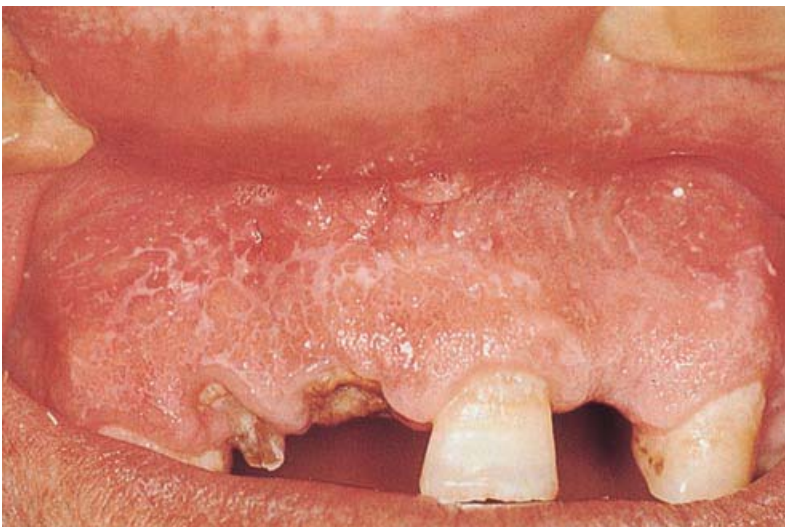


Fig. 220 Darier disease, multiple whitish confluent papules on the gingiva and alveolar mucosa.

7 Gingival Enlargement

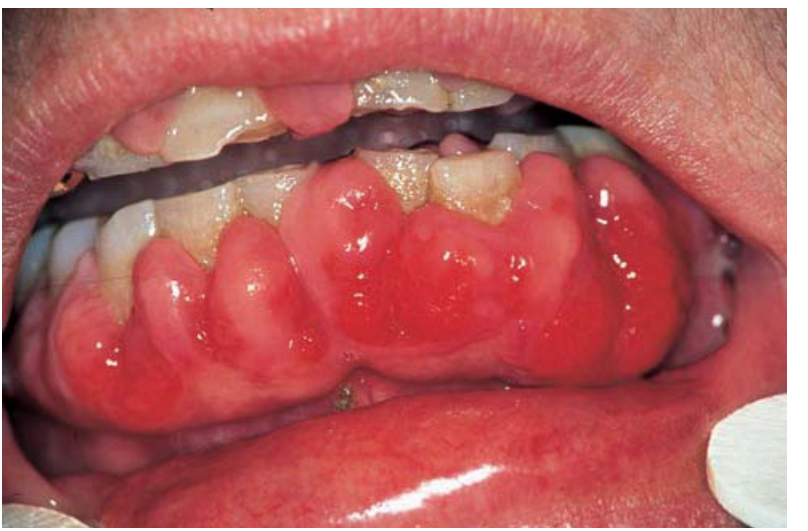
A common characteristic of this group of lesions is that they are located on the gingiva and present as a submucosal enlargement covered by normal epithelium. The lesions can be either generalized or localized. Local diseases, drug-induced lesions, systemic diseases, and tumors are included in this particular group of disorders.

I Generalized

- Hyperplastic gingivitis
- Mouth-breathing gingivitis
- Drug-induced gingival overgrowth
- Gingival overgrowth in pregnancy
- Gingival overgrowth due to leukemia
- Hereditary gingival fibromatosis
- Scurvy
- Wegener granulomatosis
- Acanthosis nigricans

II Localized

- Pyogenic granuloma
- Peripheral giant-cell granuloma
- Peripheral ossifying fibroma
- Granular-cell tumor of the newborn
- Periodontal abscess
- Parulis
- Multiple exostoses
- Gingival cyst
- Eruption cyst



Generalized

Hyperplastic Gingivitis

Definition Hyperplastic gingivitis is a chronic inflammatory process that produces gingival enlargement.

Etiology Dental plaque. Local and systemic factors may involve susceptibility to the oral microbial flora, and the host response.

Clinical features Clinically, the interdental papillae and marginal gingiva appear diffuse, red, and swollen, and significantly increased in size due to connective-tissue fibromatosis and edema (Figs. **221**, **222**, **223**). Loss of normal stippling, gingival bleeding even after mild local stimulation, and formation of pseudopockets are common findings. The diagnosis is made at the clinical level.

Differential diagnosis Gingivitis of pregnancy, drug-induced gingival overgrowth, mouth-breathing gingivitis, leukemias.

Treatment Oral hygiene improvement, elimination of causative factors, and, in severe hyperplasia, surgical reconstruction.

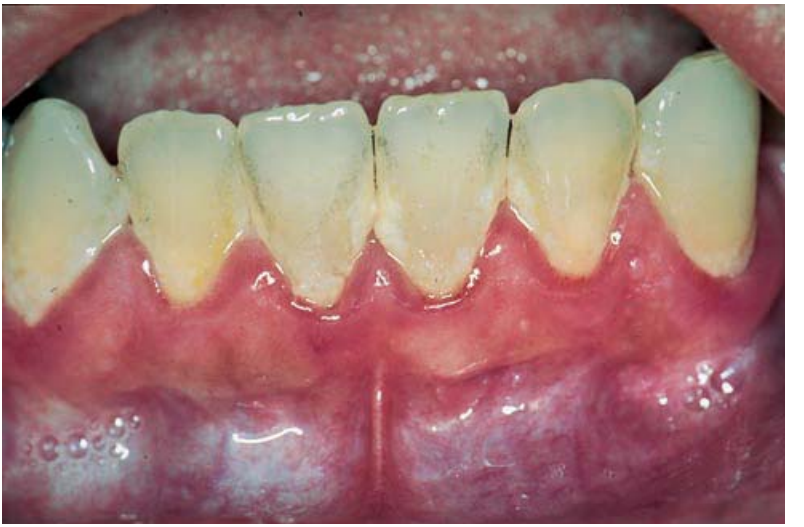


Fig. 221 Mild gingivitis

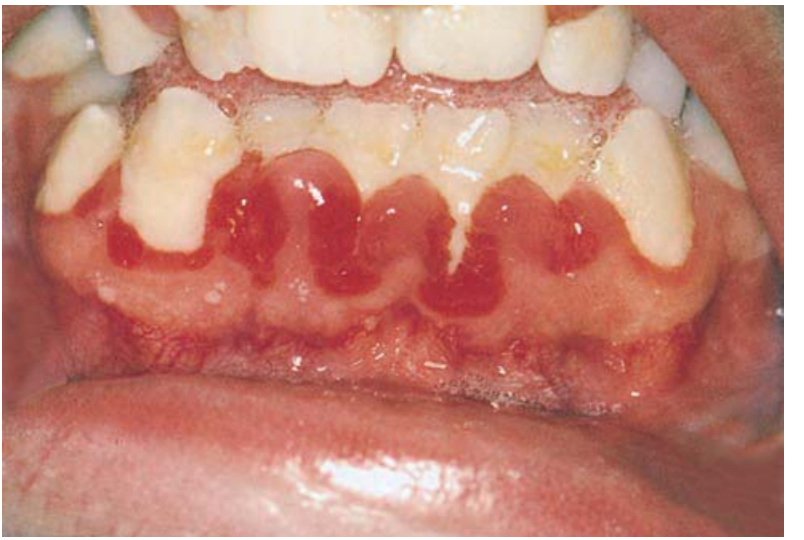


Fig. 222 Hyperplastic gingivitis.

Mouth-Breathing Gingivitis

Definition Mouth-breathing gingivitis is a unique form of hyperplastic gingivitis.

Etiology Mouth breathing or incomplete lip closure.

Clinical features This form of gingivitis affects the anterior facial gingiva in young persons. Clinically, the gingiva appear swollen, red, dry, and shiny, covering part of the crown of the teeth (Fig. **224**). The diagnosis is made using clinical criteria.

Differential diagnosis Drug-induced gingival overgrowth, hyperplastic gingivitis.

Treatment Gingivectomy and discontinuation of mouth-breathing.

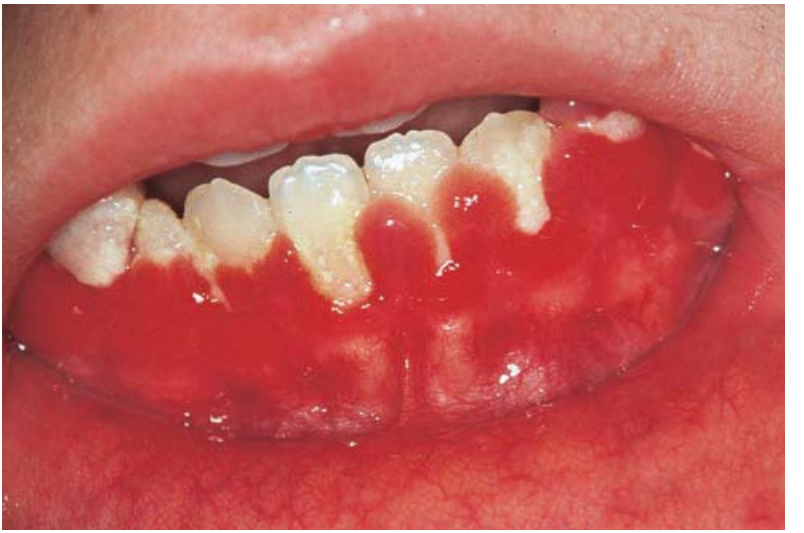


Fig. 223 Hyperplastic gingivitis.

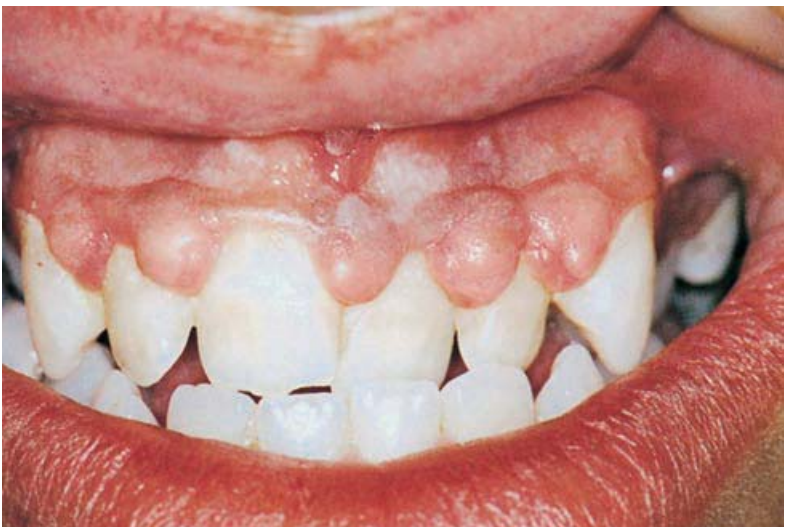


Fig. 224 Gingivitis caused by mouth breathing.

Drug-Induced Gingival Overgrowth

Definition Drug-induced gingival overgrowth is a relatively common disorder of the gingiva due to several drugs.

Etiology The most common drugs associated with the condition are phenytoin, ciclosporin, and calcium channel blockers.

Clinical features The gingival overgrowth is usually related to the dose of the drug, the duration of therapy, the serum concentration, and the presence of dental plaque. Clinically, both marginal gingiva and interdental papillae appear enlarged and firm, with a surface that may be smooth, stippled, or lobulated, with little or no inflammation (Figs. **225**, **226**, **227**, **228**, **229**). The gingival overgrowth may be localized or generalized, and can partially or entirely cover the crown of the teeth. In severe cases, difficulties in mastication and speech may occur. The diagnosis is made on the basis of the medical history and the clinical features.

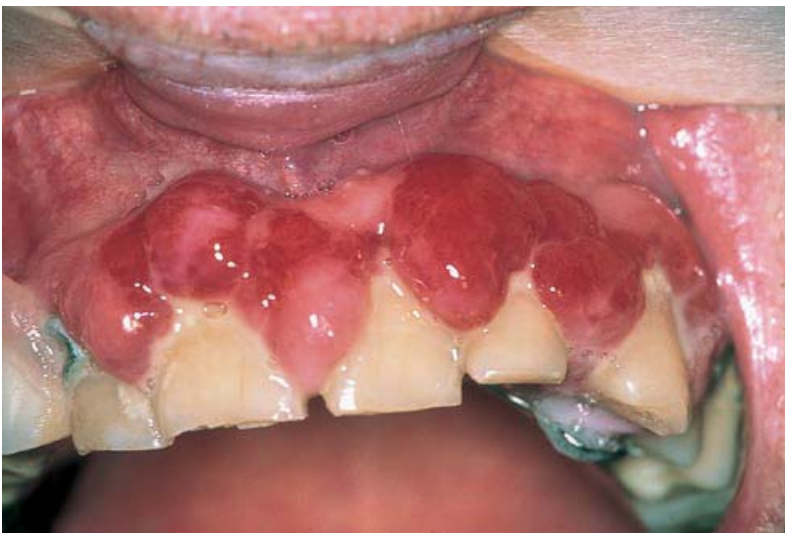


Fig. 225 Gingival overgrowth caused by felodipine.

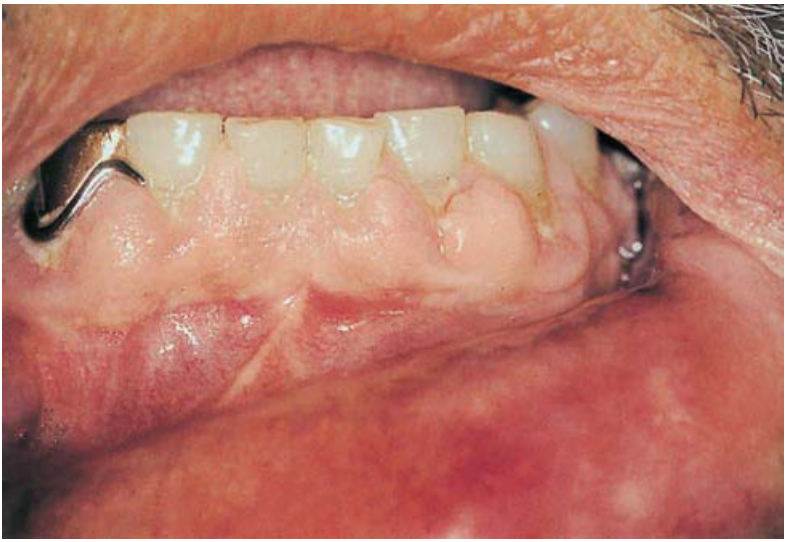


Fig. 226 Gingival overgrowth caused by nifedipine.

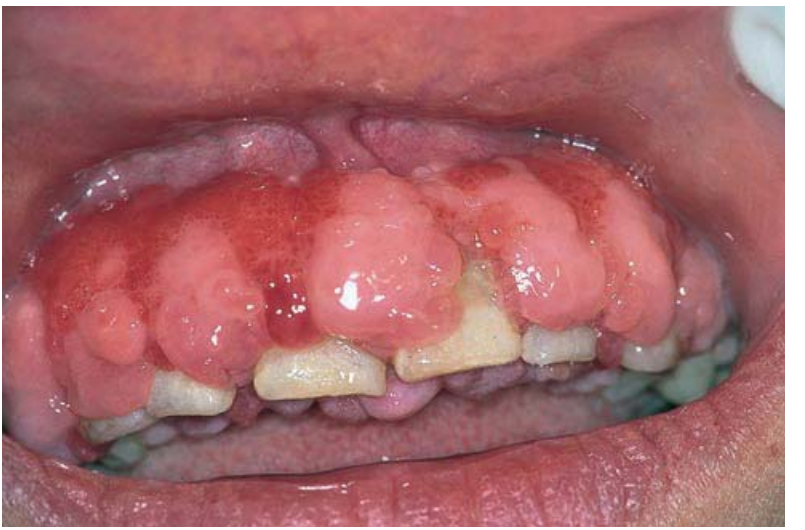


Fig. 227 Gingival overgrowth caused by ciclosporin.

Differential diagnosis Hereditary gingival fibromatosis, mouth-breathing gingivitis, leukemia, Crohn disease, amyloidosis.

Treatment Improvement of oral hygiene, gingivectomy, discontinuation of the offending drug.

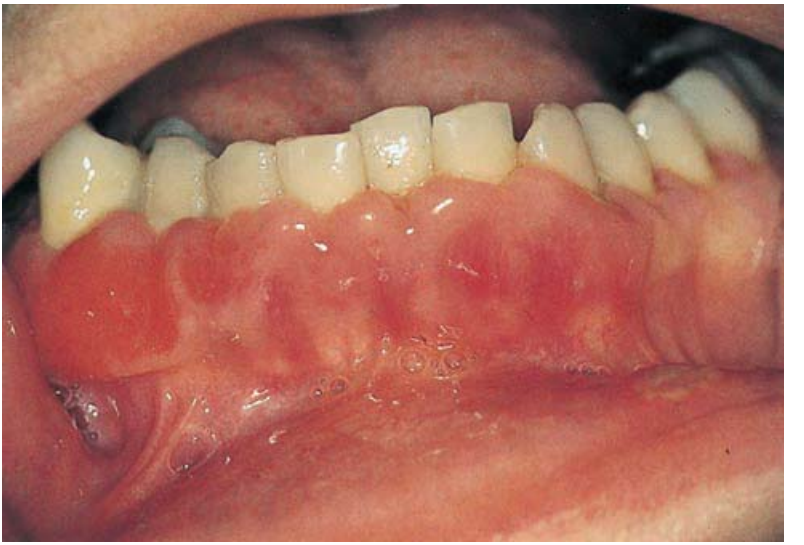


Fig. 228 Gingival overgrowth caused by ciclosporin.

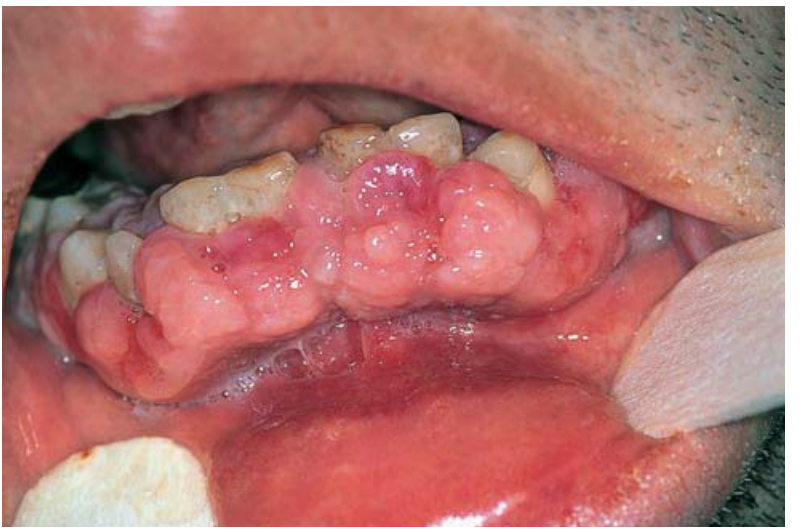


Fig. 229 Gingival overgrowth caused by phenytoin.

Gingival Overgrowth in Pregnancy

Definition Gingival overgrowth in pregnancy, or pregnancy gingivitis, is a relatively rare form of gingival hyperplasia that occurs exclusively during pregnancy.

Etiology Increased levels of estrogen and progesterone and poor oral hygiene.

Clinical features The condition presents as significant gingival enlargement, generalized or localized in one or more quadrants. The gingiva is soft, edematous, bright red, with dense inflammation, and is hyperplastic and bleeds easily (Fig. **230**). A "pregnancy granuloma" may also occur. These lesions usually appear after the first trimester.

Differential diagnosis Scurvy, dental plaque-induced gingivitis.

Treatment Good oral hygiene. The gingivitis may regress after pregnancy.

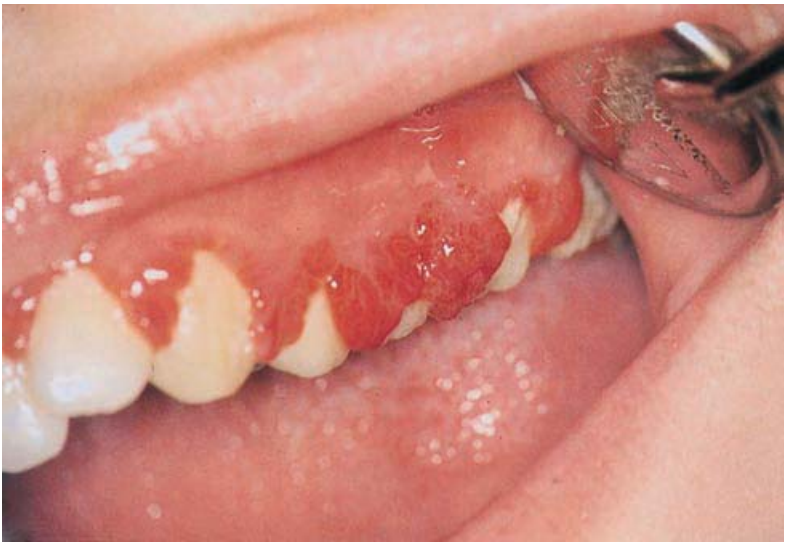


Fig. 230 Severe gingivitis during pregnancy.

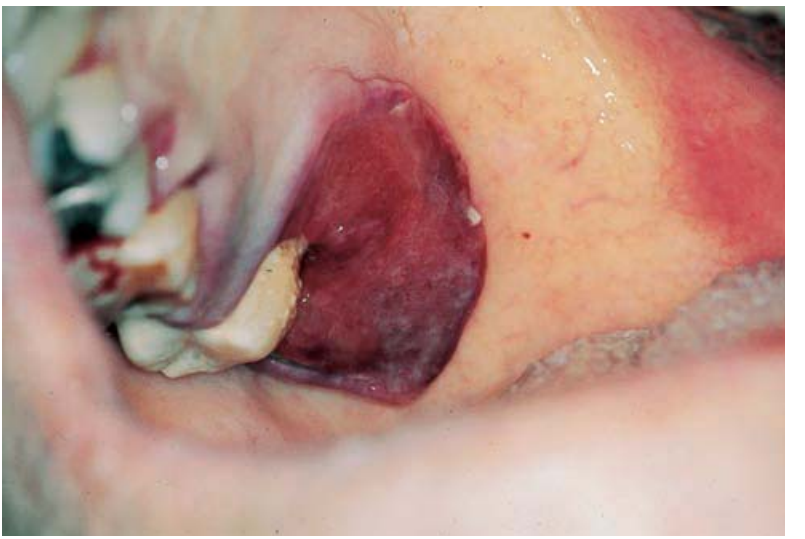


Fig. 231 Acute myelomonocytic leukemia: localized gingival overgrowth.

Gingival Overgrowth due to Leukemia

Gingival overgrowth is a common and early finding in leukemia (see also p. 184). Gingival swelling occurs most frequently in patients with myelomonocytic and myelocytic leukemia. Gingival infiltration by leukemic cells causes diffuse enlargement of the gingiva, which becomes edematous, red, and inflamed, and bleeds spontaneously (Figs. **231**, **232**, **233**).

Differential diagnosis Scurvy, agranulocytosis, drug-related gingival overgrowth, hereditary gingival fibromatosis.

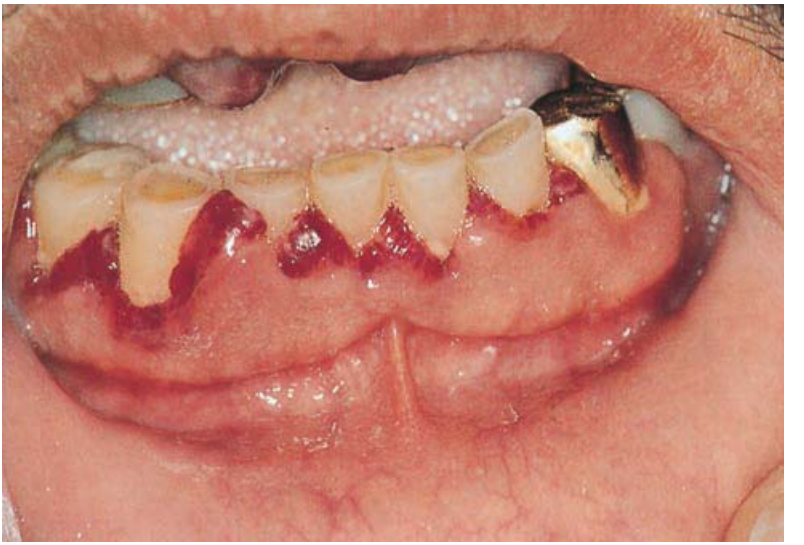


Fig. 232 Erythroleukemia: gingival overgrowth.

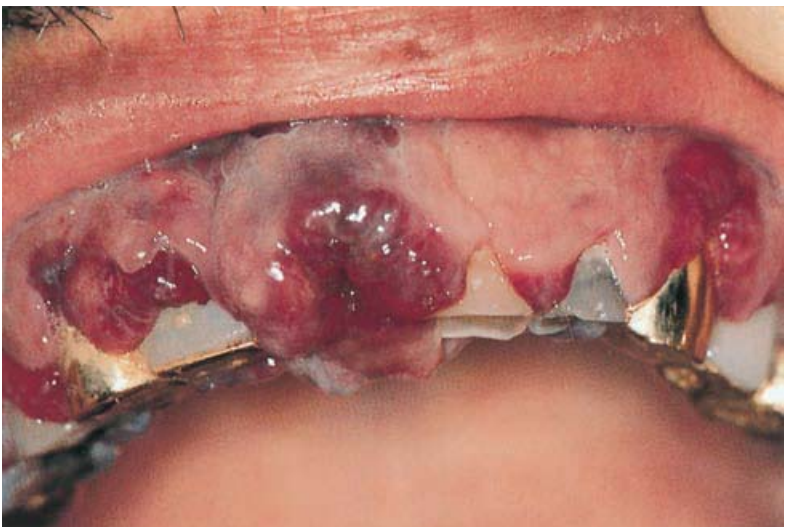


Fig. 233 Acute myelomonocytic leukemia: severe gingival overgrowth.

Hereditary Gingival Fibromatosis

Definition Hereditary gingival fibromatosis is a unique gingival enlargement caused by collagenous proliferation of the fibrous connective tissue of the gingivae.

Etiology Genetic. It is transmitted as an autosomal dominant or rarely as an autosomal recessive trait.

Clinical features The disorder usually begins before age 15 years in both sexes. The gingival enlargement is usually generalized, but less commonly may be localized in one or two quadrants. The gingiva are firm, smooth, and occasionally papillary or nodular, with no or only minimal inflammation, and a normal color (Fig. **234**). The teeth may be partially or completely covered by the overgrown gingiva (Fig. **235**). Delay or failure in teeth eruption may also be seen. Although either jaw may be involved, the maxillary gingiva are more frequently and severely affected. The diagnosis is mainly based on the history and the clinical features.

Laboratory tests Histopathological examination.

Differential diagnosis Drug-related gingival overgrowth, gingival fibromatosis associated with several genetic syndromes, Crohn disease, amyloidosis, leukemia.

Treatment Gingivectomy, good oral hygiene.

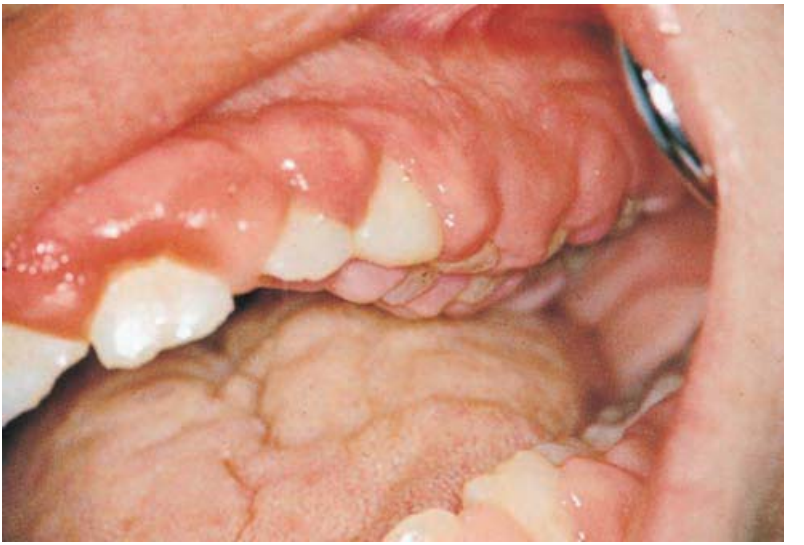


Fig. 234 Hereditary gingival fibromatosis.

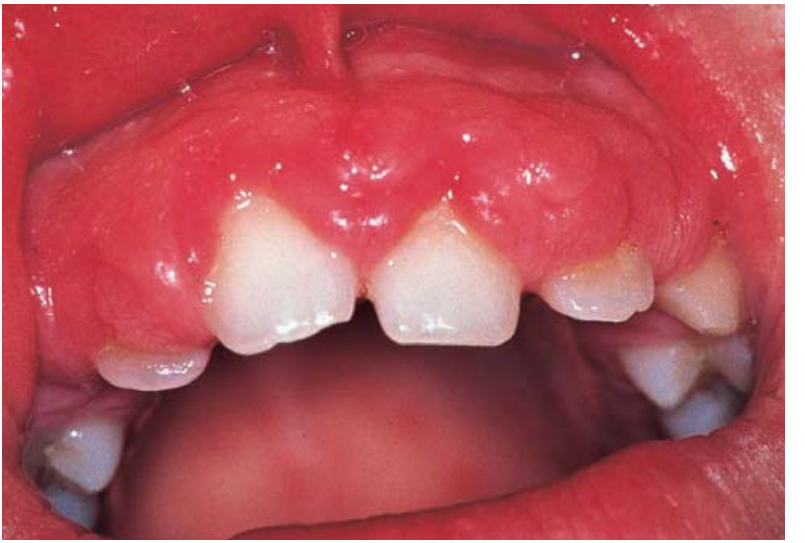


Fig. 235 Hereditary gingival fibromatosis.

Scurvy

Definition Scurvy is a rare systemic nutritional disorder that primarily affects the gingiva, skin, hair, nails, muscles, and joints.

Etiology Vitamin C (ascorbic acid) deficiency.

Clinical features The oral manifestations consist of generalized swelling and redness of the marginal and the interdental gingiva, followed by gingival bleeding, ulceration, and tooth mobility (Fig. **236**). Petechiae, ecchymoses, spontaneous hemorrhage, and delayed wound healing are commonly seen, both orally and systemically.

Laboratory tests Measurement of ascorbic acid in the blood.

Differential diagnosis Acute necrotizing ulcerative gingivitis, herpetic gingivitis, leukemia, agranulocytosis, thrombocytopenic purpura.

Treatment Vitamin C replacement.

Wegener Granulomatosis

See p. 168.

Acanthosis Nigricans

See p. 216, 218.

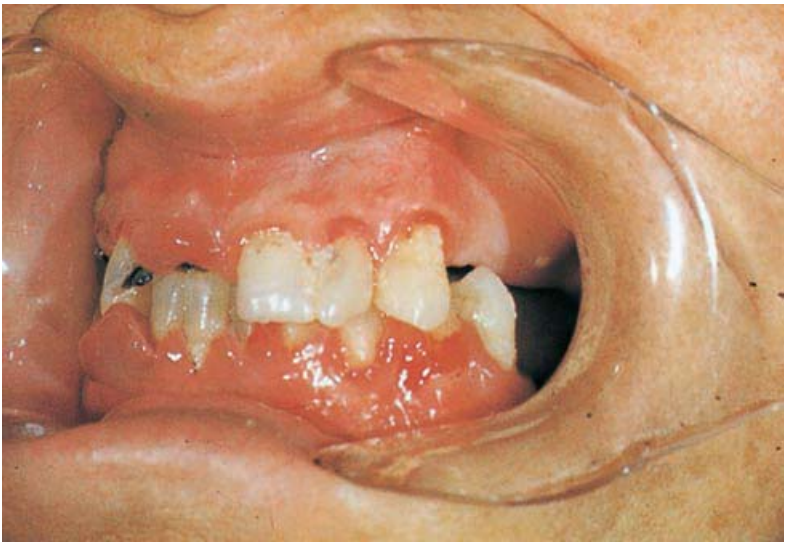


Fig. 236 Scurvy, swelling, and redness of the gingiva.

Localized

Pyogenic Granuloma

Definition Pyogenic granuloma is a common tumorlike granulation tissue overgrowth of the oral tissues in reaction to mild irritation.

Etiology Local mild irritation or trauma.

Clinical features Pyogenic granuloma presents as a painless, exophytic nodular mass that is usually pedunculated or sessile, with a deep red color (Figs. **237**, **238**). The surface of the lesion may be smooth or lobulated, is often ulcerated, and is covered by a whitish-yellowish fibrinous membrane. It is soft on palpation and has a tendency to hemorrhage easily. It grows rapidly and may range in size from a few millimeters to several centimeters. The gingiva is commonly affected (about 70–75%), followed by the tongue, lips, and buccal mucosa. Children and young adults are more frequently affected. Over 60% of patients are between 11 and 40 years of age.

Laboratory tests Histopathological examination.

Differential diagnosis Peripheral giant-cell granuloma, peripheral ossifying fibroma, hemangioma, Kaposi sarcoma, bacillary angiomatosis, leiomyoma, hemangioendothelioma, metastatic neoplasms.

Treatment Surgical excision.

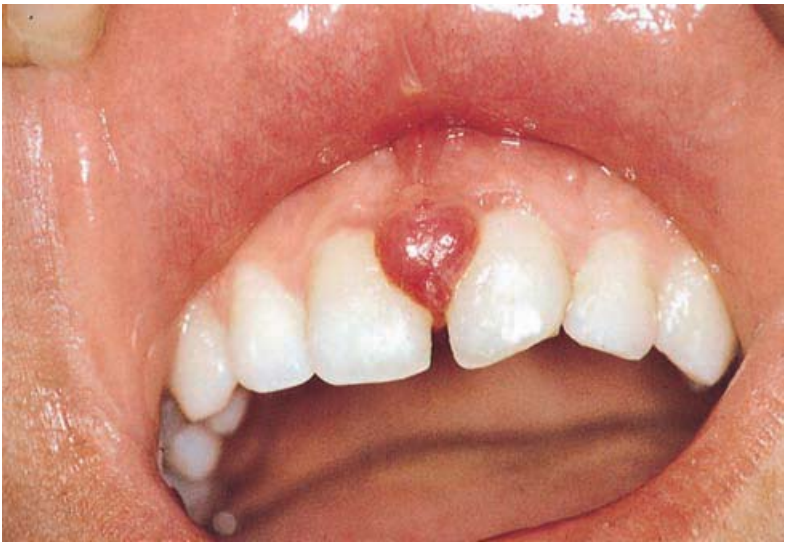


Fig. 237 Pyogenic granuloma of the gingiva.

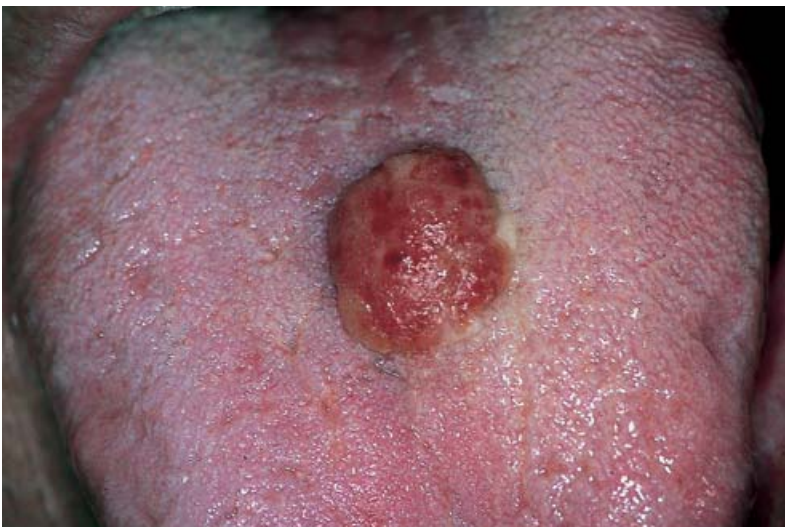


Fig. 238 Pyogenic granuloma on the dorsum of the tongue.

Peripheral Giant-Cell Granuloma

Definition Peripheral giant-cell granuloma is a relatively uncommon reactive tumor of the oral cavity.

Etiology Local irritation or trauma. It is thought to arise from a periodontal ligament or periosteum.

Clinical features The lesion occurs exclusively on the gingiva or edentulous alveolar ridge. It typically presents as a well-circumscribed sessile or pedunculated mass, dark red in color, which hemorrhages easily and may or may not be ulcerated (Figs. **239**, **240**, **241**). The lesion is relatively elastic on palpation, and the size ranges from 0.5 cm to 2 cm in diameter. It may occur at any age, and is more common in females.

Laboratory tests Histopathological examination.

Differential diagnosis Pyogenic granuloma, peripheral ossifying fibroma, brown giant-cell tumor of hyperparathyroidism, Kaposi sarcoma.

Treatment Surgical excision.

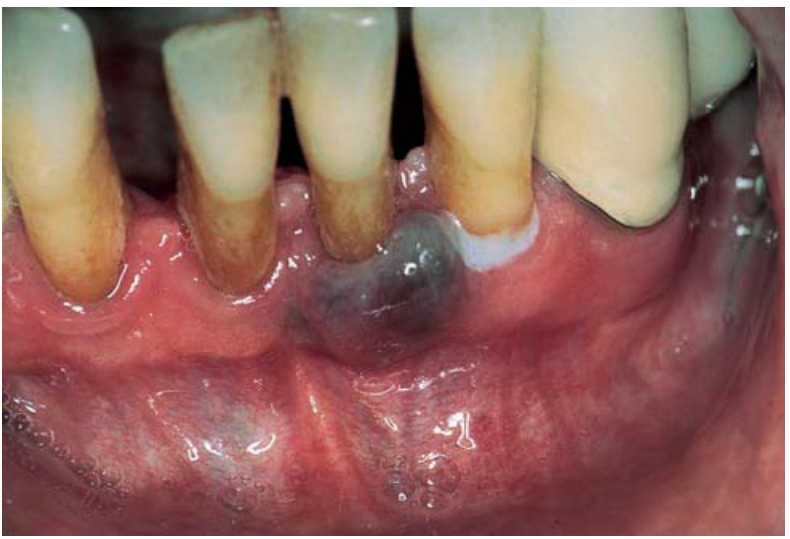


Fig. 239 Peripheral giant-cell granuloma: early lesion on the gingiva.

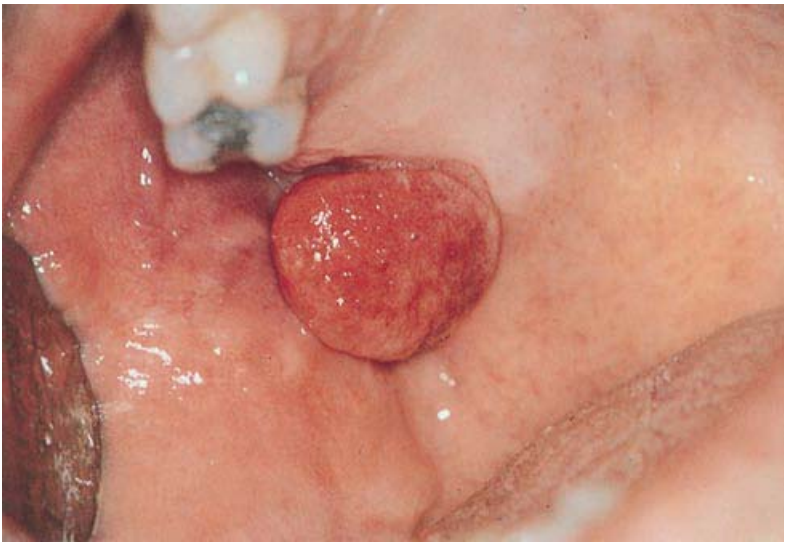


Fig. 240 Peripheral giant-cell granuloma of the maxilla.

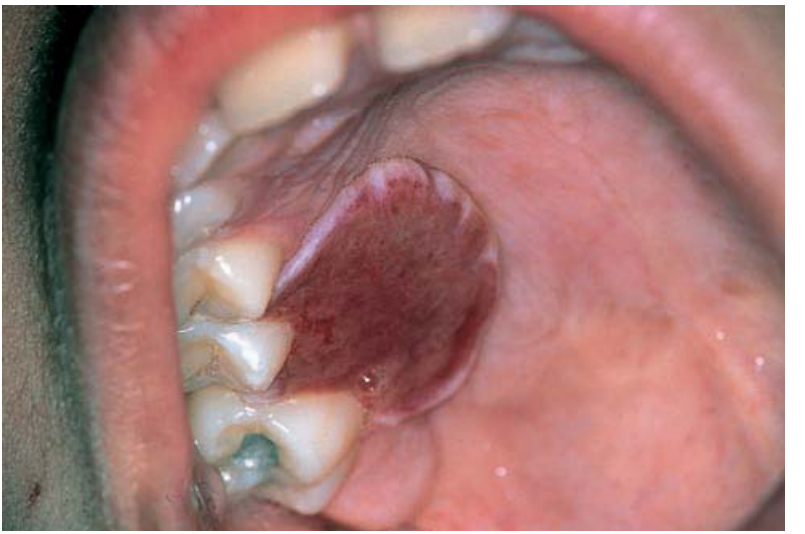


Fig. 241 Peripheral giant cell granuloma of the upper gingiva.

Peripheral Ossifying Fibroma

Definition Peripheral ossifying fibroma is a relatively common reactive growth on the gingiva, with a characteristic histomorphological pattern.

Etiology Unknown. It is thought to derive from the periodontal ligament or the periosteum.

Clinical features The lesion occurs exclusively on the gingiva, and it is more common in children and young adults, with a female predilection. It presents as a well-defined, firm mass, sessile or pedunculated, usually covered by smooth normal epithelium (Figs. **242**, **243**, **244**). The surface is frequently ulcerated due to mechanical trauma. The size varies from 0.5 cm to 2 cm in diameter. More than 50% of cases occur in the region of the incisors and canine teeth.

Laboratory tests Histopathological examination.

Differential diagnosis Pyogenic granuloma, peripheral giant-cell granuloma, fibroma, peripheral odontogenic tumors.

Treatment Surgical excision.

Granular-Cell Tumor of the Newborn

Definition Granular-cell tumor of the newborn, or congenital epulis of the newborn, is an uncommon, benign soft-tissue tumor of the mouth.

Etiology Uncertain. It probably originates from primitive mesenchymal cells.

Clinical features The lesion develops exclusively in neonates on the alveolar ridges, and is almost 9–10 times more common in girls than in boys. The maxilla is affected about twice as often as the mandible. Clinically, it appears as an asymptomatic, usually solitary, pedunculated tumor of normal or red color, with a smooth surface (Fig. **245**). The size ranges from a few millimeters to several centimeters.

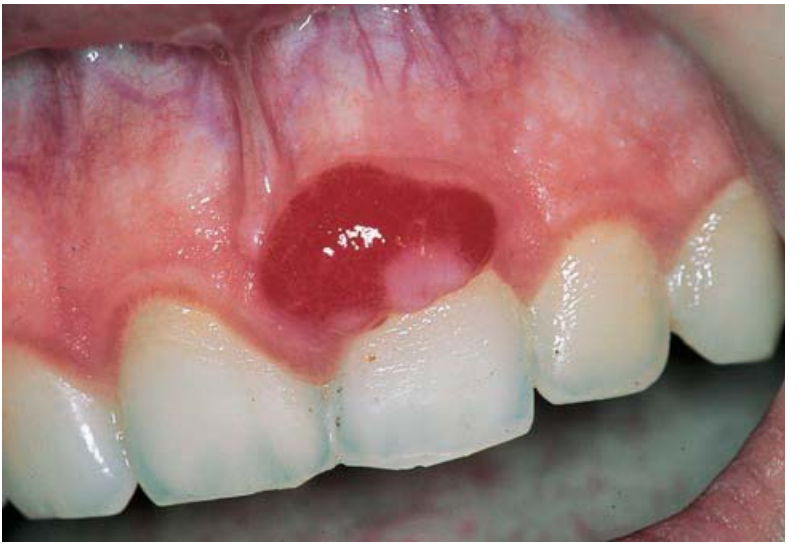


Fig. 242 Peripheral ossifying fibroma.

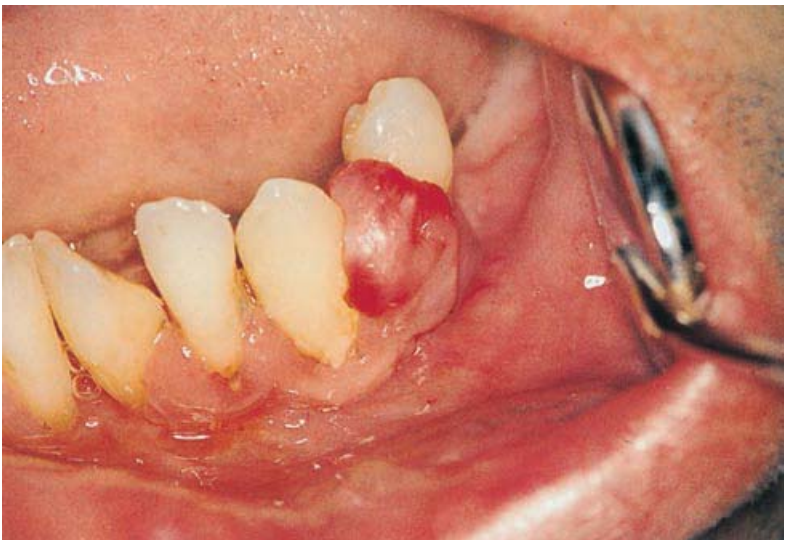


Fig. 243 Peripheral ossifying fibroma.

Laboratory tests Histopathological and immunohistochemical examination.

Differential diagnosis Melanotic neuroectodermal tumor of infancy, hamartoma, fibroma, pyogenic granuloma.

Treatment Surgical excision.

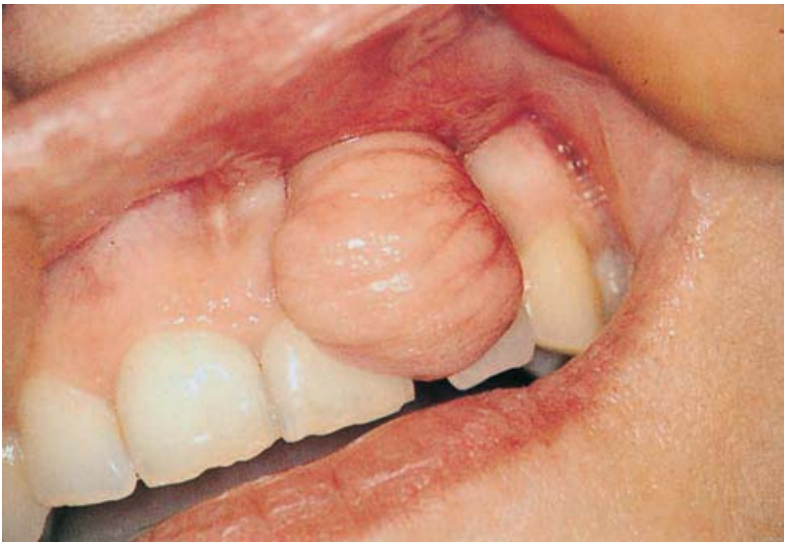


Fig. 244 Peripheral ossifying fibroma.

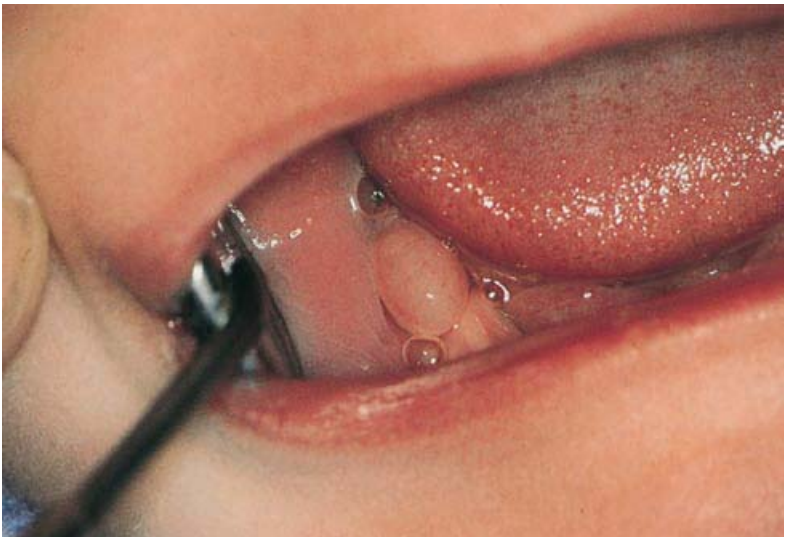


Fig. 245 Granular-cell tumor of the newborn.

Periodontal Abscess

Definition Periodontal abscess is formed by localized pus accumulation in a preexisting periodontal pocket.

Etiology Gram-positive and Gram-negative microorganisms, anaerobic microbes.

Clinical features It usually appears as a painful, soft, red gingival swelling (Fig. **246**). On pressure, pus exudes from the cervical area of the tooth. The diagnosis is made at the clinical level.

Differential diagnosis Periapical abscess, gingival cyst of the adult, actinomycosis, palatine papilla cyst, nasolabial cyst.

Treatment Antibiotics, periodontal treatment.

Parulis

Parulis, or fistula granuloma, is a common lesion that develops exclusively on the gingiva. It is characteristically found at the opening of the sinus tract of a periapical or periodontal fistula. Clinically, the lesion presents as a painless, exophytic granulation tissue mass, identical to pyogenic granuloma (Fig. **247**).

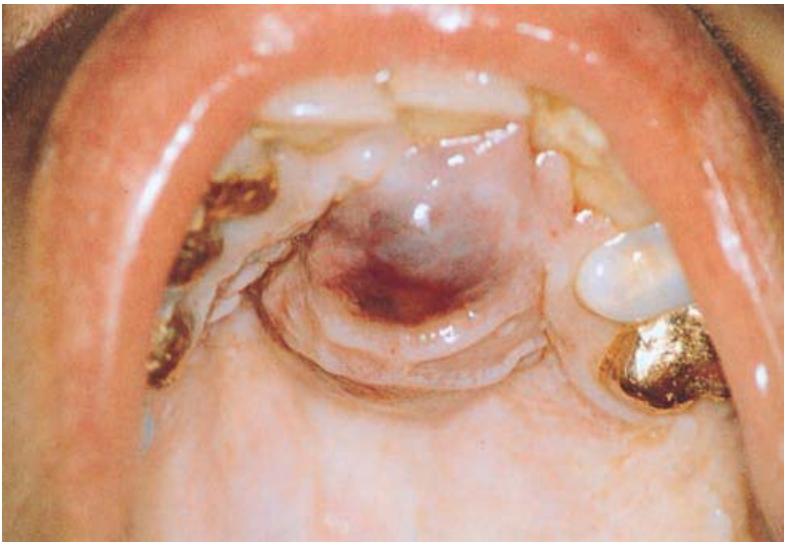


Fig. 246 Periodontal abscess.

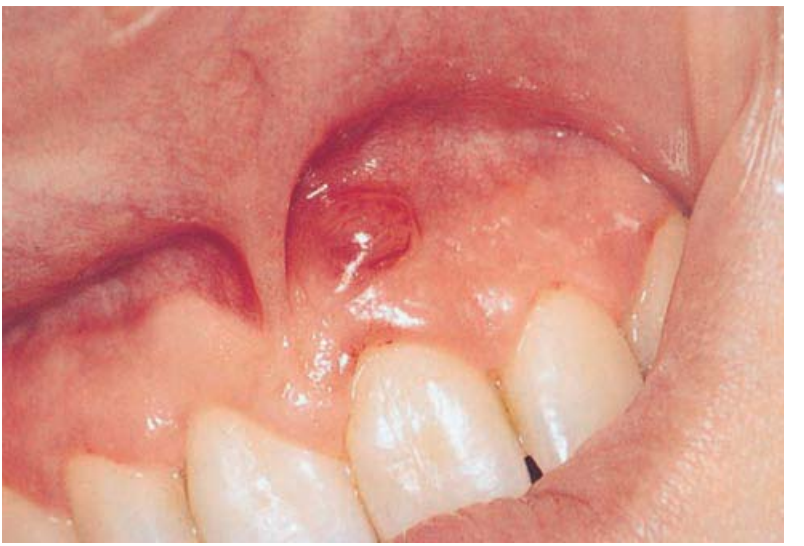


Fig. 247 Fistula granuloma at the opening of the duct of a dental fistula.

Multiple Exostoses

Definition Multiple exostoses is a rare condition that develops on the buccal surface of the jaws.

Etiology Developmental.

Clinical features The lesions appear as multiple, asymptomatic, nodular, bony elevations below the mucolabial fold, and occasionally the attached gingiva is covered with normal mucosa (Fig. **248**). Multiple exostoses may be concurrent with torus palatinus and torus mandibularis, and their occurrence is related to increasing age. The diagnosis is made at the clinical level.

Treatment No treatment is required.

Gingival Cyst

See p. 306.

Eruption Cyst

See p. 302.

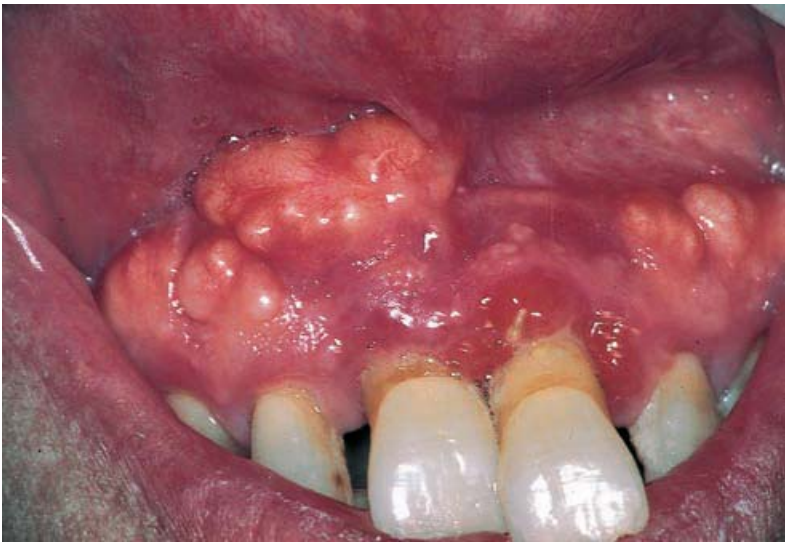
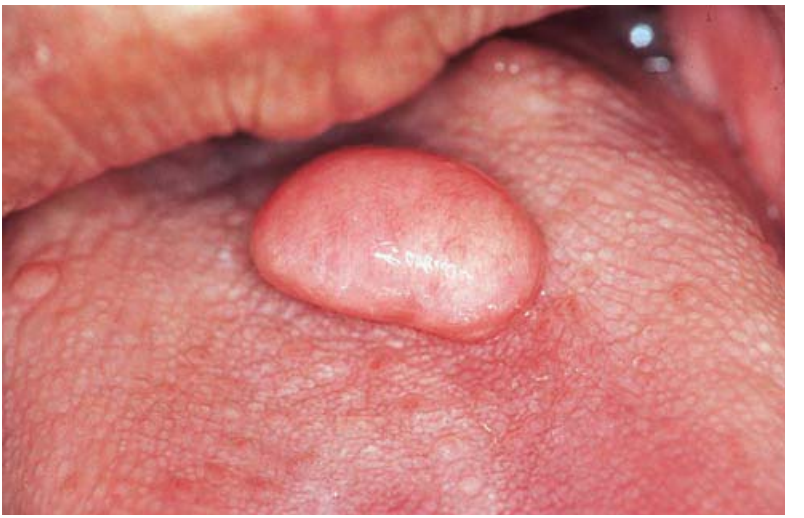


Fig. 248 Multiple exostoses of the maxilla.

8 Soft-Tissue Tumors

"Tumor" is a loose, descriptive term to characterize a firm or solid, raised, usually asymptomatic swelling that is larger than 0.5 cm in diameter. Both epithelial and mesenchymal lesions can represent a "tumor." Benign and malignant neoplasms, reactive lesions, infections, and systemic diseases are included in this group of lesions. The location, consistency, surface, inflammation, and presence or absence of pain are important clinical signs and symptoms for the differential diagnosis of a given tumor. However, clinicians should make the final diagnosis exclusively on the basis of a biopsy.

- Fibroma
- Papilloma
- Pyogenic granuloma
- Peripheral giant-cell granuloma
- Peripheral ossifying fibroma
- Lipoma
- Soft-tissue osteoma
- Traumatic neuroma
- Neurofibroma
- Schwannoma
- Leiomyoma
- Granular-cell tumor
- Melanotic neuroectodermal tumor of infancy
- Myxoma
- Benign fibrous histiocytoma
- Pleomorphic adenoma
- Keratoacanthoma
- Squamous-cell carcinoma



- Kaposi sarcoma
- Malignant fibrous histiocytoma
- Chondrosarcoma
- Fibrosarcoma
- Leiomyosarcoma
- Hemangioendothelioma
- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Other malignant salivary gland tumors
- Non-Hodgkin lymphoma
- Amyloidosis
- Actinomycosis
- Cutaneous leishmaniasis
- Oral soft-tissue chondroma

Fibroma

Definition Fibroma is the most common benign tumor of the oral cavity, and originates from the connective tissue.

Etiology It is a reactive, rather fibrous hyperplasia in response to local irritation or trauma, than a true neoplasm.

Clinical features The lesion typically presents as an asymptomatic, well-defined, firm, sessile or pedunculated tumor with a smooth surface of normal epithelium (Figs. **249**, **250**). The size usually ranges from 0.5 cm to 1.5 cm in diameter. Fibroma often occurs on the buccal mucosa, gingiva, labial mucosa, and tongue. It is more common between 40 and 60 years of age in both sexes.

Laboratory tests Histopathological examination.

Differential diagnosis Neurofibroma, peripheral ossifying fibroma, lipoma, myxoma, schwannoma, pleomorphic adenoma.

Treatment Surgical removal.

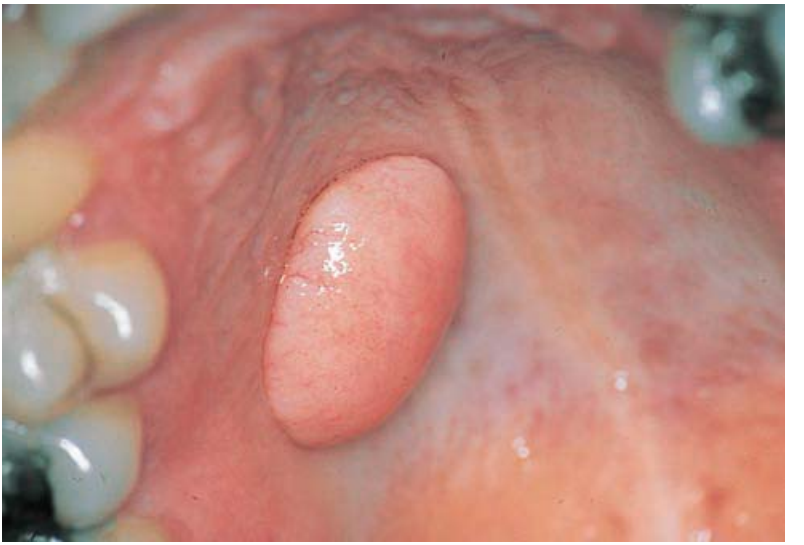


Fig. 249 Fibroma of the palate

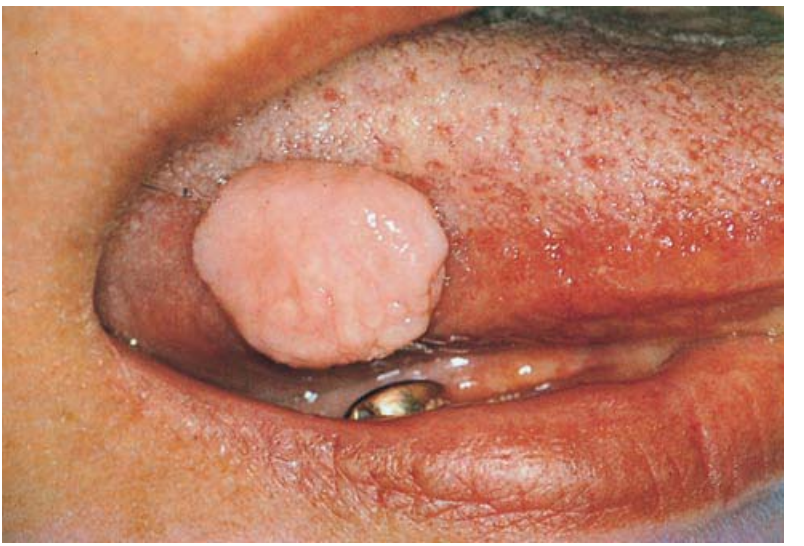


Fig. 250 Giant-cell fibroma of the tongue.

Papilloma

See pp. 34, 200.

Pyogenic Granuloma

See p. 240.

Peripheral Giant-Cell Granuloma

See p. 242.

Peripheral Ossifying Fibroma

See p. 244.

Lipoma

Definition Lipoma is a benign tumor of fat tissue, and is relatively rare in the oral cavity.

Etiology Unknown.

Clinical features It appears as an asymptomatic, well-defined tumor, sessile or pedunculated, varying in size from 0.5 cm to 3 cm, and with a yellowish or pink color (Figs. **251**, **252**). It is soft on palpation, and occasionally fluctuant. Both sexes are affected, usually between 40 and 60 years of age. The buccal mucosa, buccal vestibule, floor of the mouth, and tongue are the most common sites affected.

Laboratory tests Histopathological examination.

Differential diagnosis Myxoma, fibroma, mucocele, dermoid cyst.

Treatment Surgical removal.

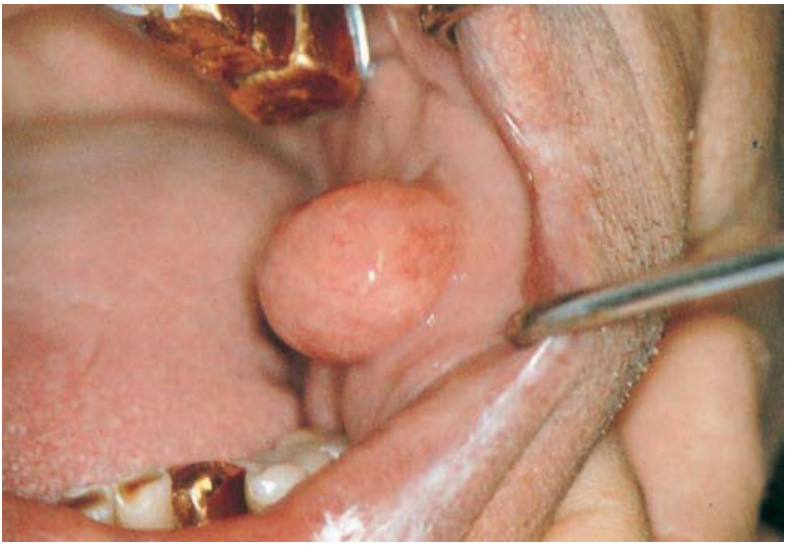


Fig. 251 Lipoma of the buccal mucosa.

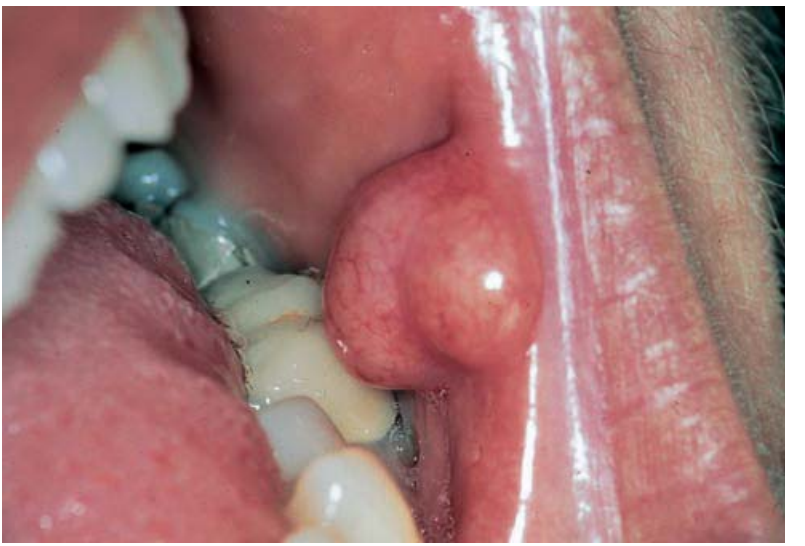


Fig. 252 Lipoma of the buccal mucosa.

Soft-Tissue Osteoma

Definition Osteoma is a benign tumor that represents a proliferation of mature cancellous or compact bone.

Etiology Unknown.

Clinical features Osteoma is rare in the jaws and extremely rare on the oral soft tissue. The latter form has been described in the palate, buccal mucosa, tongue, and alveolar process. Clinically, soft-tissue osteoma presents as an asymptomatic, well-defined, hard tumor, covered by thin and smooth epithelium (Fig. **253**). The size ranges from 0.5 to 2 cm in diameter.

Laboratory tests Histopathological examination.

Differential diagnosis Exostoses, torus palatinus, fibroma.

Treatment Surgical excision.

Traumatic Neuroma

Definition Traumatic neuroma or amputation neuroma is a reactive proliferation of nerve fibers and surrounding tissues.

Etiology Transection or injury of a nerve bundle.

Clinical features It appears as a small, usually mobile, tumor covered by normal mucosa (Fig. **254**). The lesion is usually painful, particularly on palpation, and is often located in the mental foramen area, lower lip, and tongue.

Laboratory tests Histopathological examination.

Differential diagnosis Neurofibroma, schwannoma, fibroma.

Treatment Surgical excision.

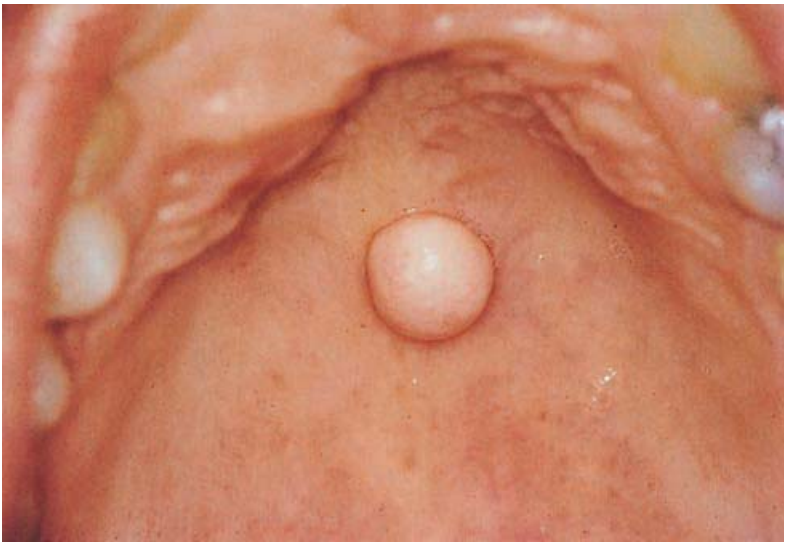


Fig. 253 Soft-tissue osteoma on the palate.

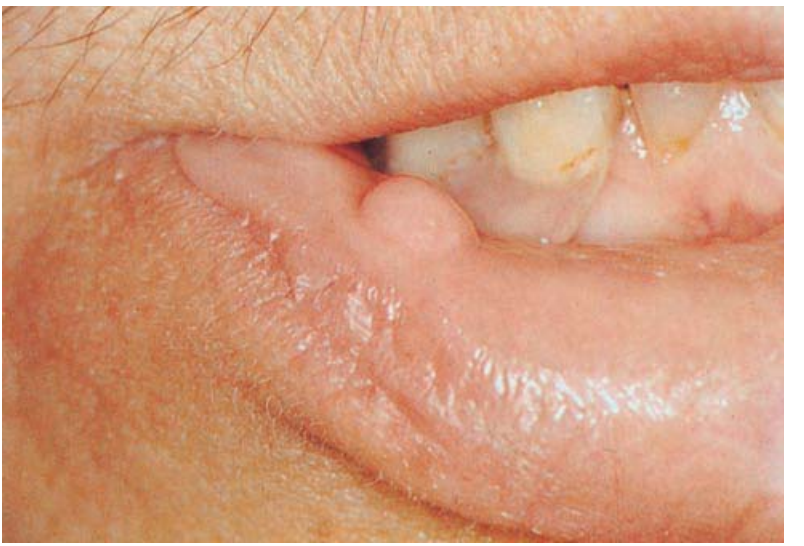


Fig. 254 Traumatic neuroma of the lower lip.

Neurofibroma

Definition Neurofibroma is a relatively rare benign neoplasm of the oral mucosa, originating in Schwann cells or perineural cells.

Etiology Unknown.

Clinical features It appears as a painless, well-defined, pedunculated and firm tumor, covered by normal epithelium (Figs. **255**, **256**). The size ranges from 0.5 cm to 1.5 cm, and the lesion is usually located on the buccal mucosa, tongue, and palate. Multiple skin and oral neurofibromas are a common finding with neurofibromatosis (Fig. **257**).

Laboratory tests Histopathological examination.

Differential diagnosis Fibroma, schwannoma, traumatic neuroma, and granular-cell tumor.

Treatment Surgical excision.

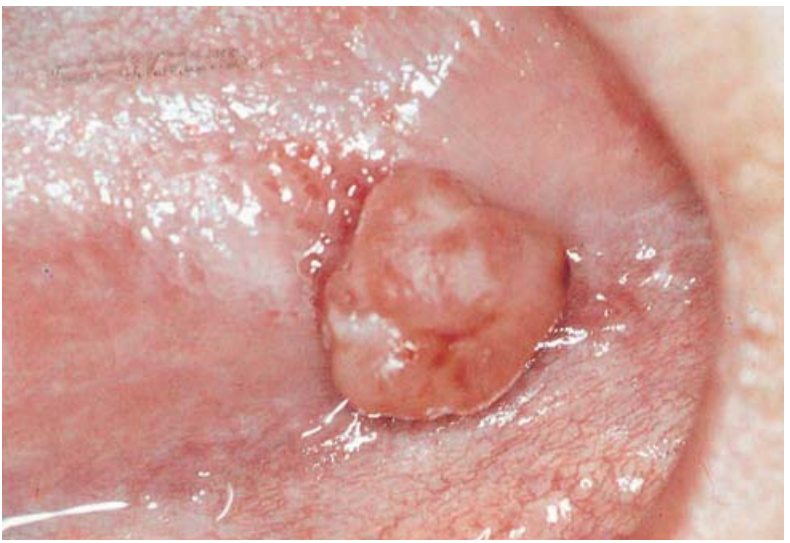


Fig. 255 Neurofibroma on the margin of the tongue.

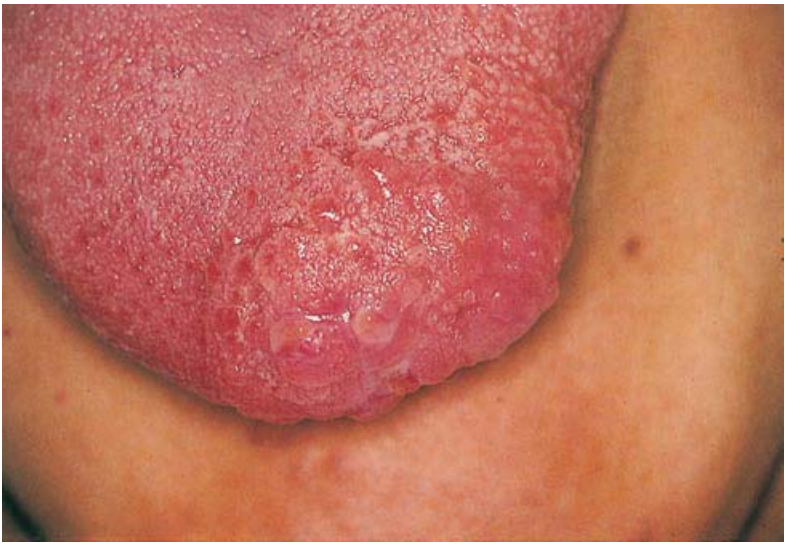


Fig. 256 Neurofibromatosis: multiple neurofibromas of the tongue.

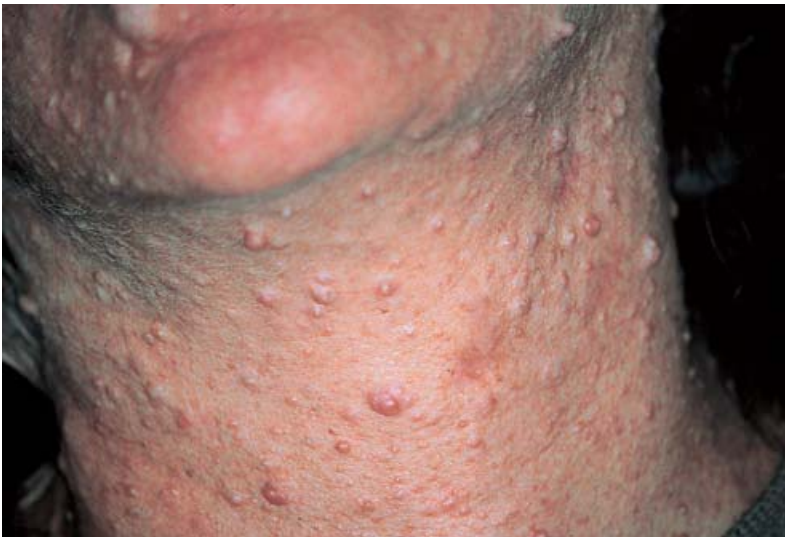


Fig. 257 Neurofibromatosis: multiple neurofibromas of the skin.

Schwannoma

Definition Schwannoma or neurilemoma is a rare benign tumor of Schwann-cell origin.

Etiology Unknown.

Clinical features It presents as an asymptomatic, well-defined, firm and sessile tumor, usually covered by normal epithelium (Fig. **258**). The size ranges from 0.5 cm to 2 cm, and the lesion is most often located on the tongue, followed by the palate, floor of the mouth, buccal mucosa, gingiva, and lips.

Laboratory tests Histopathological examination.

Differential diagnosis Neurofibroma, fibroma, granular-cell tumor, leiomyoma, pleomorphic adenoma, and other salivary gland tumors.

Treatment Surgical excision.

Leiomyoma

Definition Leiomyoma is a rare benign tumor deriving from smooth muscle. In the oral cavity it derives from the smooth muscles of blood vessels and from the circumvallate papillae of the tongue.

Etiology Unknown.

Clinical features It presents as a slow-growing, painless, firm, and well-defined tumor with a normal or reddish color (Fig. **259**). It can occur in both sexes at any age. The most common sites are the tongue, buccal mucosa, lower lip, and palate.

Laboratory tests Histopathological examination, immunohistochemistry.

Differential diagnosis Hemangioma, granular-cell tumor, hemangiopericytoma, myofibroma, schwannoma.

Treatment Surgical excision.

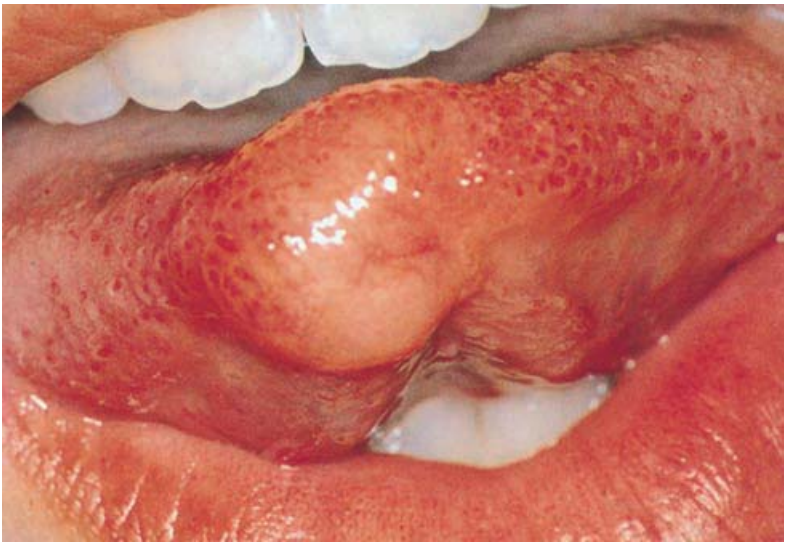


Fig. 258 Schwannoma on the tip of the tongue.

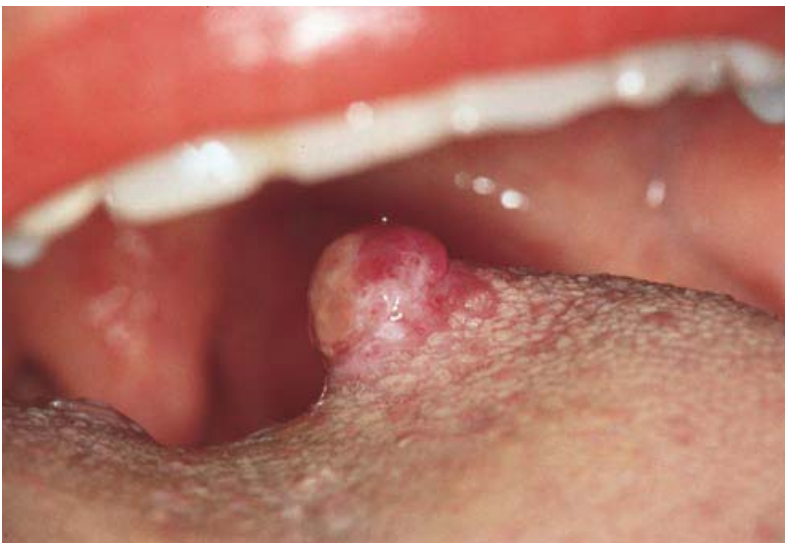


Fig. 259 Leiomyoma on the dorsum of the tongue.

Granular-Cell Tumor

Definition Granular-cell tumor, or granular-cell myoblastoma, is a relatively rare, benign tumor, probably originating in Schwann cells or undifferentiated cells.

Etiology Unknown.

Clinical features It presents as an asymptomatic, firm, well-defined tumor that may be slightly elevated, with a normal or whitish color, and 2 cm in size or smaller (Figs. **260**, **261**, **262**). The dorsum and lateral borders of the tongue are the sites of predilection, followed by the buccal mucosa. The tumor most frequently occurs between 30 and 60 years of age and is more common in women.

Laboratory tests Histopathological and immunohistochemical examination.

Differential diagnosis Rhabdomyoma, schwannoma, neurofibroma, pleomorphic adenoma, leiomyoma, granular-cell tumor of the newborn.

Treatment Surgical excision.

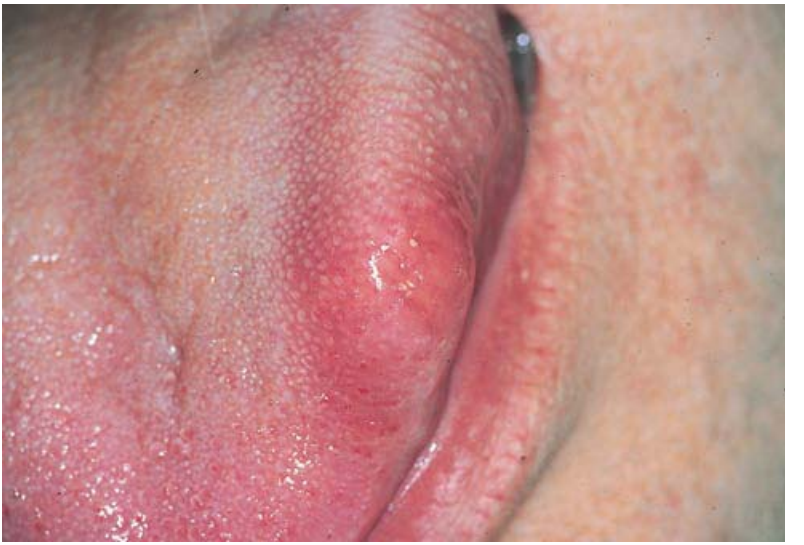


Fig. 260 Granular-cell tumor on the lateral border of the tongue.

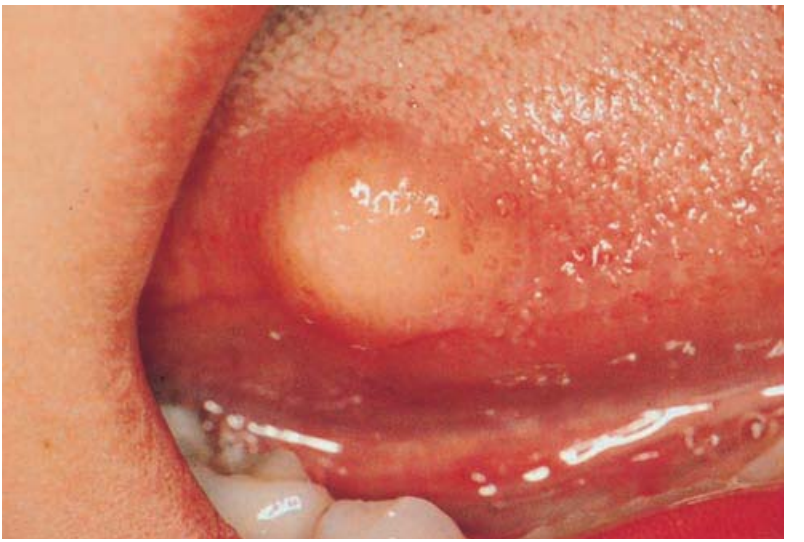


Fig. 261 Granular-cell tumor on the margin of the tongue.

Melanotic Neuroectodermal Tumor of Infancy

Definition Melanotic neuroectodermal tumor of infancy is a rare benign tumor of neural crest origin, which usually occurs in tooth-bearing areas.

Etiology Unknown.

Clinical features It presents as a rapidly expanding, painless tumor covered by normal epithelium of a normal or reddish-brown color (Fig. **263**). The lesion may cause bone destruction and displacement of the developing teeth. It occurs mostly in the anterior region of the maxilla (79%), and rarely in the mandible, skull, shoulder, skin, brain, and epididymis. The tumor appears only in infants less than 6 months of age.

Laboratory tests Histopathological examination, radiography, high urinary level of vanillylmandelic acid.

Differential diagnosis Granular-cell tumor of the newborn, odontogenic tumors, melanoma, neuroblastoma, schwannoma, sarcomas.

Treatment Surgical excision.

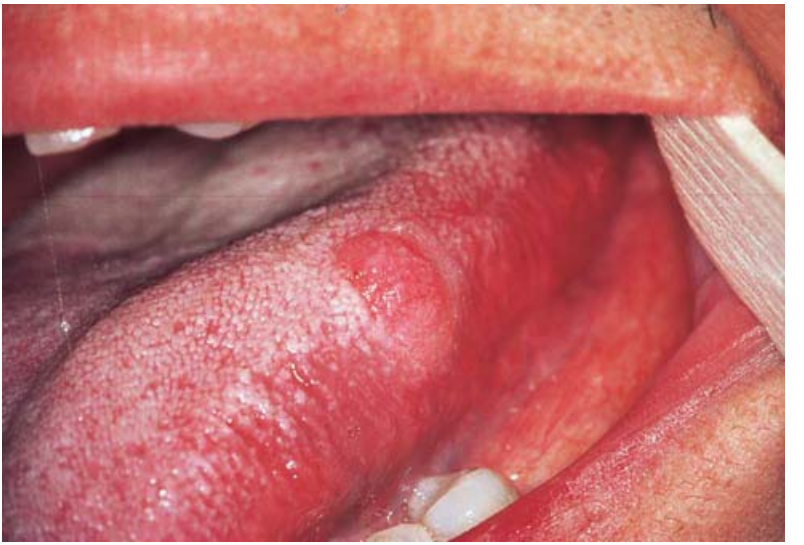


Fig. 262 Granular-cell tumor on the lateral border of the tongue.

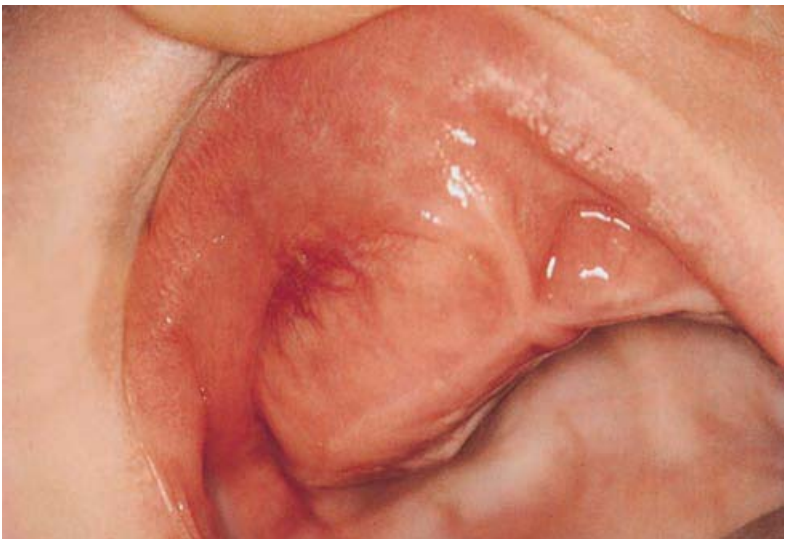


Fig. 263 Melanotic neuroectodermal tumor of infancy in the maxilla.

Myxoma

Definition Myxoma is a very rare benign tumor of the oral cavity, of mesenchymal origin.

Etiology Myxoid degeneration of the connective tissue, of unknown etiology.

Clinical features It is a well-defined, soft tumor covered by normal epithelium (Fig. **264**). It can appear at any age, and is most frequent on the buccal mucosa, the floor of the mouth, and the palate.

Laboratory tests Histopathological examination.

Differential diagnosis Lipoma, fibroma, mucoceles, focal mucinosis.

Treatment Surgical excision.

Benign Fibrous Histiocytoma

Definition Benign fibrous histiocytoma is a rare tumor, primarily composed of histiocytes and fibroblasts.

Etiology Reactive rather than a true neoplasm.

Clinical features It presents as a painless, firm tumor, covered by normal epithelium, which may be ulcerated (Fig. **265**). The size ranges from 0.5 cm to 2 cm and both sexes are affected, at any age. The buccal mucosa and tongue are most frequently affected.

Laboratory tests Histopathological and immunohistochemical examination.

Differential diagnosis Fibroma, neurofibroma, schwannoma, lipoma, granular-cell tumor, leiomyoma, malignant fibrous histiocytoma.

Treatment Surgical excision.

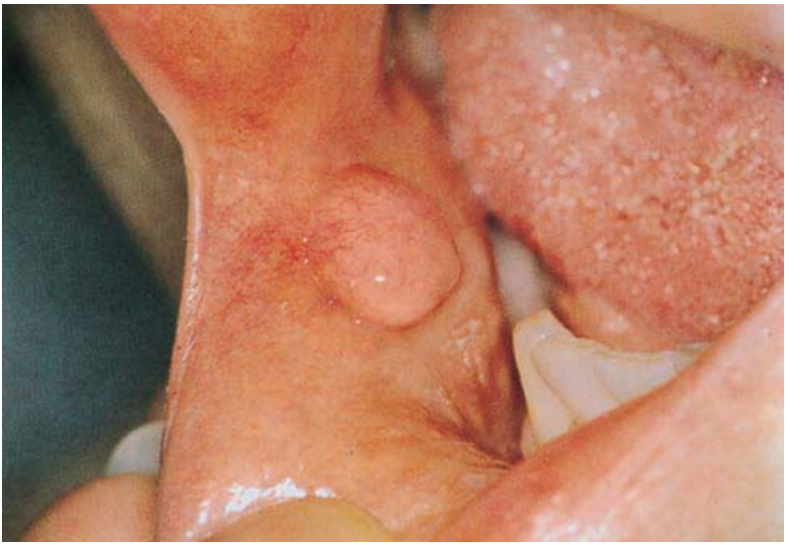


Fig. 264 Myxoma of the buccal mucosa.

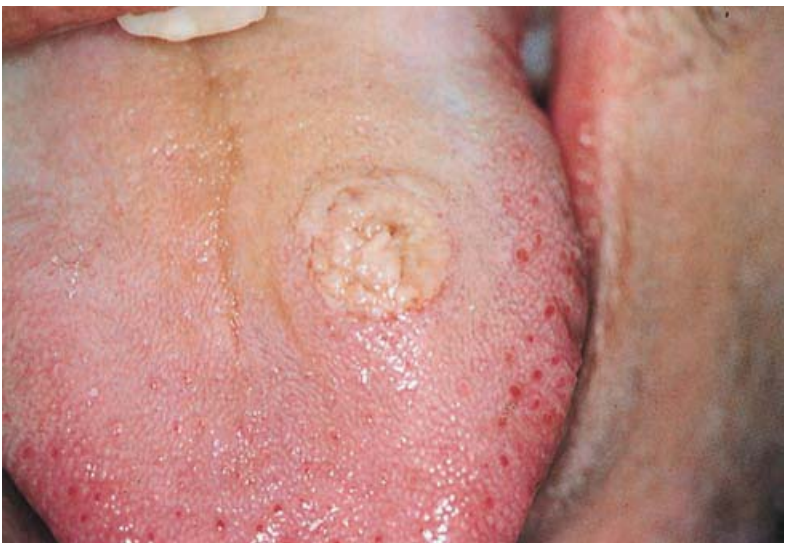


Fig. 265 Benign fibrous histiocytoma on the dorsum of the tongue.

Pleomorphic Adenoma

Definition Pleomorphic adenoma is the most common benign tumor of the salivary glands, and originates from ductal and myoepithelial elements.

Etiology Unknown.

Clinical features Pleomorphic adenoma in the minor salivary glands presents as an asymptomatic, slow-growing, firm swelling, 2–3 cm in size (Figs. **266**, **267**, **268**). The tumor is usually covered by normal epithelium. It accounts for 40–45% or more of minor salivary gland tumors. The posterior palate is the most common intraoral site, followed by the upper lip and buccal mucosa.

Laboratory tests Histopathological examination.

Differential diagnosis Other benign and malignant salivary gland tumors, necrotizing sialadenometaplasia, lipoma.

Treatment Surgical excision.

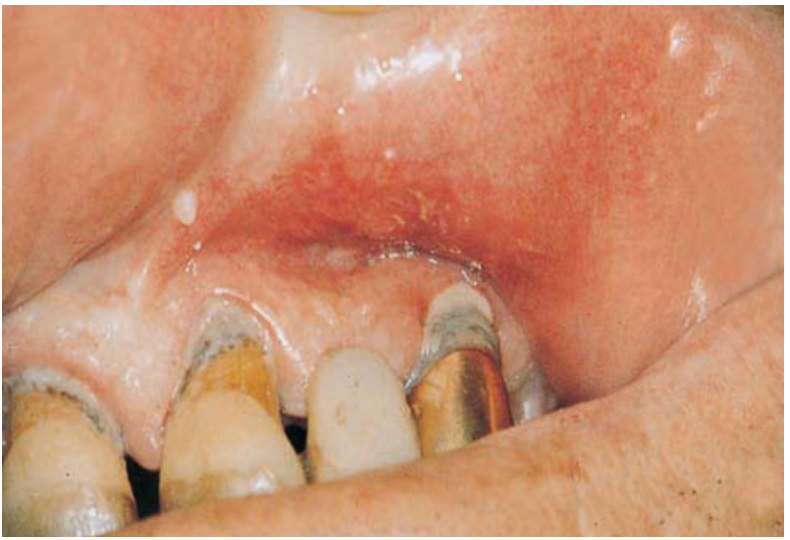


Fig. 266 Pleomorphic adenoma of the upper labial mucosa.

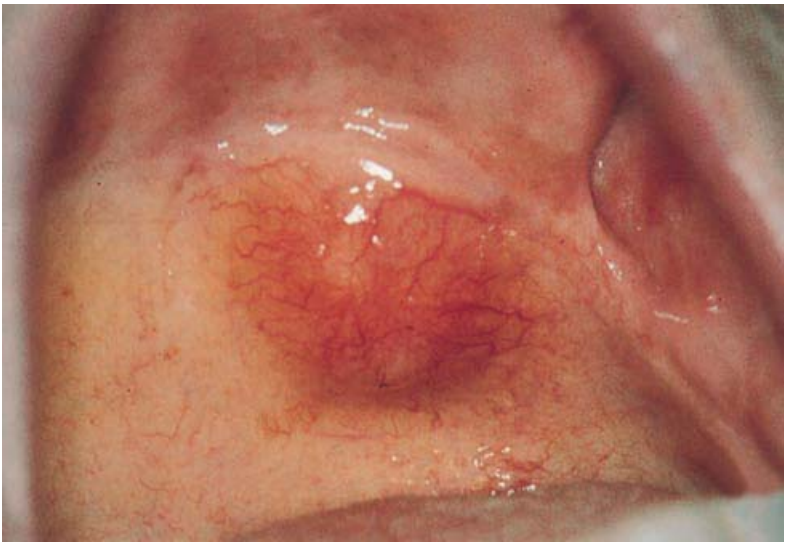


Fig. 267 Pleomorphic adenoma of the palate.

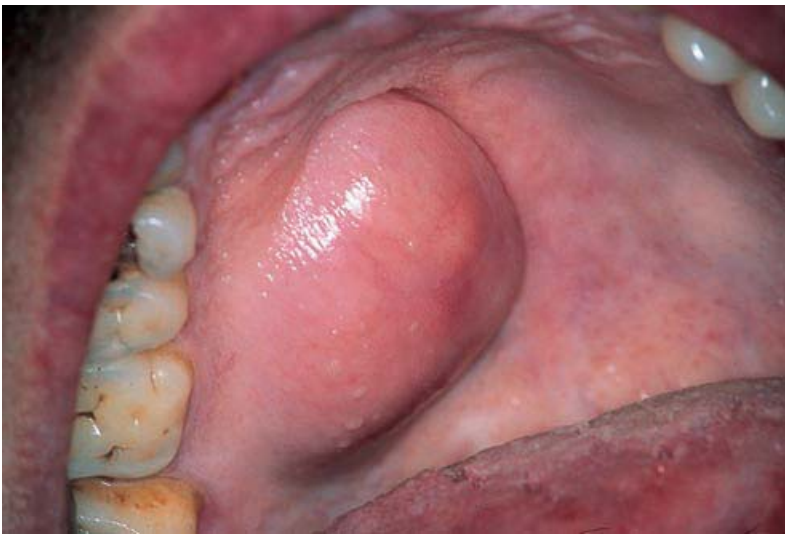


Fig. 268 Pleomorphic adenoma of the palate.

Keratoacanthoma

Definition Keratoacanthoma is a fairly common benign tumor that originates from hair follicles.

Etiology Uncertain; sunlight probably plays a role.

Clinical features It appears as a rapidly growing, painless, well-circumscribed dome- or bud-shaped tumor, 1–2 cm in diameter, with a keratin crater at the center (Fig. **269**). The tumor reaches its full size within 4–8 weeks, persists for a period of one or two months, and may then undergo spontaneous regression. Almost 10% of keratoacanthomas are located on the lips, and only a few cases have been reported intraorally.

Laboratory tests Histopathological examination.

Differential diagnosis Basal-cell carcinoma, squamous-cell carcinoma, warty dyskeratoma, papillary syringadenoma, cutaneous horn.

Treatment Surgical excision, radiation. Some lesions may regress spontaneously.

Squamous-Cell Carcinoma

Squamous-cell carcinoma of the oral cavity has a varied clinical presentation and may mimic a variety of diseases, leading to diagnostic dilemmas. A relatively common clinical pattern for the disease is an exophytic irregular mass or tumor (Figs. **270**, **271**). The surface of the tumor may or may be not ulcerated, and it is indurated on palpation. A biopsy and histopathological examination are essential for accurate diagnosis.

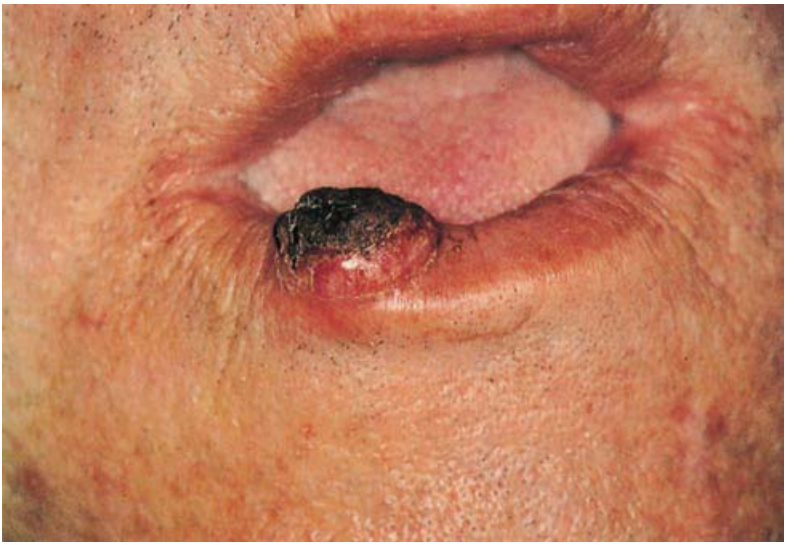


Fig. 269 Keratoacanthoma of the vermilion border of the lower lip.

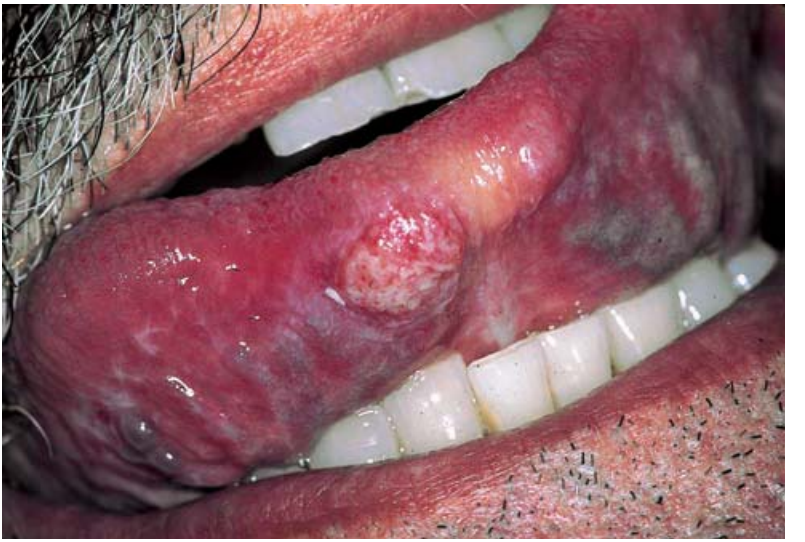


Fig. 270 Squamous-cell carcinoma of the tip of the tongue, presenting as a small tumor.

Kaposi Sarcoma

Definition Kaposi sarcoma is a malignant neoplasm, probably of endothelial cell origin.

Etiology Presumably herpesvirus type 8, immunosuppression.

Clinical features Four forms are recognized.

Classic: This is most common in Jewish and other Mediterranean individuals, and primarily involves the skin and rarely the oral mucosa, usually in men over 60 years of age.

African (endemic): This primarily involves the skin and lymph nodes, and rarely the oral mucosa.

Immunosuppression-associated (iatrogenic): This occurs in recipients of organ transplants, and may have an aggressive course. The oral mucosa is rarely affected.

AIDS-related (epidemic): This has a high incidence among AIDS patients, and primarily involves the skin, lymph nodes, viscera, and frequently the oral mucosa.

The skin lesions appear as multiple or solitary macules, nodules, or tumors with deep red or dark blue color (Fig. **272**). The feet, hands, nose, and ears are the most common sites of involvement.

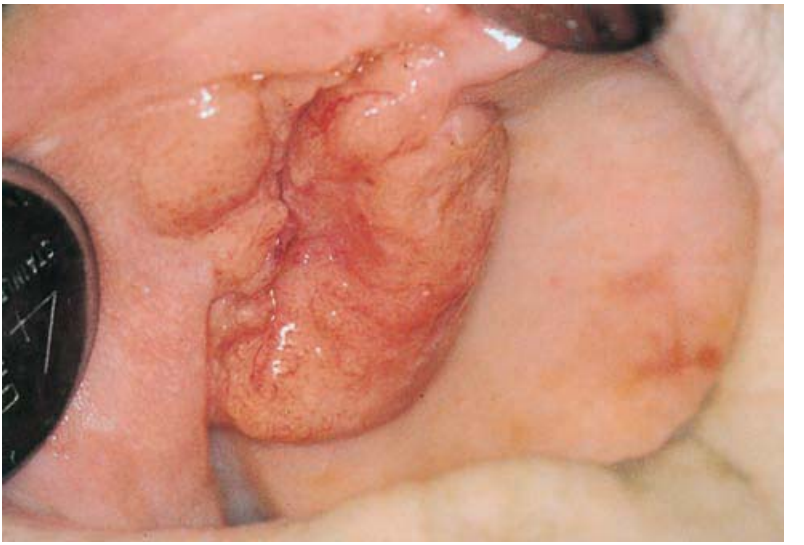


Fig. 271 Squamous-cell carcinoma of the alveolar mucosa.

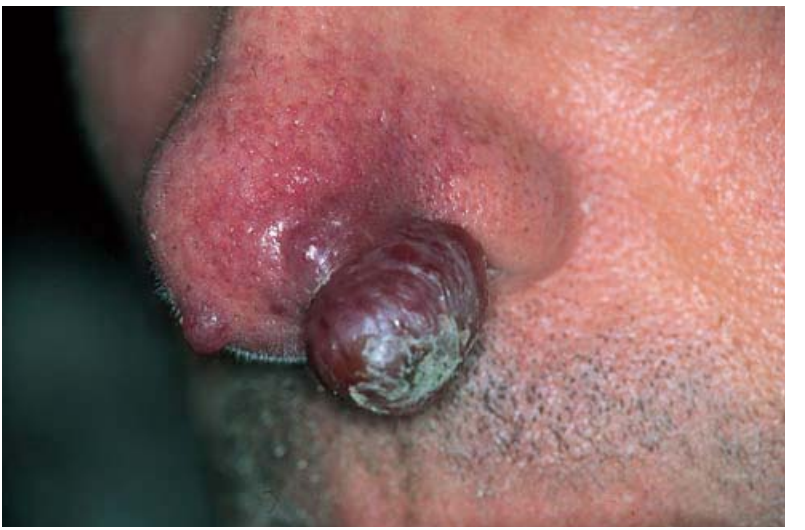


Fig. 272 Classic Kaposi sarcoma of the nose.

Clinically, the oral lesions present as multiple or solitary red or brownish-red patches or elevated plaques or tumors (Figs. **273**, **274**). The palate and gingiva are the most common sites affected, followed by buccal mucosa, tongue, and lips.

Laboratory tests Histopathological examination.

Differential diagnosis Pyogenic granuloma, peripheral giant-cell granuloma, bacillary angiomatosis, hemangioma, angiosarcomas.

Treatment Interferon, chemotherapy, radiotherapy, or surgical excision in small, localized lesions.

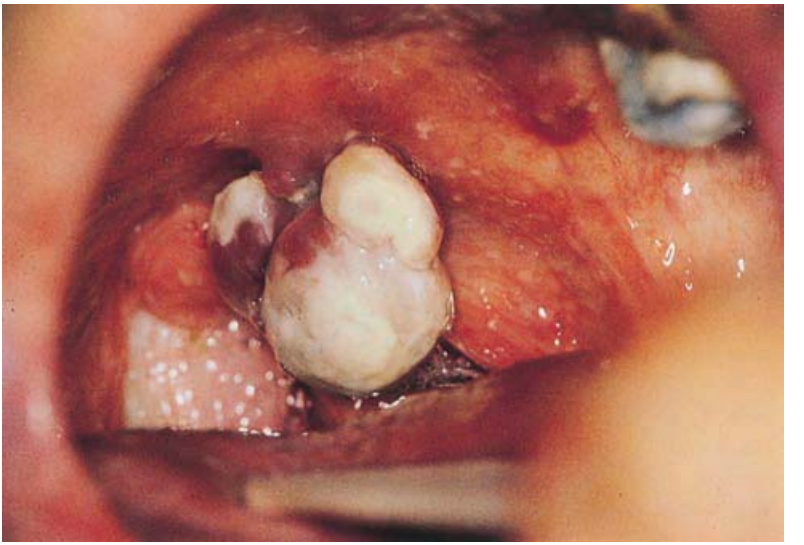


Fig. 273 Multiple Kaposi sarcoma lesions of the soft palate.

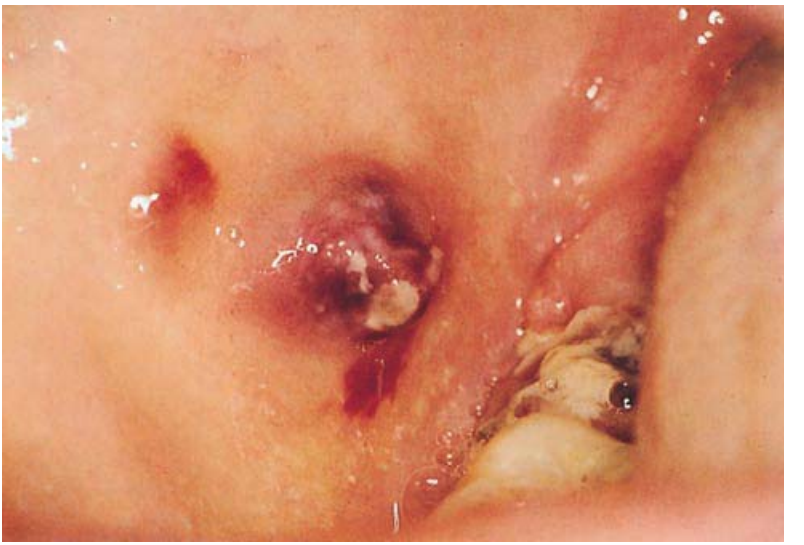


Fig. 274 Kaposi sarcoma: early lesions on the buccal mucosa in a 33-year-old man with AIDS.

Malignant Fibrous Histiocytoma

Definition Malignant fibrous histiocytoma is a common malignant soft-tissue neoplasm in older individuals; it rarely involves the oral cavity.

Etiology Unknown.

Clinical features The oral lesion presents as a quickly growing, painless exophytic tumor of a reddish or brown color, with or without ulceration (Fig. **275**). The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests Histopathological examination.

Differential diagnosis Chondrosarcoma, fibrosarcoma, squamous-cell carcinoma, peripheral giant-cell granuloma, pyogenic granuloma.

Treatment Surgical excision.

Chondrosarcoma

Definition Chondrosarcoma is a malignant neoplasm characterized by the formation of aberrant cartilage by the tumor cells.

Etiology Unknown.

Clinical features Chondrosarcoma of the jaws is rare, and may involve either jaw. It presents as a painless hard swelling that progressively enlarges, causing extensive destruction and loosening of teeth. A large, erythematous, lobulated, and ulcerated soft mass may present in the oral cavity (Fig. **276**).

Laboratory tests Histopathological examination, radiograph.

Differential diagnosis Osteosarcoma, fibrosarcoma, peripheral giant-cell granuloma, chondroma, odontogenic tumors.

Treatment Surgical excision.

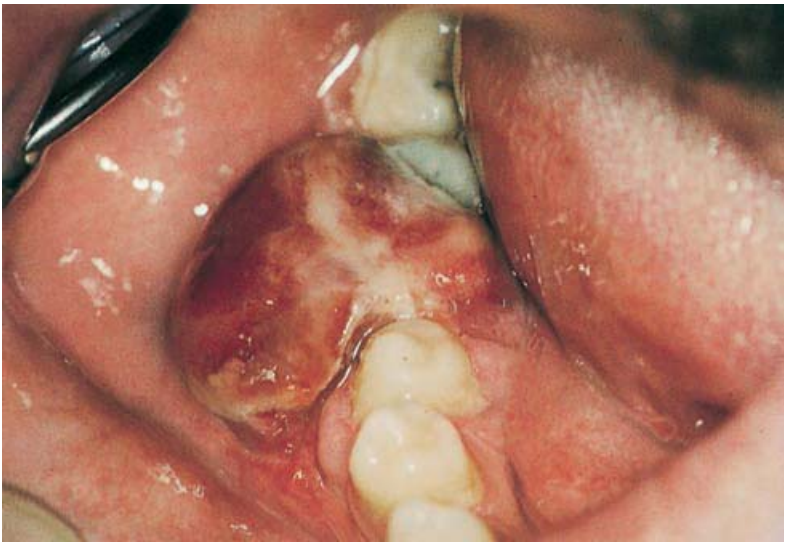


Fig. 275 Malignant fibrous histiocytoma of the alveolar mucosa of the mandible.

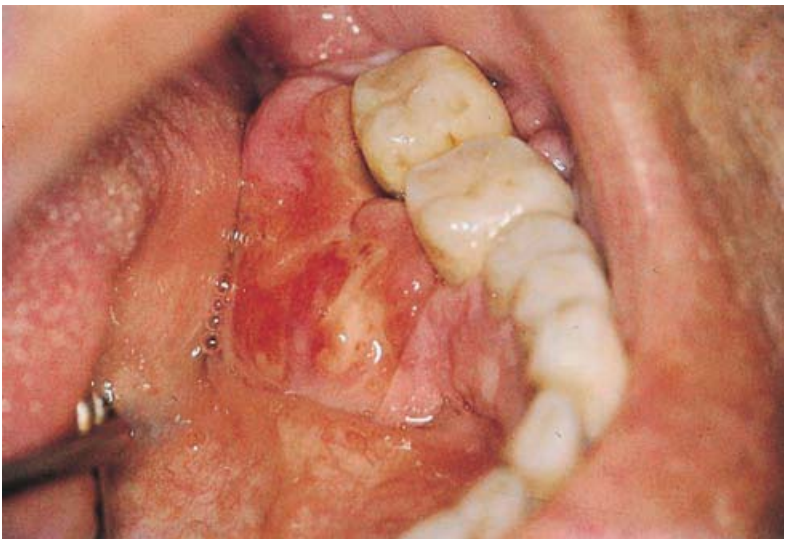


Fig. 276 Chondrosarcoma of the mandible, presenting as a lobulated and ulcerated mass.

Fibrosarcoma

Definition Oral soft-tissue fibrosarcoma is an extremely rare malignant neoplasm.

Etiology Unknown.

Clinical features It presents as a soft or semi-hard tumor, usually of a reddish color and with a smooth or ulcerated surface (Fig. **277**). The tongue, buccal mucosa, lips, and gingiva may be involved.

Laboratory tests Histopathological examination.

Differential diagnosis Malignant fibrous histiocytoma, Kaposi sarcoma, chondrosarcoma, other malignant connective-tissue tumors.

Treatment Surgical excision.

Leiomyosarcoma

Definition Leiomyosarcoma is a malignant smooth-muscle tumor that commonly develops in the gastrointestinal tract, uterus, and skin.

Etiology Unknown.

Clinical features Oral leiomyosarcoma is an uncommon malignant tumor and may arise from smooth-muscle cells of the blood vessels and the circumvallate papillae of the tongue. Clinically, it appears as a painless or painful, nonspecific, slow-growing, rubbery firm mass with smooth surface with or without ulceration (Fig. **278**). The neoplasm more frequently affects females 50–70 years of age. The clinical diagnosis should be confirmed by histopathological examination.

Differential diagnosis Pyogenic granuloma, peripheral giant-cell granuloma, leiomyoma, peripheral ossifying fibroma, angiosarcoma, Kaposi sarcoma, benign and malignant neoplasms of the minor salivary glands.

Treatment Radical surgical excision.

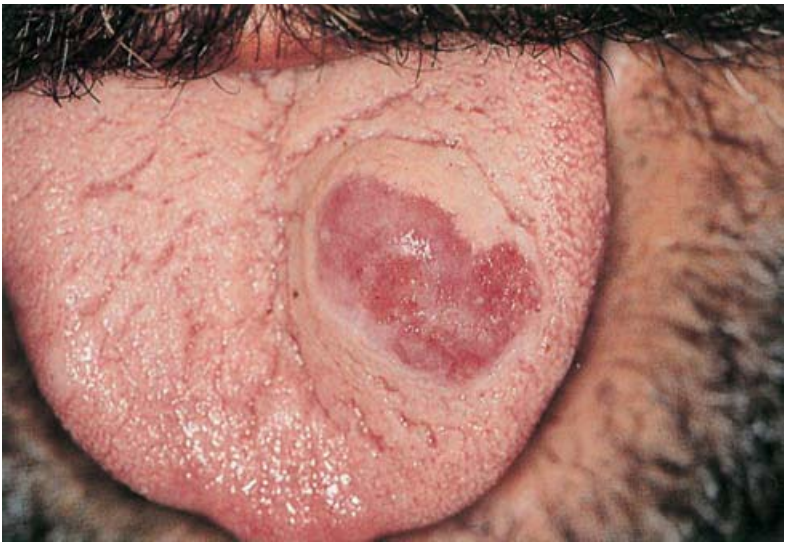


Fig. 277 Fibrosarcoma of the dorsum of the tongue.

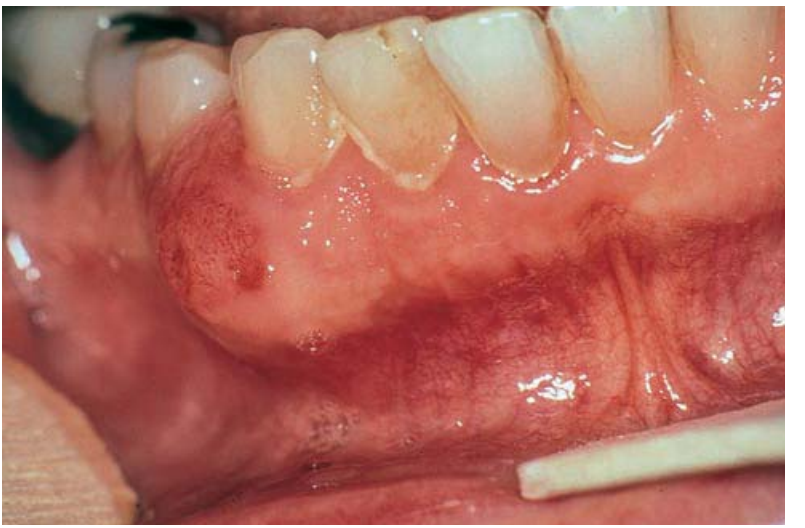


Fig. 278 Leiomyosarcoma of the gingiva.

Hemangioendothelioma

Definition Hemangioendothelioma is a rare malignant neoplasm that is derived from the endothelial cells of blood vessels.

Etiology Unknown.

Clinical features Oral hemangioendothelioma is extremely rare and presents as an elevated, firm, painless tumor with a reddish color (Fig. **279**). The palate, tongue, gingiva, and lips may be involved.

Laboratory tests Histopathological examination.

Differential diagnosis Kaposi sarcoma, leiomyoma, cavernous hemangioma, pyogenic granuloma, peripheral giant-cell granuloma.

Treatment Surgical excision.

Mucoepidermoid Carcinoma

Definition Mucoepidermoid carcinoma is one of the most frequent neoplasms of the minor salivary glands.

Etiology Unknown.

Clinical features It presents as a painless, proliferating, rubbery swelling that may be ulcerated (Fig. **280**). Often, the tumor is fluctuant and has a bluish color, resembling a mucocele. The palate, retromolar pad, tongue, and lips are the most common intraoral sites of involvement.

Laboratory tests Histopathological examination.

Differential diagnosis Pleomorphic adenoma, mucocele, necrotizing sialadenometaplasia.

Treatment Surgical excision.

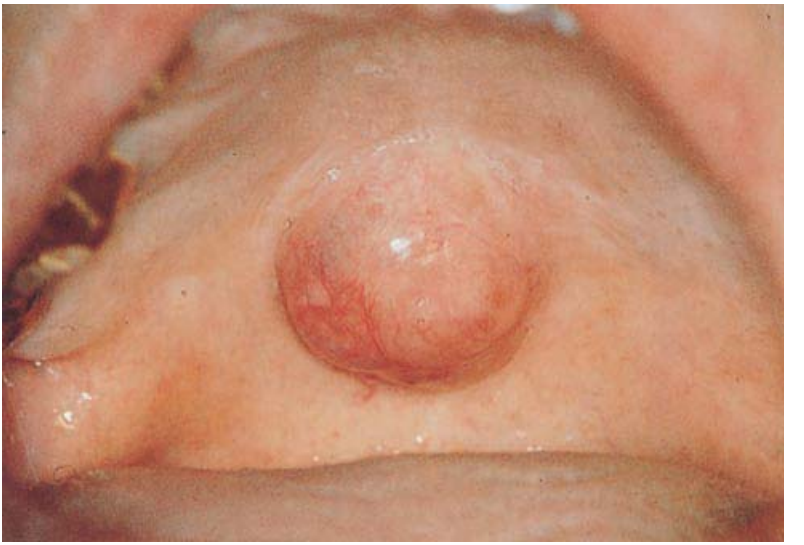


Fig. 279 Hemangioendothelioma of the palate.

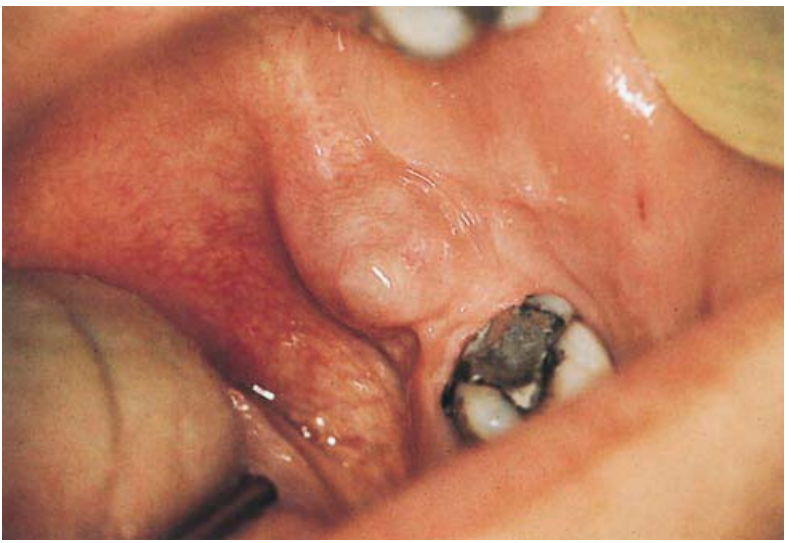


Fig. 280 Mucoepidermoid carcinoma of the retromolar area.

Adenoid Cystic Carcinoma

Definition Adenoid cystic carcinoma is the most common malignant neoplasm of minor gland, with a distinct histopathological pattern.

Etiology Unknown.

Clinical features It usually presents as a slightly painful, slow-growing tumor that may later ulcerate (Fig. **281**). The palate is most frequently affected, usually in patients over 50 years of age. The lesion is prone to infiltrate the perineural spaces, and usually has a poor prognosis.

Laboratory tests Histopathological examination.

Differential diagnosis Pleomorphic adenoma, necrotizing sialadenometaplasia, other malignant salivary gland tumors.

Treatment Surgical excision, radiation.

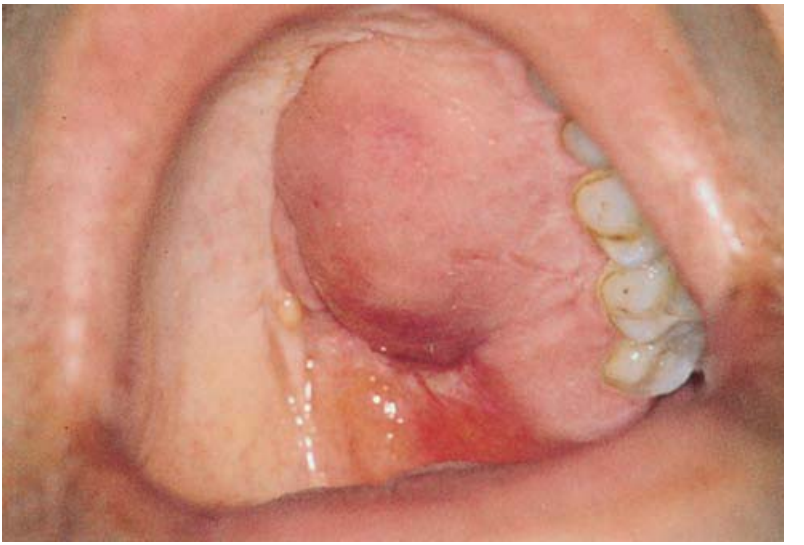


Fig. 281 Adenoid cystic carcinoma of the palate.

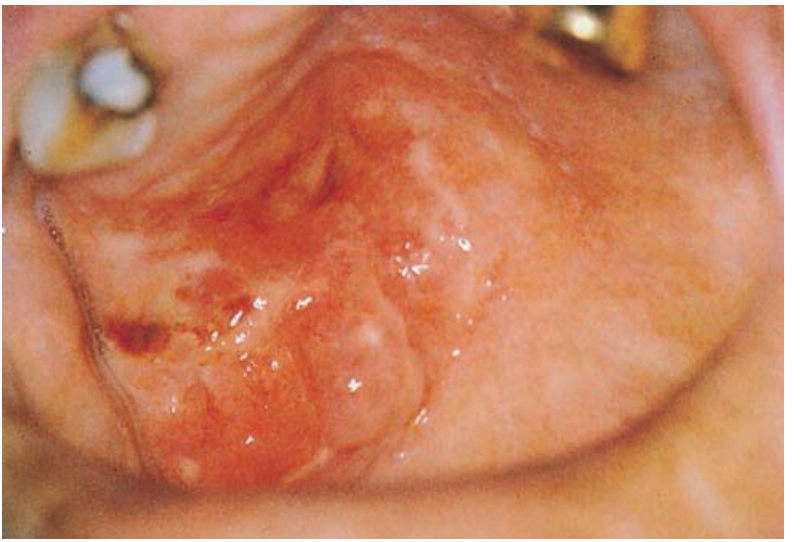


Fig. 282 Adenocarcinoma of the palate.

Other Malignant Salivary Gland Tumors

Acinic-cell adenocarcinoma, malignant pleomorphic adenoma, adenocarcinoma, clear-cell adenocarcinoma, polymorphous low-grade adenocarcinoma, and some others are included in this category of minor salivary gland malignant neoplasms. Clinically, almost all of them present as a firm swelling or tumor that may be ulcerated (Figs. **282**, **283**, **284**). It should be remembered that the clinical features are not characteristic, and the final diagnosis is made on the basis of the biopsy and histopathological examination.

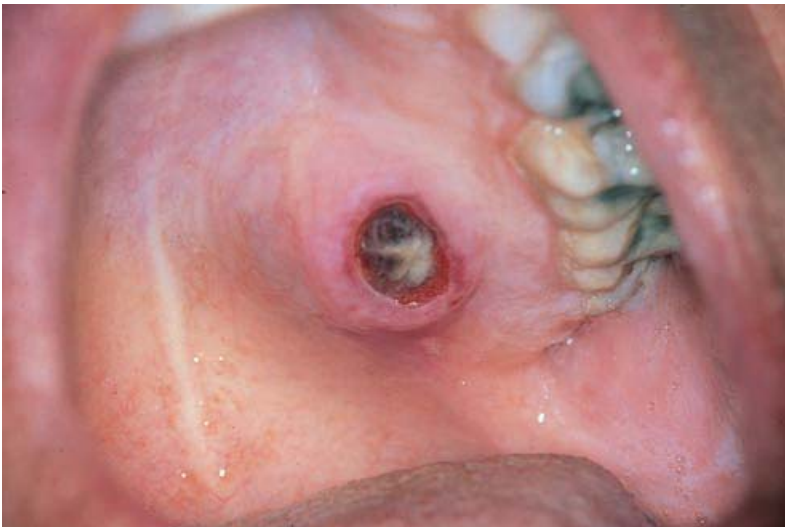


Fig. 283 Adenocarcinoma of the palate, ulcerated.

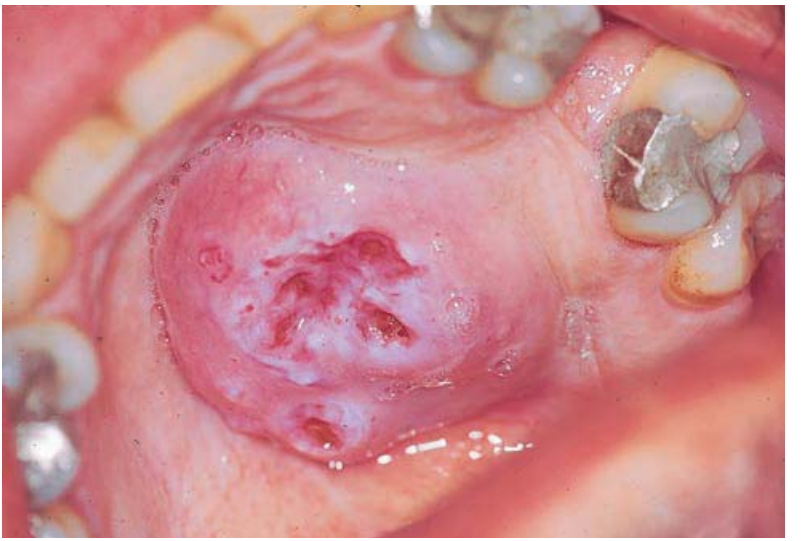


Fig. 284 Clear-cell adenocarcinoma of the minor salivary glands of the palate.

Non-Hodgkin Lymphoma

Definition Non-Hodgkin lymphoma is a heterogeneous group of neoplastic disorders that originate from lymphocytic cell lines.

Etiology Unknown. Viruses and radiation may sometimes be responsible.

Clinical features Oral involvement may be the only manifestation, or it may be part of a disseminated disease. It presents as a diffuse painless swelling, which may ulcerate (Fig. **285**). The palate, tonsillar area, base of the tongue, posterior gingiva, and floor of the mouth are most frequently affected.

Laboratory tests Histopathological and immunohistochemical examination.

Differential diagnosis Eosinophilic ulcer, minor salivary gland neoplasms, squamous-cell carcinoma, dental abscess, systemic mycoses.

Treatment Radiotherapy, chemotherapy.

Amyloidosis

Definition Amyloidosis is a rare metabolic disorder characterized by an abnormal extracellular deposition of amyloid, a fibrillar proteinaceous material, in tissues.

Etiology The etiology is not fully understood.

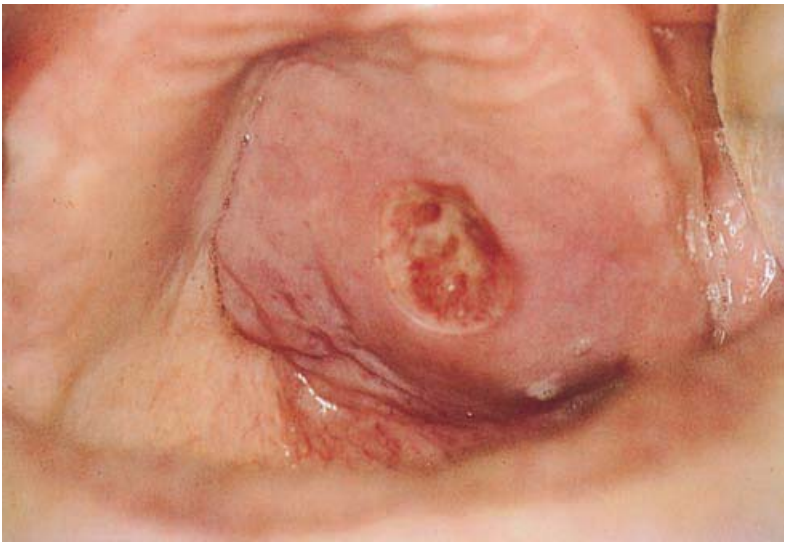


Fig. 285 Non-Hodgkin lymphoma: swelling and ulcer on the palate.

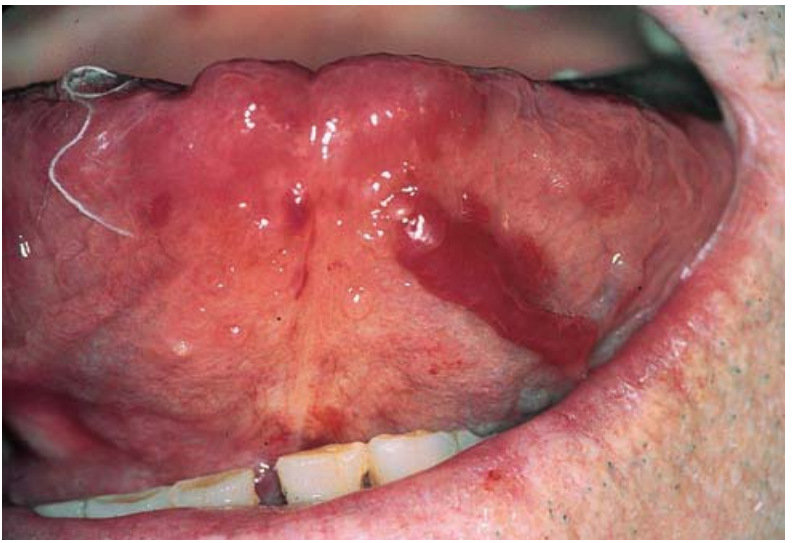


Fig. 286 Primary systemic amyloidosis: hemorrhagic bulla on the tongue.

Clinical features Four major forms are recognized: *primary*, *secondary*, *senile*, and *familial*. Primary and secondary amyloidosis may be either systemic or localized. The primary systemic form is the most serious form of the disease, affecting individuals older than 50 years. Oral lesions are common, and present as multiple deep red tumors, with petechiae, ecchymoses, macroglossia, ulcers, bullae, salivary gland infiltration, and xerostomia (Figs. **286**, **287**, **288**). Skin (purpura, petechiae, papules, nodules, bullae, alopecia) and systemic disorders are common. In 10–25% of cases, the disease is associated with multiple myeloma.

Laboratory tests Histopathological examination with special stains (Congo red, methyl violet, thioflavine T).

Differential diagnosis Kaposi sarcoma, Crohn disease, lipoid proteinosis, sarcoidosis, Crohn disease, multiple neurofibromatosis.

Treatment Symptomatic.

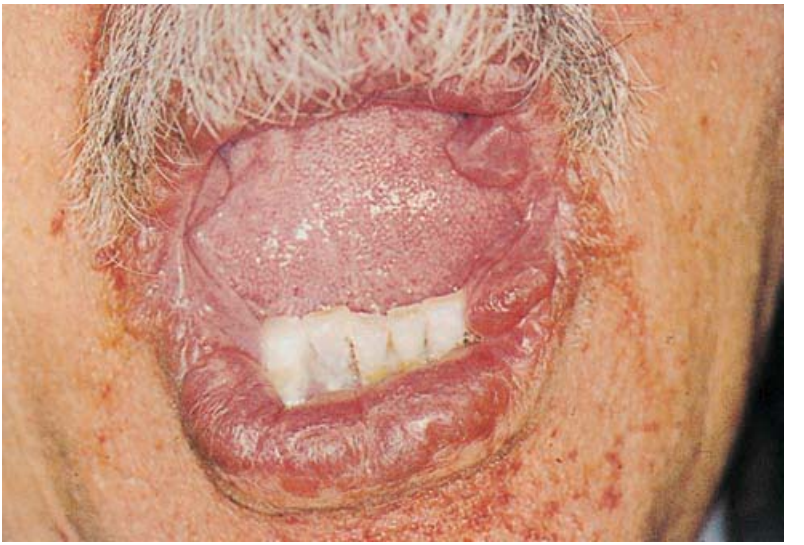


Fig. 287 Primary systemic amyloidosis: deep red nodules on the lips.

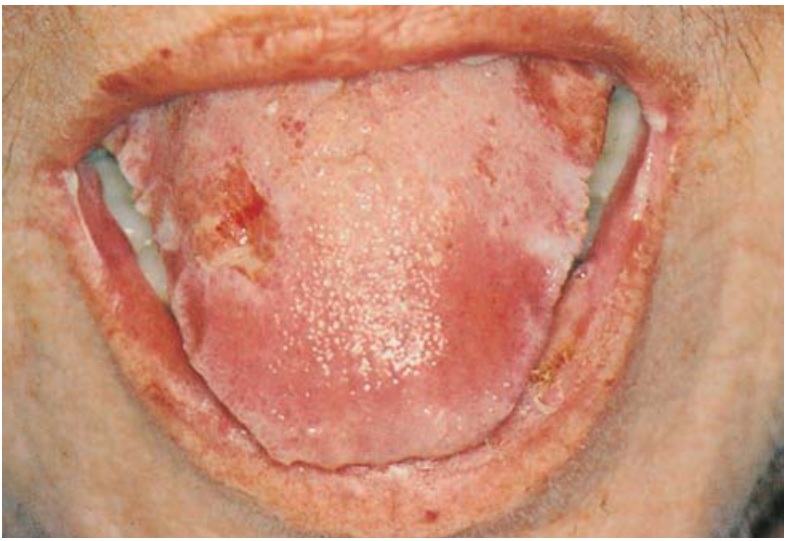


Fig. 288 Primary systemic amyloidosis: macroglossia, ecchymoses, and ulcer on the tongue.

Actinomycosis

Definition Actinomycosis is a chronic granulomatous infectious disease.

Etiology *Actinomyces israelii*.

Clinical features Oral lesions appear in the cervicofacial form of the disease, and present as an inflammatory, hard swelling that grows slowly (Fig. **289**). Multiple abscesses and draining sinuses intraorally and on the skin are common (Figs. **290**, **291**). New abscesses and sinuses may develop, while jaw and salivary gland involvement is common. The tongue, buccal mucosa, gingiva, tonsils, and lips are the most common sites involved.

Laboratory tests Bacteriological and histopathological examination.

Differential diagnosis Periapical and periodontal abscess, tuberculosis, systemic mycoses, other infections, benign and malignant tumors.

Treatment Penicillin or erythromycin or tetracycline, surgery.

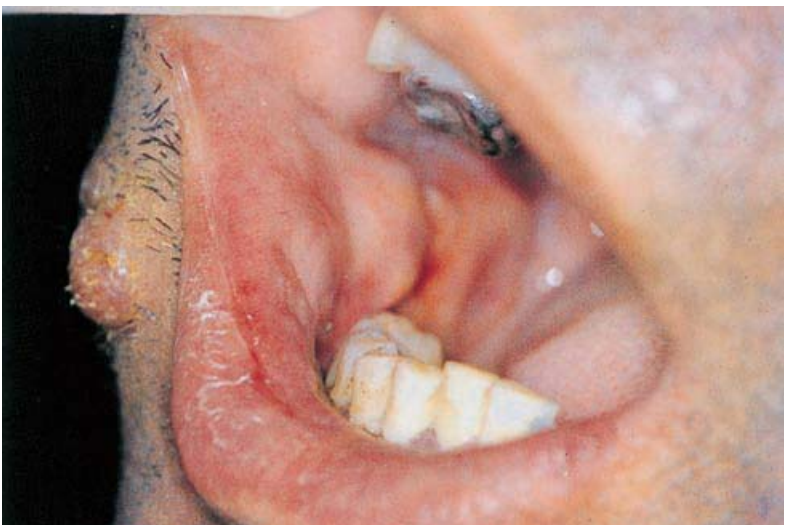


Fig. 289 Actinomycosis, nodules and sinus of the buccal mucosa.

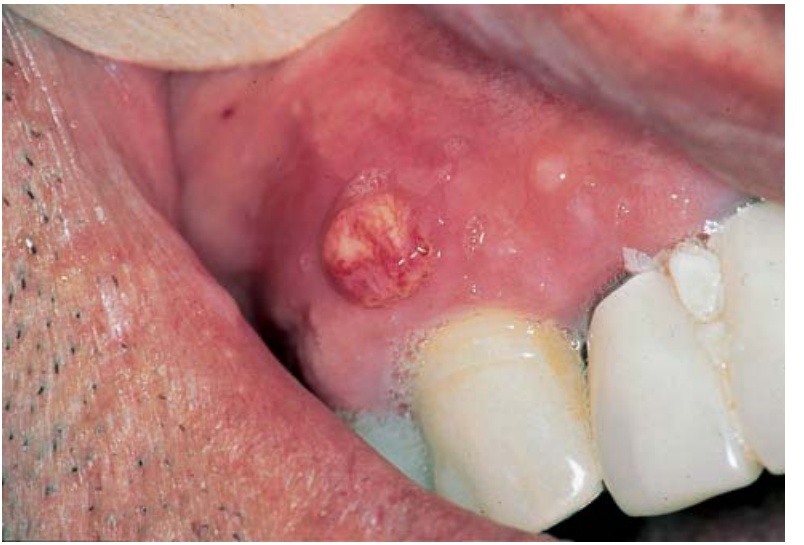


Fig. 290 Actinomycosis, abscess and draining sinus of the maxilla.

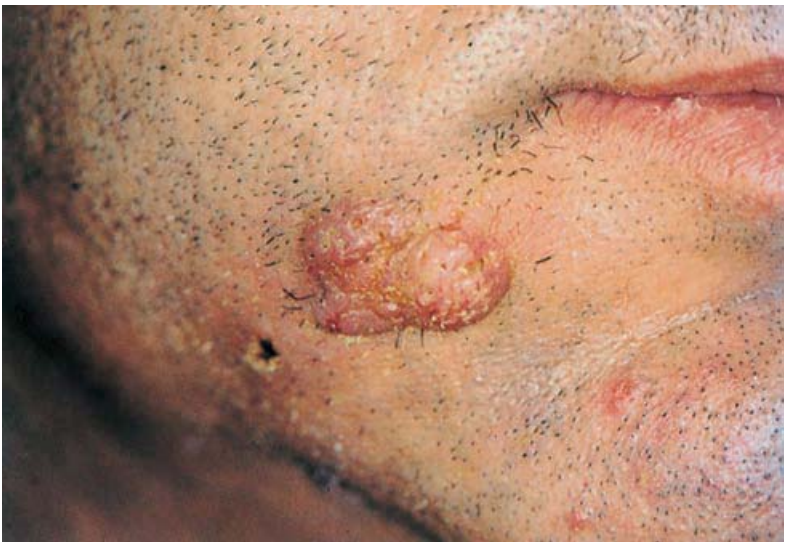


Fig. 291 Actinomycosis, multiple nodules and sinus of the skin.

Cutaneous Leishmaniasis

Definition Leishmaniasis is a parasitic infection that is endemic in the tropical and subtropical areas and around the Mediterranean.

Etiology *Leishmania tropica*.

Clinical features It initially appears as a small papule that grows slowly. Progressively, a red or brownish-red large nodule or tumor is formed, with a smooth and glistening surface, which finally ulcerates. The surrounding tissues are inflamed. The lips may be a site of cutaneous leishmaniasis, but it is extremely rare intraorally (Fig. **292**). The face, neck, arms, and legs are more frequently affected cutaneous areas.

Laboratory tests Histopathological examination, microbiological identification of the organism, leishmanin skin tests.

Differential diagnosis Basal-cell carcinoma, squamous-cell carcinoma, chancre, erysipelas, keratoacanthoma, systemic mycoses, sarcoidosis.

Treatment Meglumine antimonate, sodium stibogluconate, antimalarials.

Oral Soft-Tissue Chondroma

Definition Chondroma is a benign neoplasm composed of cartilage tissue.

Etiology Unknown. Oral soft-tissue chondroma may originate from ectopic cartilage or pluripotential cells of mesenchymal origin.

Clinical features Oral soft-tissue chondroma is very uncommon and appears as a painless, sessile or pedunculated, firm tumor, covered with intact normal mucosa (Fig. **293**). The lateral borders and the dorsum of the tongue, buccal mucosa, palate, and gingiva are the sites of predilection. It affects females more frequently than males. The clinical diagnosis should be confirmed by histopathological examination.

Differential diagnosis Fibroma, neurofibroma, schwannoma, granular cell tumor, peripheral ossifying fibroma.

Treatment Local surgical excision

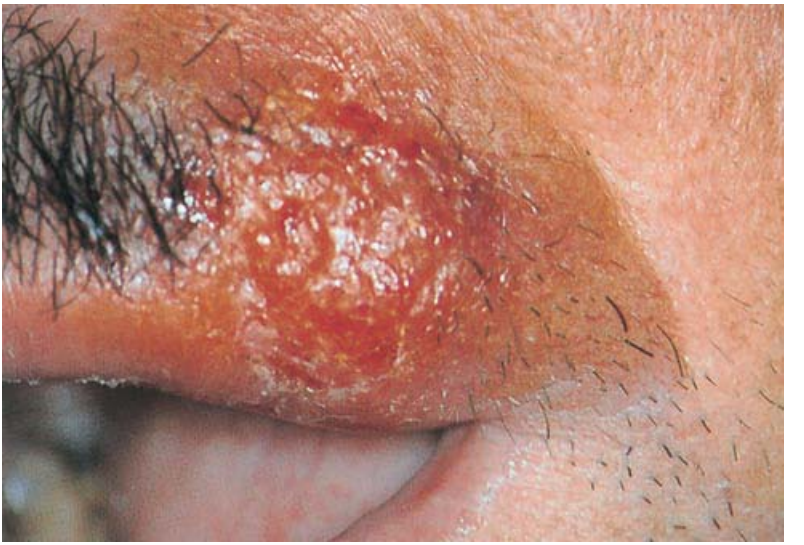


Fig. 292 Cutaneous leishmaniasis of the upper lip.

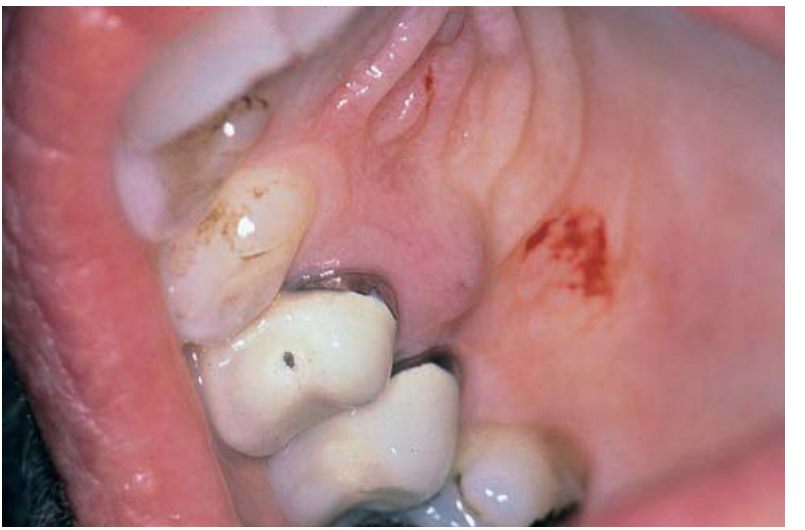
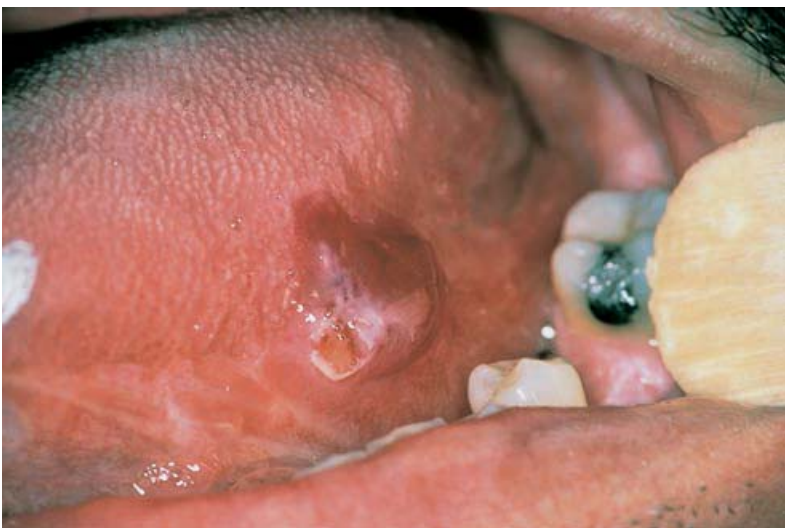


Fig. 293 Soft-tissue chondroma of the palatal gingiva.

9 Soft-Tissue Cysts

Cysts are epithelium-lined pathological cavities, usually filled with fluid, semi-solid material, or cellular debris. Soft-tissue cysts are a histogenetically heterogeneous group, characterized by the location on the soft tissues. Clinically, they present as a soft or fluctuant swelling. The cysts that are included in this group may be developmental, odontogenic, and traumatic in origin.

- Mucocele
- Ranula
- Dermoid cyst
- Lymphoepithelial cyst
- Eruption cyst
- Gingival cyst of the newborn
- Gingival cyst of the adult
- Thyroglossal duct cyst
- Nasolabial cyst
- Palatine papilla cyst



Mucocele

Definition Mucoceles, or mucous cysts, are a common phenomenon or lesion of the oral mucosa, originating from minor salivary glands and their ducts.

Etiology Local minor trauma and duct rupture or ductal obstruction, probably due to a mucous plug.

Clinical features Two main types of mucocele are recognized, according to their pathogenesis: *extravasation mucocele* (common), which results from duct rupture due to trauma and spillage of mucin into the surrounding soft tissues; and *mucous retention cyst* (uncommon), which usually results from ductal dilation due to ductal obstruction. Clinically, mucocele presents as a painless, dome-shaped, solitary, bluish or translucent, fluctuant swelling that ranges in size from a few millimeters to several centimeters in diameter (Figs. **294**, **295**). A common finding is that the cyst partially empties and then re-forms due to the accumulation of new fluid. The lower lip is the most common site of involvement, usually laterally, at the level of the bicuspids. Less common sites are the buccal mucosa, tongue, floor of the mouth, and soft palate. Extravasation mucoceles display a peak incidence during the second and third decades, while the mucous retention types are more common in older age groups.

Laboratory tests Histopathological examination.

Differential diagnosis Lymphangioma, hemangioma, lipoma, mucoepidermoid carcinoma, Sjögren syndrome, lymphoepithelial cyst.

Treatment Surgical excision or cryosurgery.

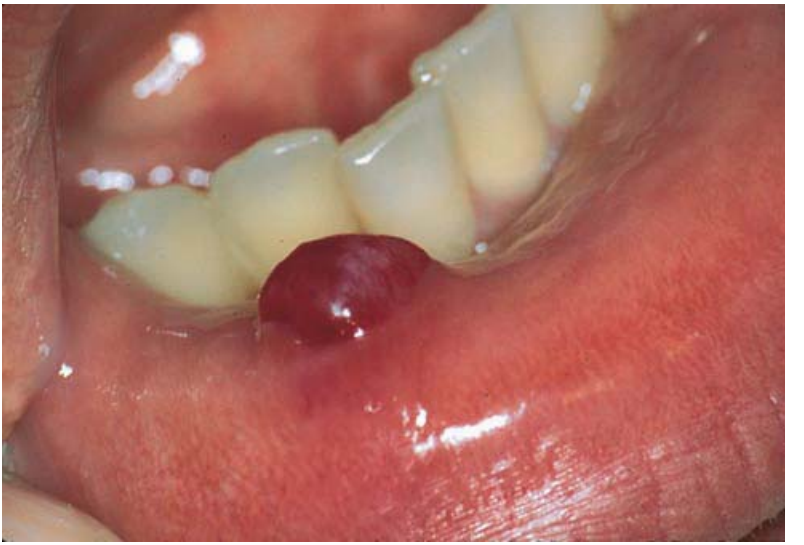


Fig. 294 Mucocele of the lower lip.

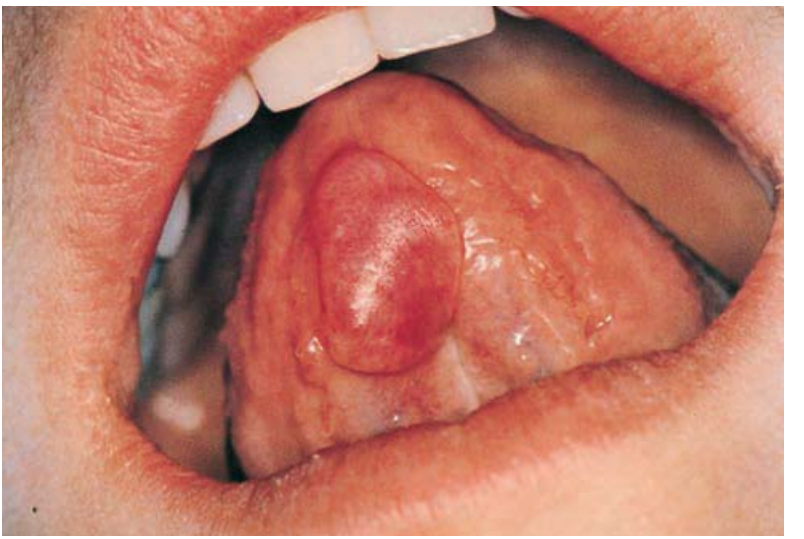


Fig. 295 Mucocele of the tongue.

Ranula

Definition Ranula is a form of mucocele that occurs exclusively on the floor of the mouth.

Etiology Trauma or ductal obstruction.

Clinical features It presents as a smooth, fluctuant, painless swelling on the floor of the mouth, lateral to the midline (Fig. **296**). The color ranges from normal to a translucent bluish, and the size is usually in the range of 1–3 cm, or larger. The diagnosis is usually based on clinical criteria.

Laboratory tests Histopathological examination.

Differential diagnosis Dermoid cyst, abscess, hemangioma, lymphangioma, lymphoepithelial cyst.

Treatment Surgical removal or marsupialization.

Dermoid Cyst

Definition and etiology Dermoid cyst is an uncommon developmental cystic lesion arising from embryonic epithelial remnants.

Clinical features It presents as a slow-growing, painless swelling with a normal or yellowish-red color and a characteristic soft doughlike consistency on palpation. The size varies from a few millimeters to 10 cm in diameter, and the lesion usually occurs in the midline of the floor of the mouth (Fig. **297**). If the cyst is located above the geniohyoid muscle, it can displace the tongue upward and create difficulty in mastication, speech, and swallowing. When the cyst occurs below the geniohyoid muscle, it may protrude submentally. Rarely, dermoid or epidermoid cysts may develop in the lips. The cyst frequently appears in early adulthood.

Laboratory tests Histopathological examination.

Differential diagnosis Ranula, abscess, lymphoepithelial cyst, cystic hygroma.

Treatment Surgical removal.

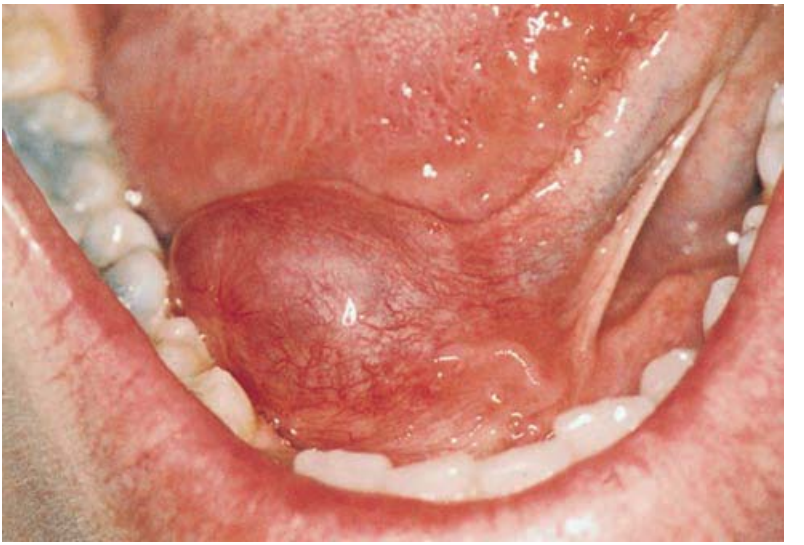


Fig. 296 Ranula.

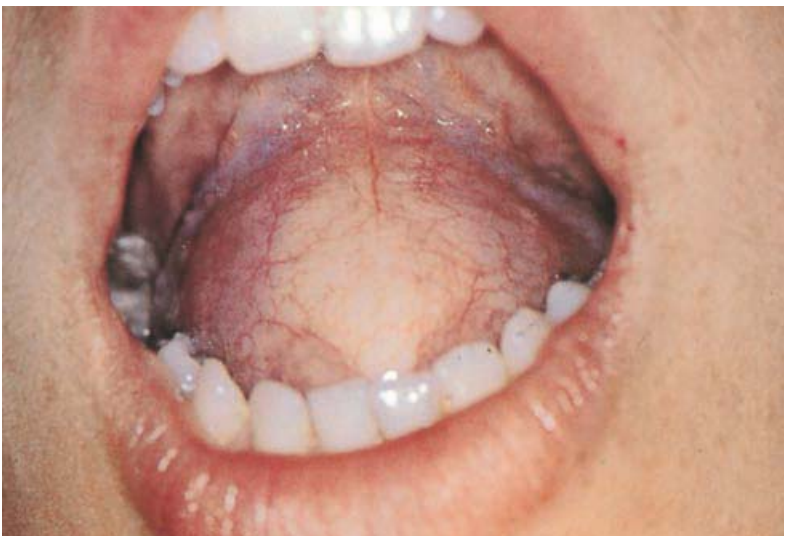


Fig. 297 Dermoid cyst.

Lymphoepithelial Cyst

Definition Lymphoepithelial cyst is an uncommon developmental lesion of the oral mucosa.

Etiology Probably caused by cystic degeneration of glandular or surface epithelium entrapped in lymphoid tissue during embryogenesis.

Clinical features It presents as an asymptomatic, mobile, well-defined nodule, usually firm on palpation and elevated, with a yellowish or whitish color. The size ranges from 0.5 cm to 2 cm in diameter. The floor of the mouth is the most frequent location, followed by the posterior lateral border and the ventral surface of the tongue (Figs. **298**, **299**, **300**). Lymphoepithelial cysts are histologically similar to the branchial cleft cysts that develop in the lateral neck.

Laboratory tests Histopathological examination.

Differential diagnosis Lymphoid tissue aggregation, dermoid cyst, mucocele, lipoma, fibroma and other benign tumors.

Treatment Surgical removal.

Eruption Cyst

Definition Eruption cyst is a soft-tissue form of dentigerous cyst and is associated with an erupting deciduous or permanent tooth.

Etiology Separation of the dental follicle from around the crown of the tooth.

Clinical features It presents as a well-demarcated, fluctuant, and soft swelling directly overlying the crown of an erupting tooth. Usually, the color is blue or dark red, depending on the amount of blood in the cystic fluid (Fig. **301**). The diagnosis is usually made on the basis of clinical criteria.

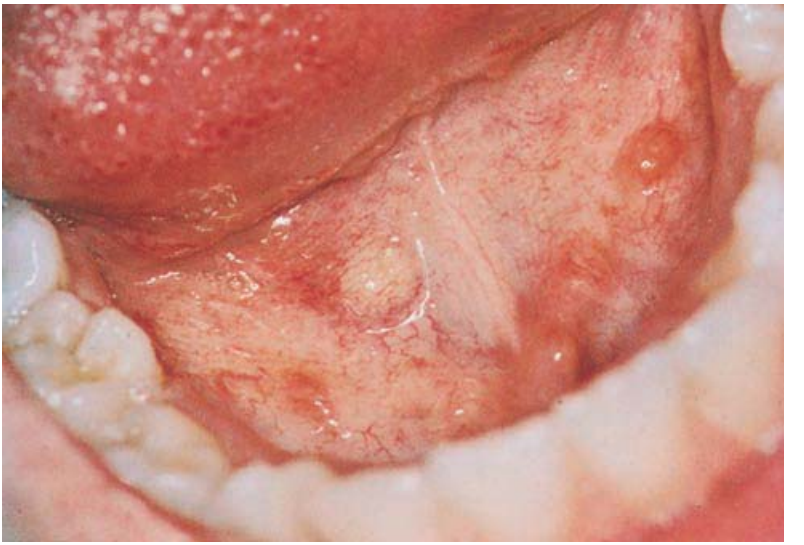


Fig. 298 Lymphoepithelial cyst in the floor of the mouth.

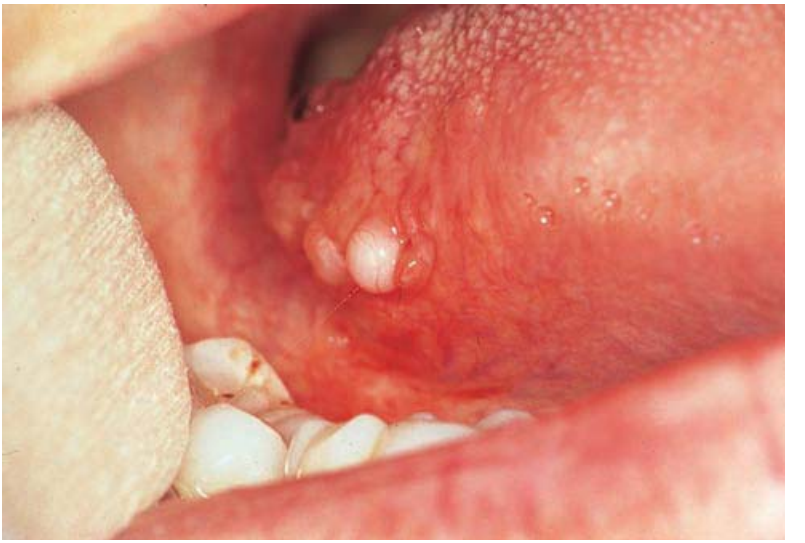


Fig. 299 Lymphoepithelial cyst on the posterior lateral border of the tongue, between the foliate papillae.

Laboratory tests Histopathological examination.

Differential diagnosis Hematoma, hemangioma, amalgam tattoo, pigmented nevi, melanoma, melanotic neuroectodermal tumor of infancy.

Treatment Usually not required, as the cyst often ruptures spontaneously.

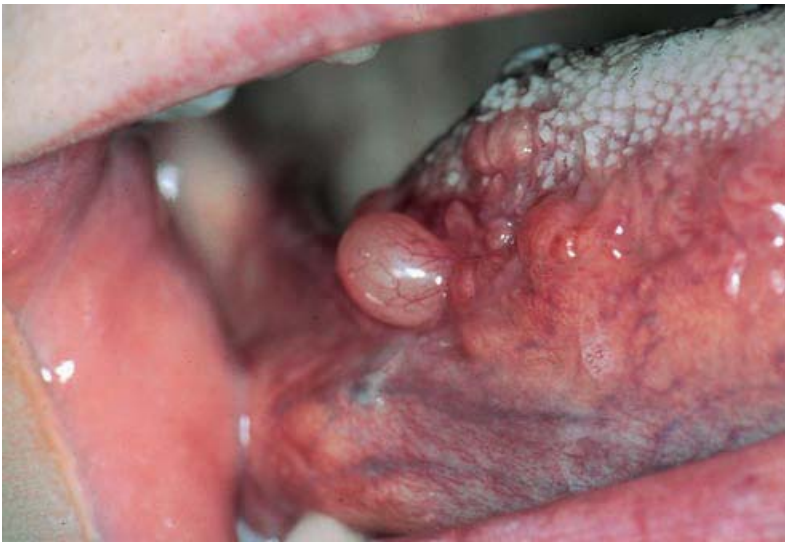


Fig. 300 Lymphoepithelial cyst of the lateral border of the tongue.

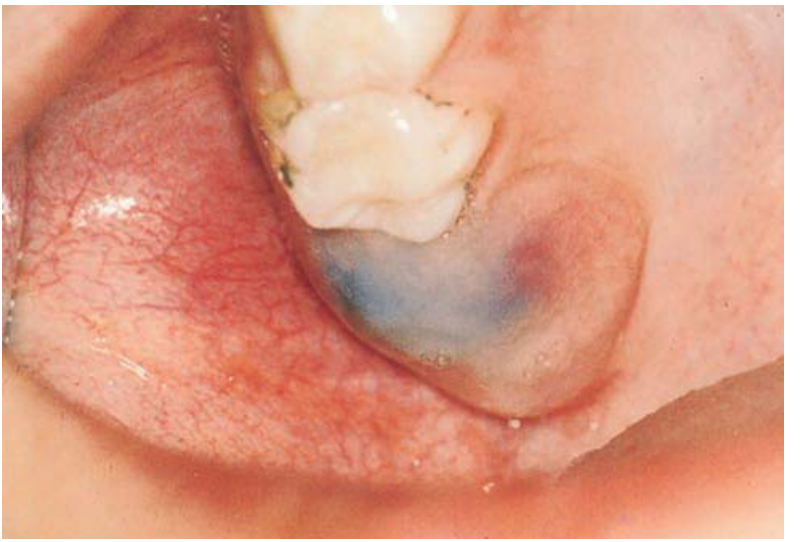


Fig. 301 Eruption cyst.

Gingival Cyst of the Newborn

Definition Gingival cysts of the newborn are small keratin-filled cysts on the alveolar mucosa of infants.

Etiology Remnant of the dental lamina.

Clinical features They appear as multiple or solitary, asymptomatic whitish nodules 1–3 mm in diameter, usually on the maxillary alveolus (Fig. **302**). The cysts contain keratin and regress spontaneously within a few weeks. The diagnosis is made at the clinical level.

Laboratory tests Histopathological examination.

Differential diagnosis Lymphangioma, granular-cell tumor of the newborn.

Treatment No treatment is required.

Gingival Cyst of the Adult

Definition Gingival cyst of the adult is a rare lesion located in the gingiva.

Etiology Remnants of the dental lamina.

Clinical features It appears as a painless, well-circumscribed swelling, 0.5–1 cm in diameter (Fig. **303**). The mandibular premolar and canine area is the site of predilection, and the condition is more frequent in patients over 40 years of age. The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests Histopathological examination.

Differential diagnosis Lateral periodontal cyst, periodontal abscess, mucocele, fibroma, peripheral ossifying fibroma, neurofibroma.

Treatment Surgical removal.

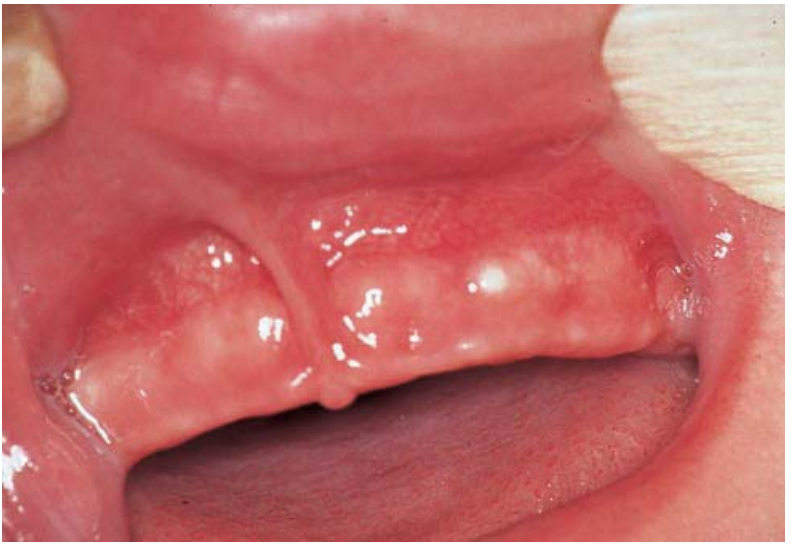


Fig. 302 Gingival cyst of the newborn: solitary whitish nodule on the maxillary alveolus.

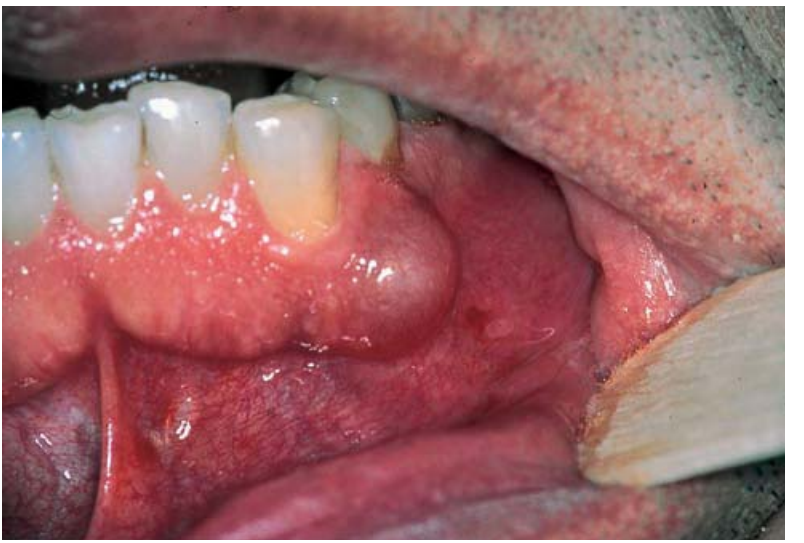


Fig. 303 Gingival cyst of the adult in the mandible.

Thyroglossal Duct Cyst

Definition Thyroglossal duct cyst is a rare developmental lesion that may form along the thyroglossal tract.

Etiology Remnants of thyroglossal duct epithelium.

Clinical features The cyst is usually located under the hyoid bone but can be located anywhere from the suprasternal notch to the foramen cecum of the dorsal tongue. Intraorally, it appears as a painless, fluctuant swelling usually 1–3 cm in diameter, located in the midline of the dorsum of the tongue close to the foramen cecum (Fig. **304**). Occasionally, a fistula may form following infection (Figs. **305**, **306**). The cyst is most often diagnosed in patients under 20 years of age.

Laboratory tests Histopathological examination, 99mTc or 125I scan.

Differential diagnosis Median rhomboid glossitis, benign and malignant tumors.

Treatment Surgical removal.

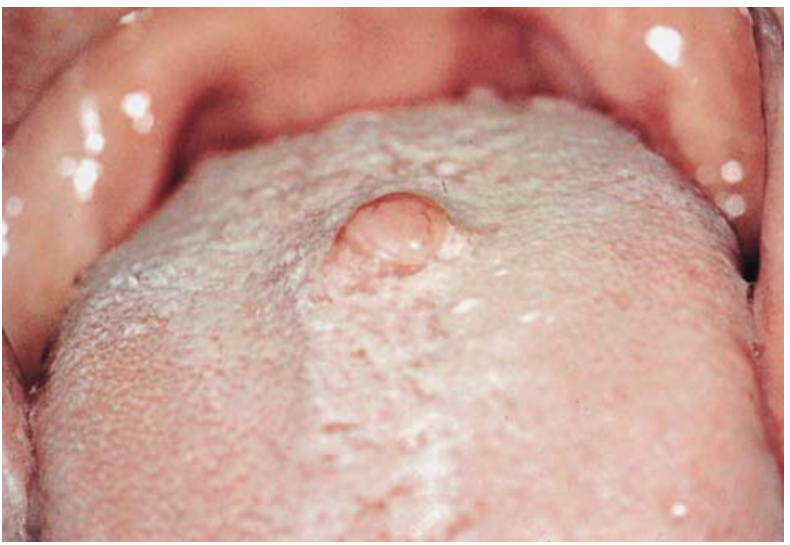


Fig. 304 Thyroglossal duct cyst on the dorsum of the tongue.

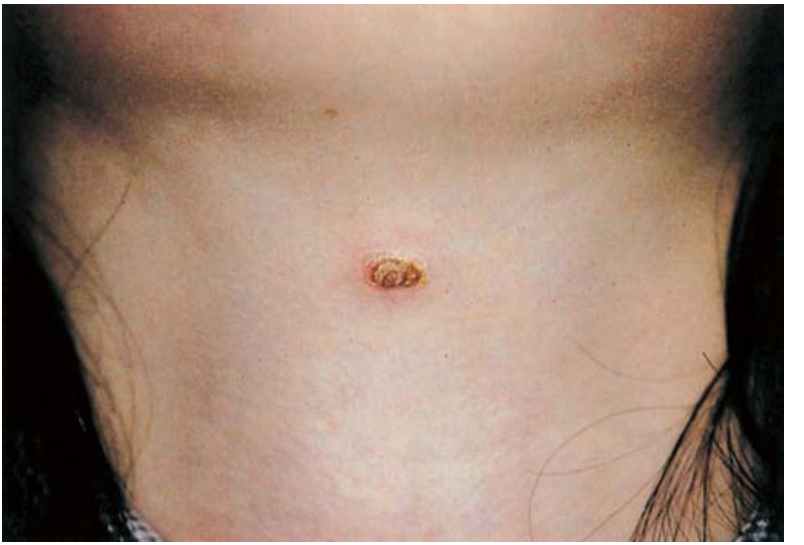


Fig. 305 Thyroglossal duct cyst and fistula in the midline of the neck.

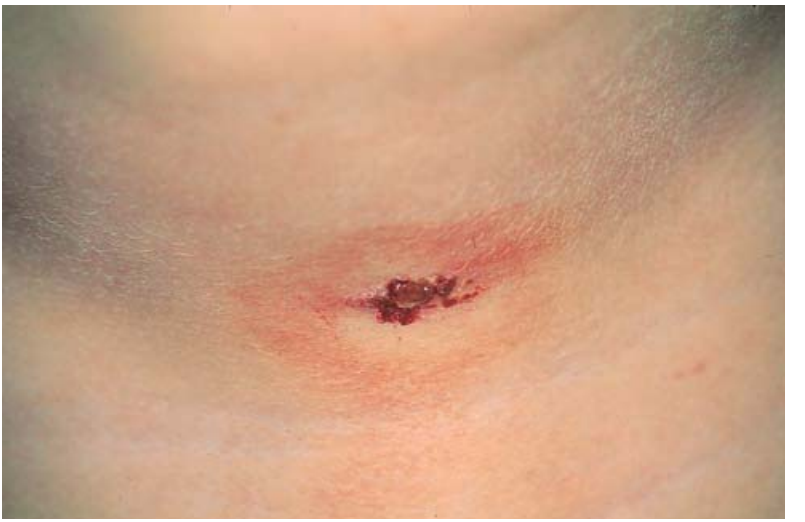


Fig. 306 Thyroglossal duct cyst and fistula in the midline of the neck.

Nasolabial Cyst

Definition Nasolabial cyst is a rare developmental soft-tissue cyst that develops in the upper lip in the canine region.

Etiology Unclear. Presumably it develops from the epithelium of the nasolacrimal duct.

Clinical features It appears as a soft-tissue swelling in the mucobuccal fold of the maxilla, lateral to the midline (Fig. **307**). Occasionally, the patient may complain of nasal obstruction, discomfort, or difficulties in wearing dentures. The cyst is more common in women, usually between 40 and 50 years of age.

Laboratory tests Histopathological examination.

Differential diagnosis Soft-tissue abscess, tooth abscess, mucocele, radicular cyst, salivary gland neoplasms, mesenchymal neoplasms.

Treatment Surgical excision.

Palatine Papilla Cyst

Definition Palatine papilla cyst is a variety of the nasopalatine cyst.

Etiology It arises from epithelial rests in the incisive foramen.

Clinical features It appears as a slow-growing soft swelling of the palatine papilla, covered with normal mucosa (Fig. **308**). The cyst, after mechanical irritation, may be inflamed and becomes painful due to local infection. The clinical diagnosis should be confirmed by histopathological examination.

Differential diagnosis Tooth and periodontal abscesses, mechanical trauma of the palatine papilla, fibroma, lipoma.

Treatment Surgical removal.

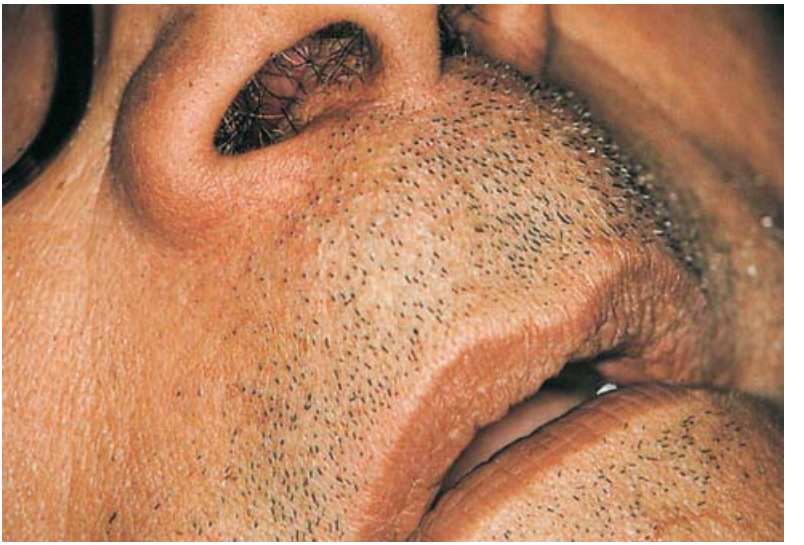


Fig. 307 Nasolabial cyst: swelling at the nasolabial fold.

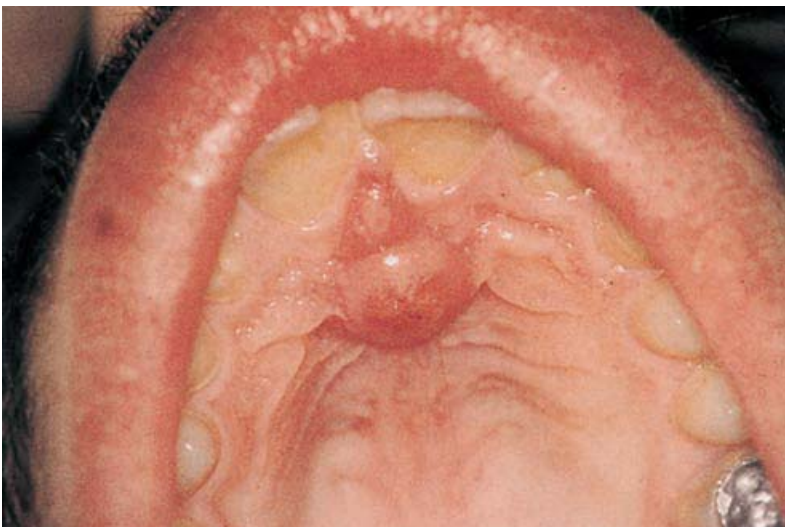
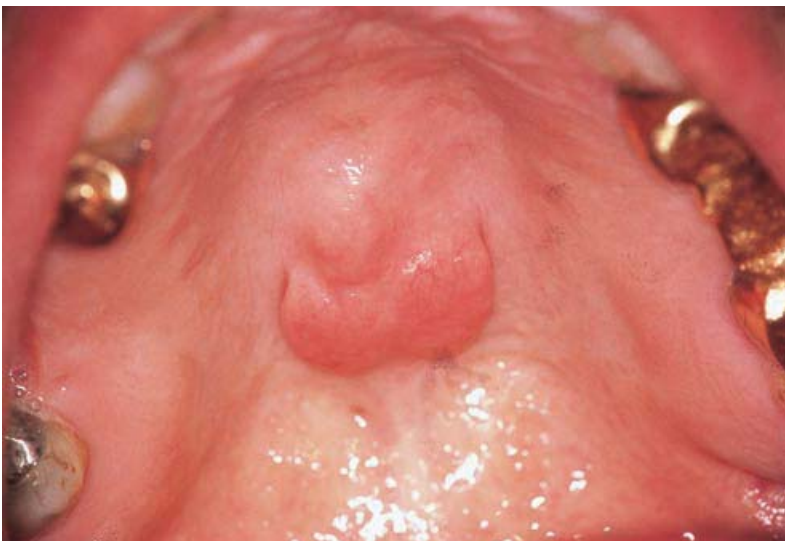


Fig. 308 Palatine papilla cyst.

10 Bone Swellings

Bone swellings are lesions that characteristically present as asymptomatic hard lumps, covered by normal epithelium. Developmental disorders, benign and malignant tumors are included in this group of lesions.

- Torus mandibularis
- Torus palatinus
- Multiple exostoses
- Osteoma
- Osteosarcoma
- Chondrosarcoma
- Burkitt lymphoma
- Multiple myeloma
- Paget disease
- Odontogenic tumors



Torus Mandibularis

Definition and etiology Torus mandibularis is a developmental malformation of unknown etiology.

Clinical features It presents as an asymptomatic bony swelling, covered by normal mucosa. The lesion displays slow growth during the second and third decades of life. Characteristically, the lesions appear bilaterally on the lingual surface of the mandible, usually in the area adjacent to the bicuspids (Fig. **309**). The diagnosis is based on clinical criteria.

Treatment Unnecessary unless full denture construction is required.

Torus Palatinus

Definition and etiology Torus palatinus is a developmental malformation of unknown etiology.

Clinical features It presents as a slow-growing, nodular, lobular or spindled, asymptomatic bony swelling covered by normal mucosa. Characteristically, the lesion appears along the midline of the hard palate (Fig. **310**). It occurs more often in women, and usually appears during the third decade of life. The diagnosis is based on the clinical findings.

Treatment Unnecessary unless full denture construction is required.

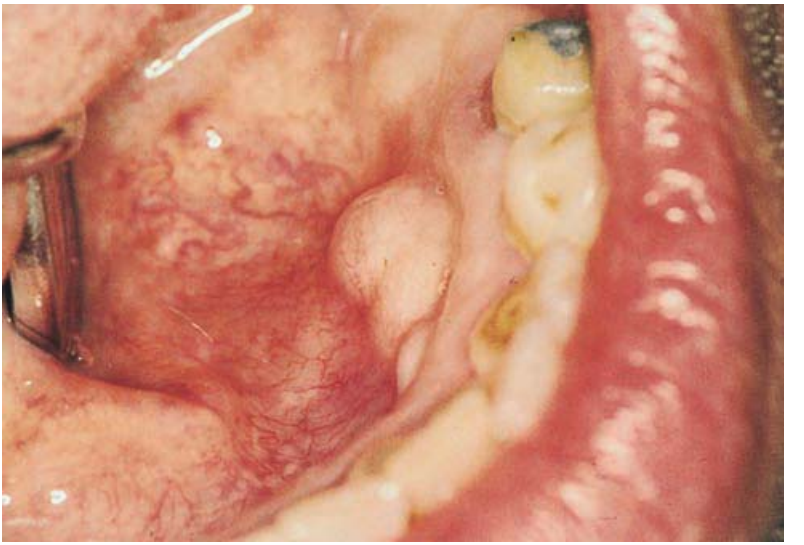


Fig. 309 Torus mandibularis.

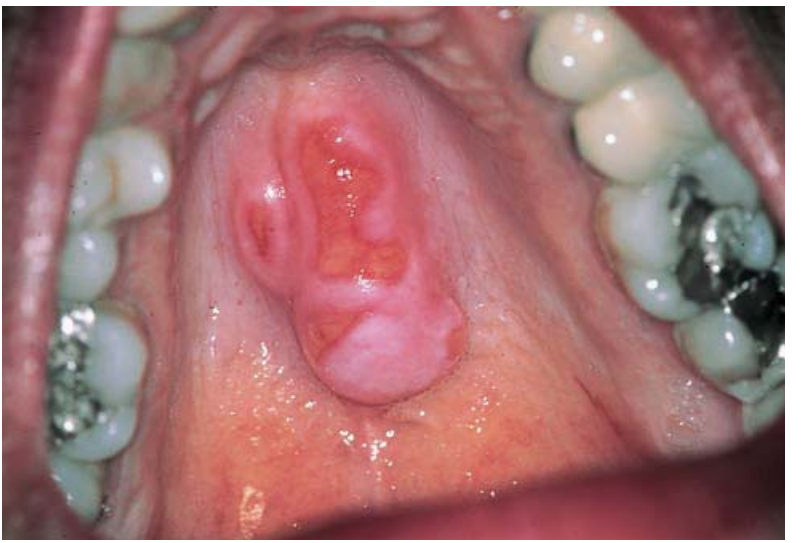


Fig. 310 Torus palatinus at the midline of the hard palate.

Multiple Exostoses

Multiple exostoses (see p. 250) may occur on the buccal surface of the maxilla, and rarely on the mandible. Clinically, the lesions appear as multiple asymptomatic bony swellings (Fig. **311**). The diagnosis is based on the clinical findings.

Treatment Unnecessary unless full denture preparation is required.

Osteoma

Definition Osteoma is a benign neoplasm that consists of mature compact or cancellous bone.

Etiology Unknown.

Clinical features It presents as an asymptomatic, slow-growing bony swelling of the jaws. The size ranges from a few millimeters to several centimeters. Multiple jaw osteomas are a common feature of Gardner syndrome (Fig. **312**).

Laboratory tests Histopathological examination, radiography.

Differential diagnosis Exostoses, osteosarcoma.

Treatment Surgical excision.

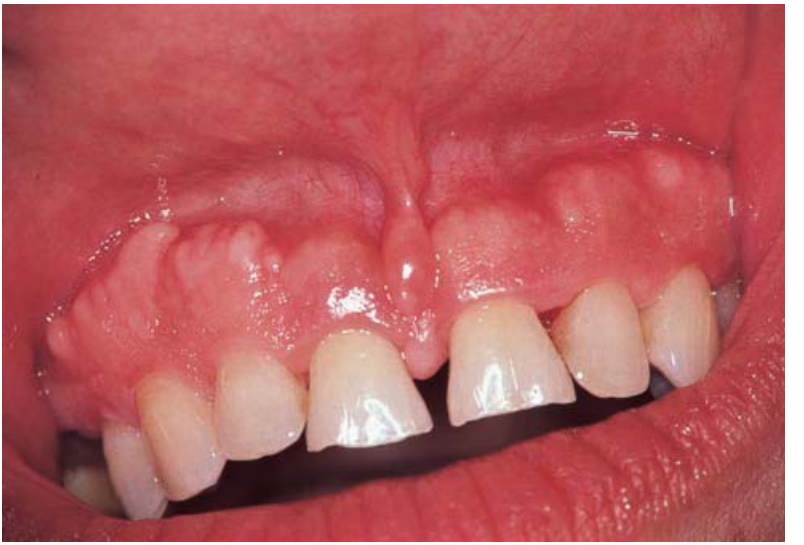


Fig. 311 Multiple exostoses on the maxilla.

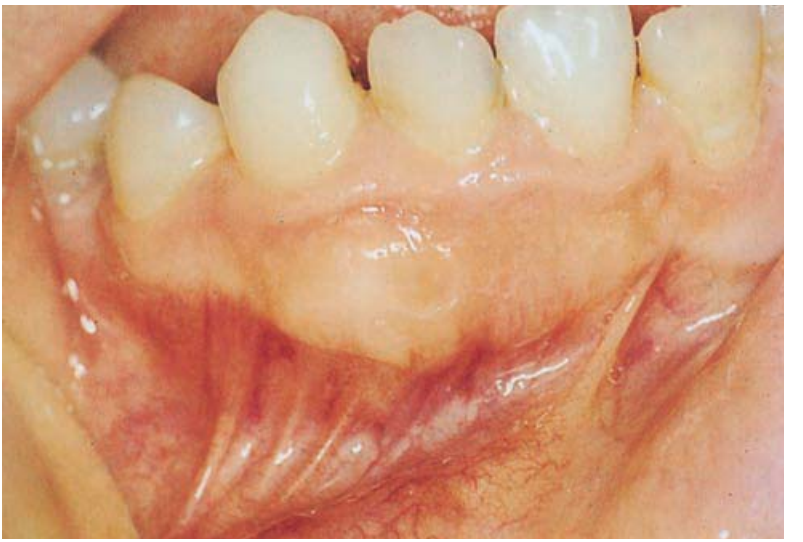


Fig. 312 Gardner syndrome: osteoma of the mandible.

Osteosarcoma

Definition Osteosarcoma is the most common primary malignant neoplasm of bone.

Etiology Unknown.

Clinical features The jaws are affected in 6–7% of cases, and usually during the third decade of life. Both jaws are affected equally and it is more common in men. Clinically, the lesion presents as a rapidly growing hard swelling that progressively produces facial deformity (Fig. **313**). Pain, paresthesia, tooth loosening, and nasal obstruction may also occur.

Laboratory tests Histopathological examination, radiography, CT scans.

Differential diagnosis Chondrosarcoma, Ewing sarcoma, metastatic tumors, odontogenic tumors and cysts, giant-cell tumor.

Treatment Surgical excision and supplementary radiotherapy and chemotherapy.

Chondrosarcoma

Chondrosarcoma (see p. 278) is more common in men than in women, between 30 and 60 years of age. Clinically, it appears as a painless hard swelling that progressively enlarges, causing extensive bone destruction with pain and loosening of the teeth.

Burkitt Lymphoma

Definition Burkitt lymphoma is a high-grade malignant B-lymphocyte lymphoma.

Etiology Epstein–Barr virus is closely associated.

Clinical features The malignancy is prevalent in central Africa (the endemic form), and usually affects children 2–12 years of age. Cases have also been observed in other countries (the nonendemic form), and recently in patients with AIDS. The jaws are the most common site of

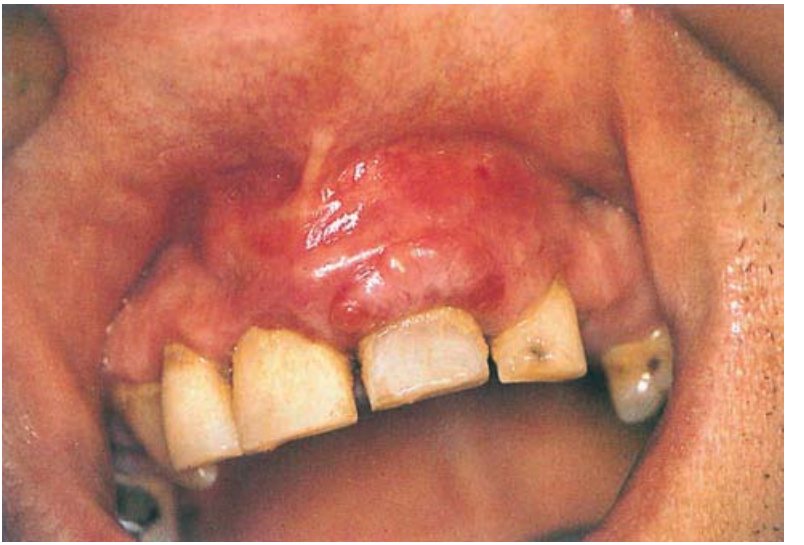


Fig. 313 Osteosarcoma of the upper jaw, presenting as a hard swelling.

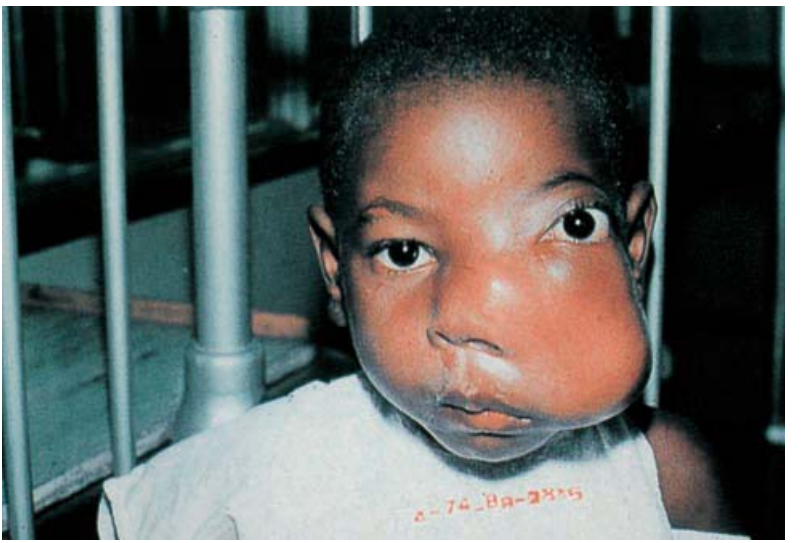


Fig. 314 Burkitt lymphoma, facial deformity.

lymphoma (60–70%). Clinically, it presents as a rapidly growing hard swelling that causes bone destruction, tooth loss, and facial deformity (Fig. **314**). Pain, paresthesia and large ulcerating or nonulcerating masses may also be seen (Figs. **315**, **316**).

Laboratory tests Histopathological examination, radiography.

Differential diagnosis Central giant-cell granuloma, ossifying fibroma, other non-Hodgkin lymphomas, and odontogenic tumors.

Treatment Chemotherapy, radiotherapy.

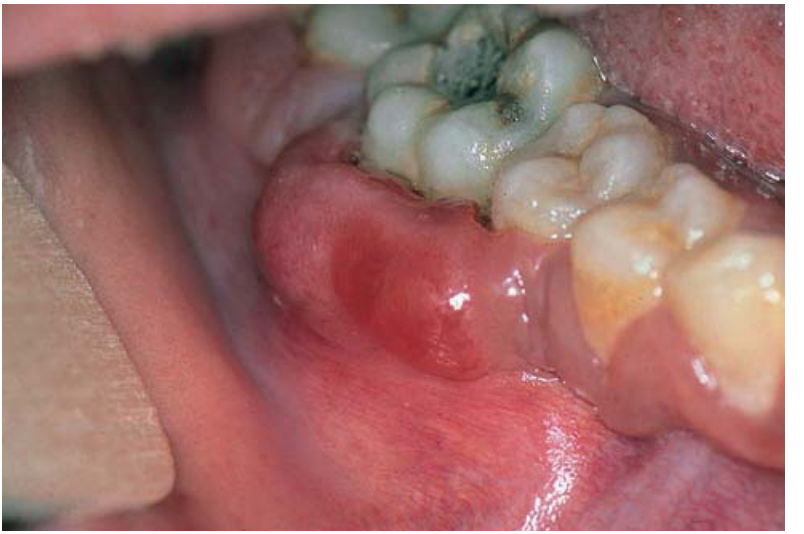


Fig. 315 Burkitt lymphoma, gingival mass.

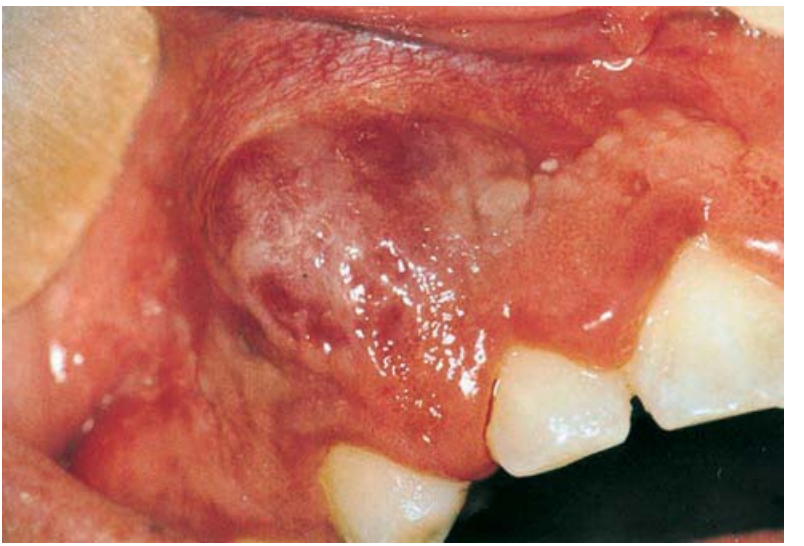


Fig. 316 Burkitt lymphoma on the gingiva in a young patient with AIDS.

Multiple Myeloma

Definition Multiple myeloma is a relatively rare malignant plasma-cell disorder.

Etiology Unknown.

Clinical features The malignancy is more common in men over 50 years of age, and the jaws are affected in about 30% of cases. Clinically, it presents with bone swelling, tooth mobility, pain, and paresthesia. A painless soft swelling, usually on the alveolar mucosa and gingiva, may develop as part of the overall disease spectrum (Fig. **317**).

Laboratory tests Bone-marrow biopsy, radiography, serum and urine protein electrophoresis.

Differential diagnosis Plasmacytoma, non-Hodgkin lymphoma, Ewing sarcoma, leukemia, Langerhans cell histiocytosis.

Treatment Chemotherapy, radiotherapy.

Paget Disease

Definition Paget disease, or osteitis deformans, is a chronic, relatively common disorder characterized by uncoordinated bone resorption and deposition.

Etiology Unknown.

Clinical features Clinically, the signs and symptoms develop gradually and are characterized by bone pain, headache, deafness, visual disorders, dizziness, and progressive bone enlargement. Progressive expansion of the maxilla and the mandible lead to symmetrical thickening of the alveolar ridges (Fig. **318**). Edentulous patients may complain that their dentures do not fit due to alveolar enlargement (Fig. **319**). Delayed wound healing, bleeding, and osteomyelitis after tooth extraction may occur. The maxilla is more frequently affected than the mandible. Males are more often affected than females. Two major forms of the disease are recognized: (a) the *monostotic*, and (b) the *polyostotic*.

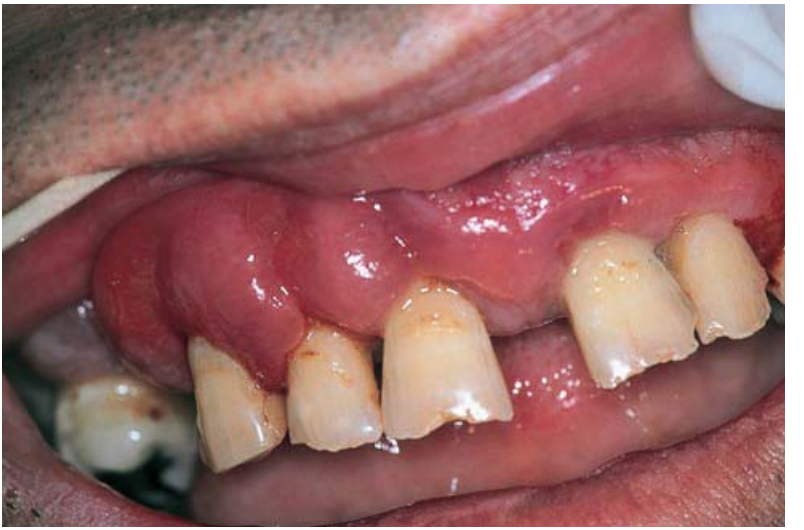


Fig. 317 Multiple myeloma, swelling on the gingiva.

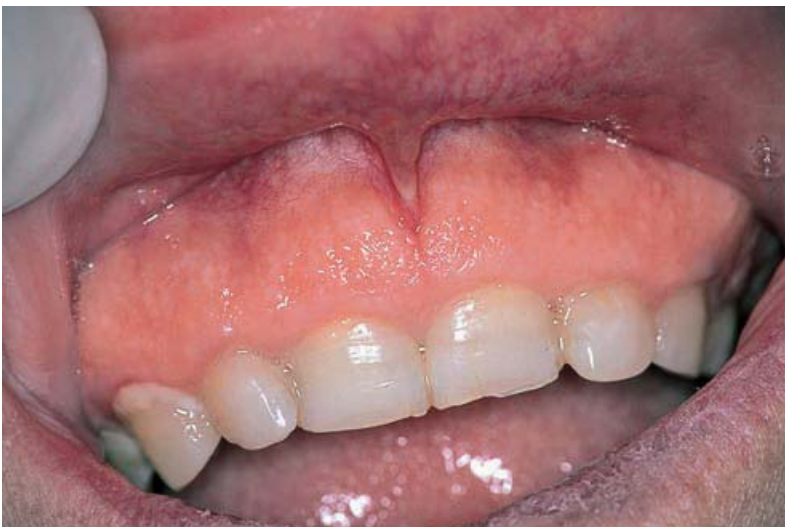


Fig. 318 Paget disease, enlarged maxilla.

The clinical diagnosis should be confirmed by a histopathological and radiographic examination. Elevations of serum alkaline phosphatase and urinary hydroxyproline levels are common findings.

Differential diagnosis Fibrous dysplasia, osteosarcoma, multiple exostoses, fibro-osseous lesions.

Treatment Most cases require no treatment. Calcitonin and bisphosphonates may slow the pathological process.

Odontogenic Tumors

Definition Odontogenic tumors are a group of lesions that originate from odontogenic epithelium and ectomesenchyme.

Etiology Unknown. Some are neoplasms and others hamartomas.

Classification On the basis of the tissue of origin, three major varieties are recognized: (a) *tumors of odontogenic epithelium*, (b) *tumors of odontogenic ectomesenchyme*, and (c) *mixed odontogenic tumors*.

Clinical features Most odontogenic tumors are usually asymptomatic for long time and are discovered only during a routine radiographic examination. However, with time they may form a usually painless slow-growing swelling or expansion of the mandible or the maxilla (Figs. **320**, **321**). The clinical signs and symptoms are not diagnostic and the final diagnosis should be made by radiographic and histopathological examinations.

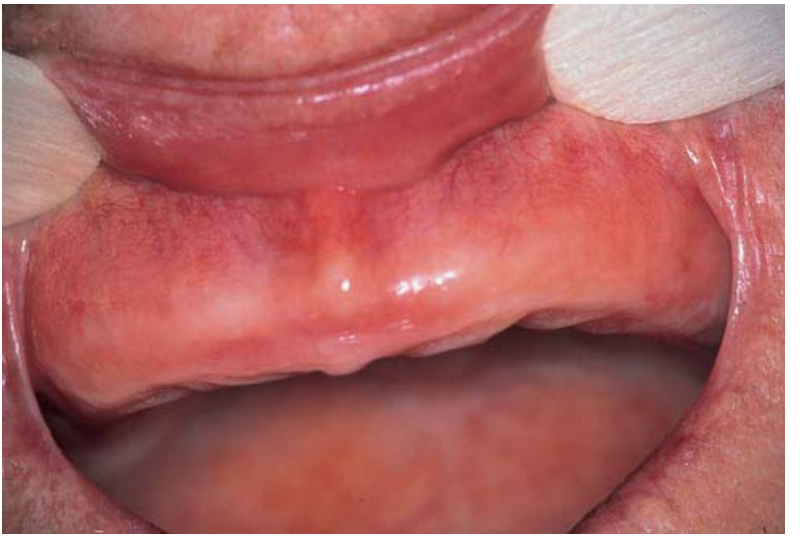


Fig. 319 Paget disease, alveolar enlargement.

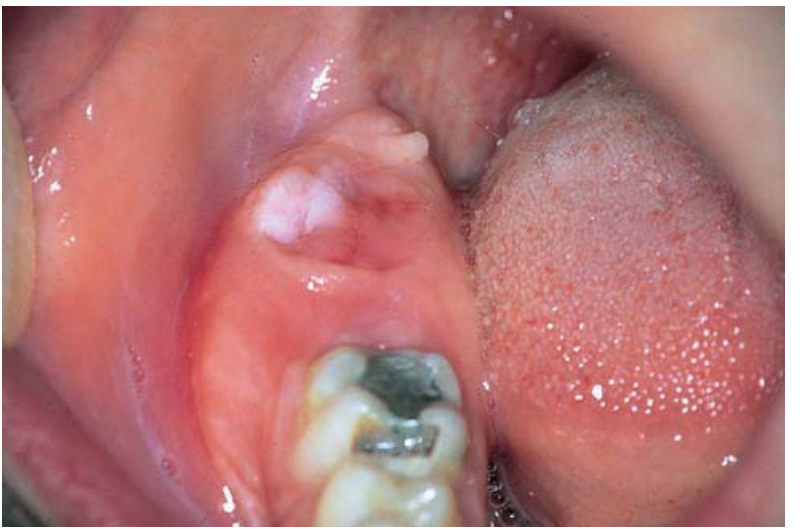


Fig. 320 Odontogenic myxoma, expansion of the retromolar area.

Differential diagnosis Different varieties of odontogenic tumors, odontogenic cysts, osteosarcomas, chondrosarcomas, multiple myeloma.

Treatment Surgical excision.

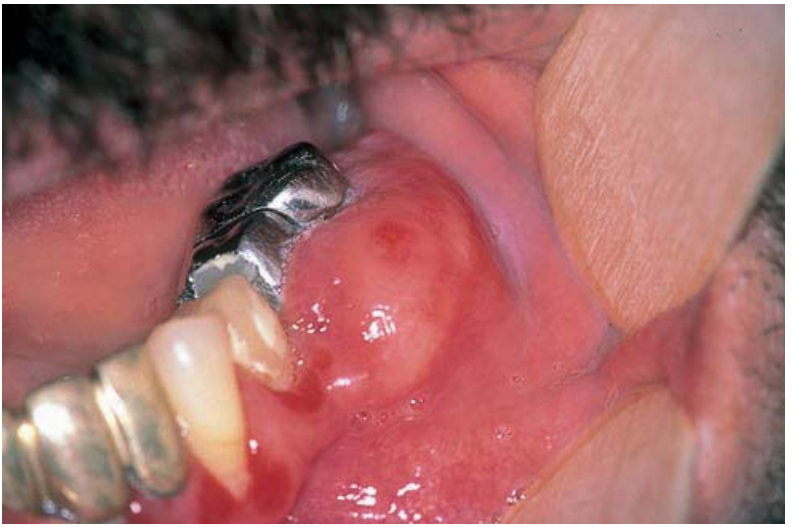
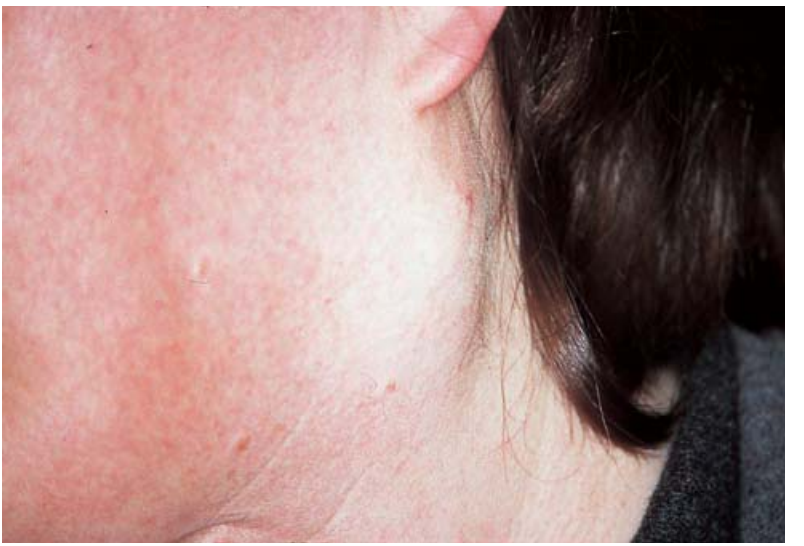


Fig. 321 Extraosseous calcifying epithelial odontogenic tumor presenting as a gingival mass.

11 Neck Swellings

This is a heterogeneous group of lesions, presenting clinically as fluctuant, soft or firm, lateral or midline neck swellings. The lesions may be asymptomatic, sensitive or painful, movable or fixed, solitary or multiple. Cysts, infectious diseases, autoimmune and systemic diseases, and neoplasms are included in this group of lesions, which usually cause diagnostic problems.

- Branchial cyst
- Thyroglossal duct cyst
- Dermoid cyst
- Cystic hygroma
- Nonspecific lymphadenitis
- Submandibular sialadenitis
- Tuberculosis
- Heerfordt syndrome
- Sjögren syndrome
- Hodgkin disease
- Metastatic carcinoma in the lymph nodes



Branchial Cyst

Definition Branchial cyst or cervical lymphoepithelial cyst is a relatively rare lesion, located in the upper lateral neck along the anterior border of the sternocleidomastoid muscle.

Etiology Developmental, like lymphoepithelial cysts.

Clinical features It appears as an asymptomatic, soft, fluctuant swelling 1–10 cm in diameter, usually lateral (Fig. **322**). It usually becomes apparent between the ages of 20 and 40 years.

Laboratory tests Histopathological examination.

Differential diagnosis Dermoid cyst, lymph-node enlargement, sialadenitis, salivary gland tumors, soft-tissue benign tumors.

Treatment Surgical removal.

Thyroglossal Duct Cyst

Thyroglossal duct cysts (see p. 308) very often appear in the midline of the neck, usually below the hyoid bone and submentally. Clinically, the lesion presents as a painless, fluctuant, movable swelling (Fig. **323**).

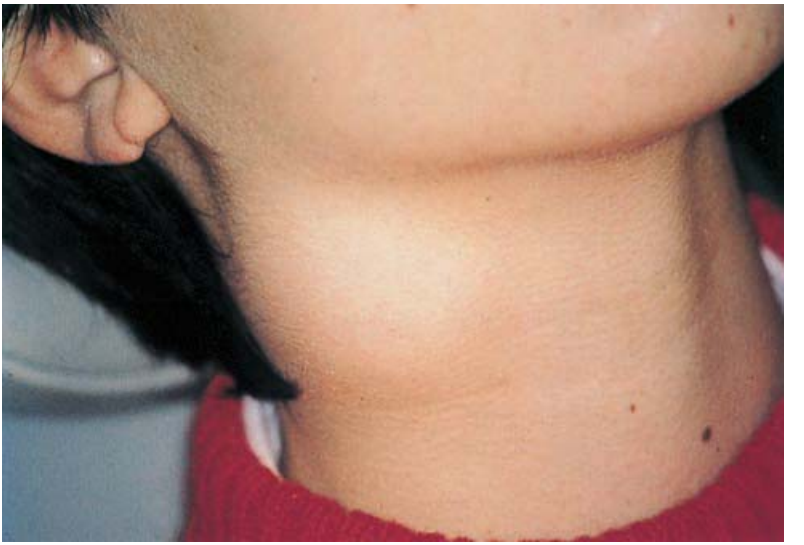


Fig. 322 Branchial cyst on the lateral side of the neck.

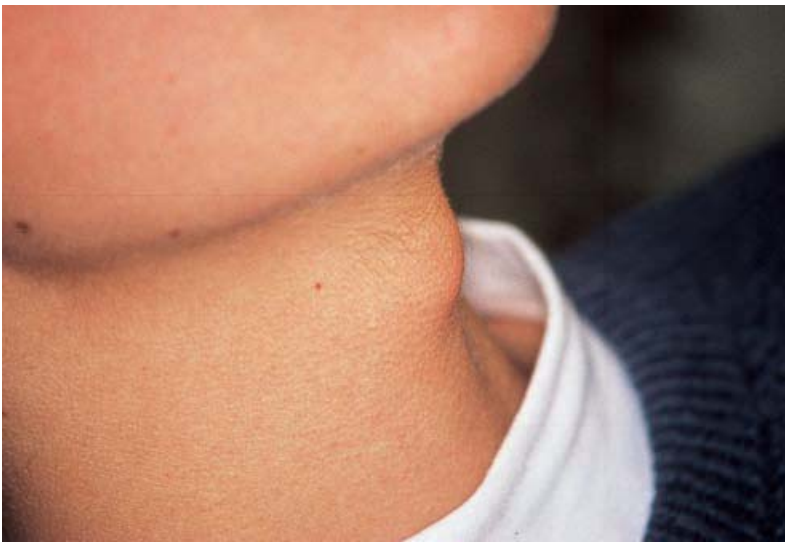


Fig. 323 Thyroglossal duct cyst: swelling of the midline of the neck.

Dermoid Cyst

Dermoid cysts (see p. 300), when they develop below the geniohyoid muscle, protrude submentally as a painless, doughy swelling (Fig. **324**). In such cases, the differential diagnosis should include thyroglossal duct cyst, periapical and soft-tissue abscesses, and sublingual sialadenitis.

Cystic Hygroma

Definition Cystic hygroma is a form of lymphangioma that consists of large cystic spaces.

Etiology Developmental.

Clinical features It appears as a large, soft swelling of the neck, extending to the submandibular or submental area, and occasionally to the buccal and the parotid area (Fig. **325**). It usually appears at birth or by 3 years of age, and may cause aesthetic or respiratory problems.

Differential diagnosis Branchial cyst, diffuse lymphadenopathy, parotitis, submandibular sialadenitis, hemangioma.

Treatment Surgical removal.

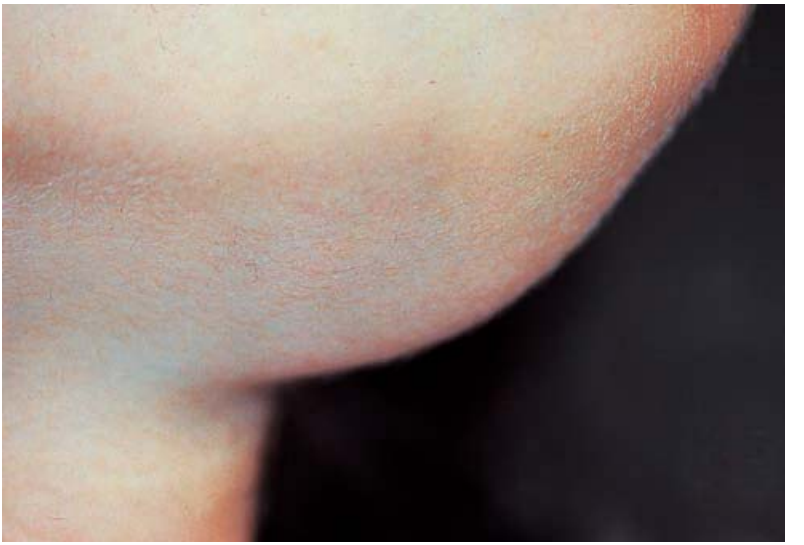


Fig. 324 Dermoid cyst: submental swelling, with a double-chin appearance.

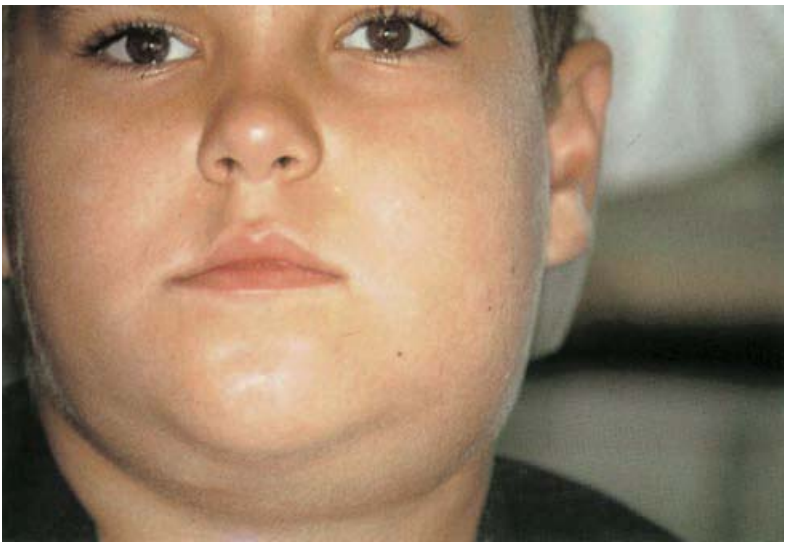


Fig. 325 Cystic hygroma: diffuse swelling of the neck.

Nonspecific Lymphadenitis

Definition Lymphadenitis is a lymphoid hyperplasia of the lymph nodes.

Etiology Infections (bacterial, viral, fungal).

Clinical features Lymph nodes in the neck area (submandibular, subdigastric, mid-jugular, low jugular, cervical) may produce neck swellings (Fig. **326**). In acute infections, the lymph nodes appear enlarged, tender, soft, and movable, while in chronic conditions they are enlarged, but not tender, and are firm, and occasionally fixed. Enlarged lymph nodes may be single or multiple.

Differential diagnosis Submandibular sialadenitis, non-Hodgkin lymphoma, Hodgkin disease, HIV infection, bacterial infections.

Treatment Treatment of the specific infection.

Submandibular Sialadenitis

Definition This is an inflammatory disorder of the submandibular salivary glands.

Etiology Infections, and rarely sialoliths, trauma.

Clinical features The condition presents as a tender swelling, usually unilateral, at the angle and the body of the mandible (Fig. **327**). The overlying skin is usually erythematous, and the duct orifice is red intraorally.

Differential diagnosis Lymph-node enlargement, buccal cellulitis, lymphomas, tuberculosis, sarcoidosis, Sjögren syndrome.

Treatment Antibiotics.

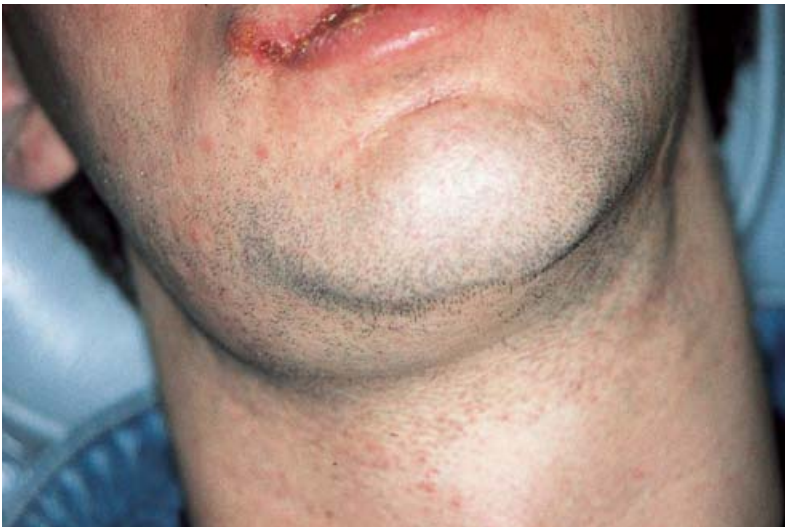


Fig. 326 Submandibular and cervical lymph-node enlargement due to herpetic oral infection.

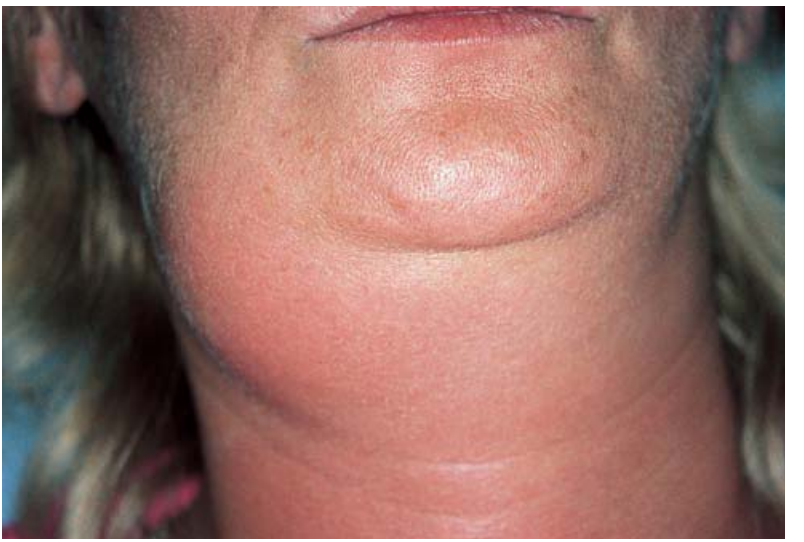


Fig. 327 Submandibular sialadenitis: swelling at the angle of the mandible and the neck.

Tuberculosis

Oral manifestations of tuberculosis are uncommon and present as a wide spectrum of lesions, usually secondary to pulmonary infection (see p. 154). Regional lymphadenopathy usually accompanies the oral lesions. A particular form of cervical lymph-node tuberculosis is known as *scrofula*. Clinically, it presents as a swelling of numerous cervical lymph nodes that occasionally leads to the formation of numerous fistulas though the overlying skin (Fig. **328**, **329**, **330**). The differential diagnosis should include lymphoma, submandibular sialadenitis, and actinomycosis.

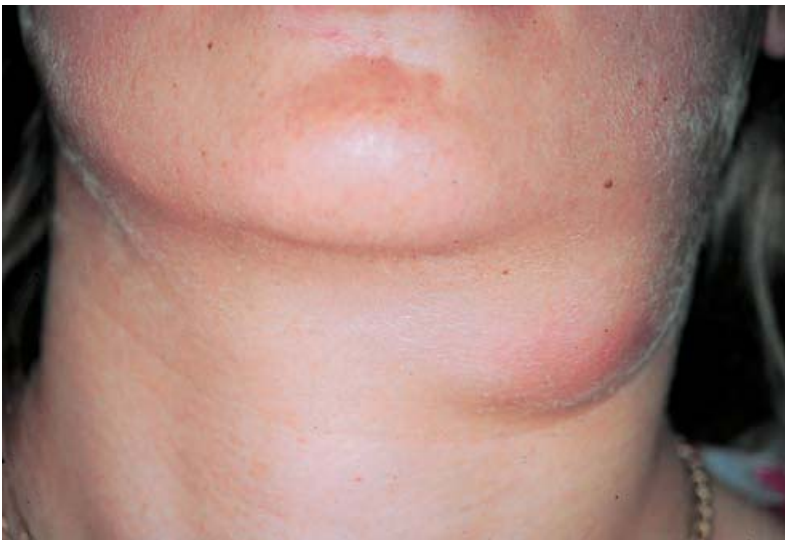


Fig. 328 Tuberculosis, submandibular and cervical lymph-node swelling.

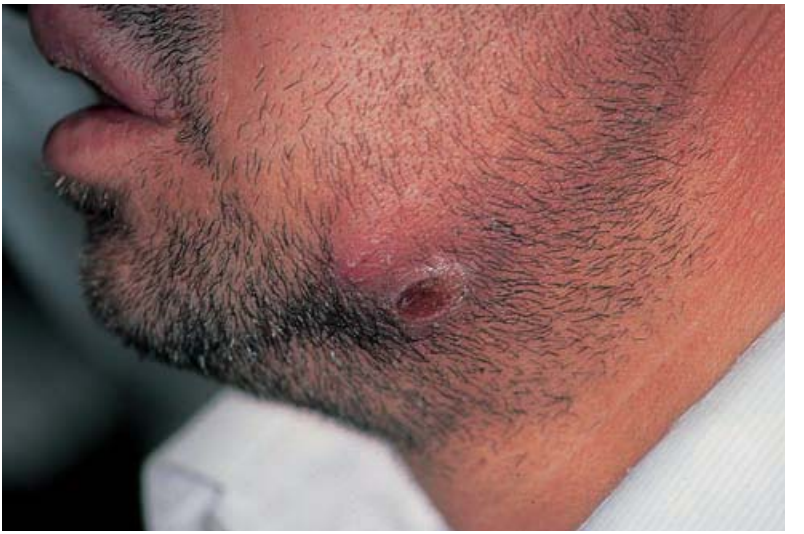


Fig. 329 Tuberculosis, lymph node involvement and fistula formation.

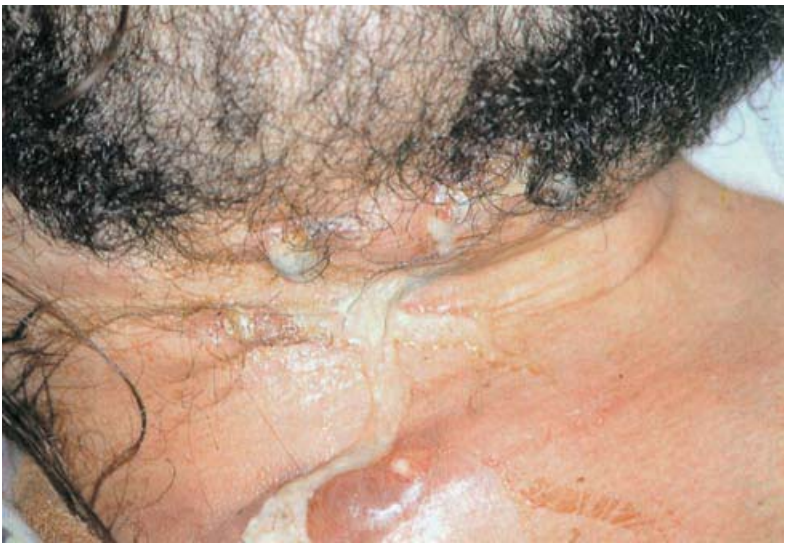


Fig. 330 Scrofula: multiple fistulas on the neck.

Heerfordt Syndrome

Definition Heerfordt syndrome, or uveoparotid fever, is a rare form of sarcoidosis.

Etiology Unknown. It is presumably related to an infectious agent.

Clinical features The condition is characterized by a bilateral, firm, painless swelling of the parotid glands, ocular lesions (uveitis, conjunctivitis, keratitis), facial paralysis, skin lesions, and low-grade fever (Fig. **331**, **332**). Submandibular and sublingual salivary gland enlargement may also occur (Fig. **333**).

Laboratory tests Histopathological examination, Kveim skin test, radiography.

Differential diagnosis Sjögren syndrome, Mikulicz syndrome.

Treatment Steroids. Often the symptoms resolve spontaneously within two or three years.

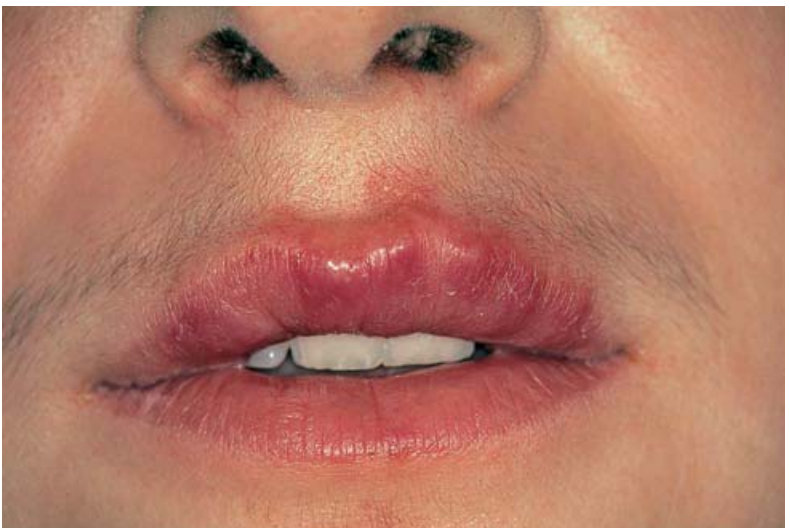


Fig. 331 Sarcoidosis, multiple red nodules on the upper lip.

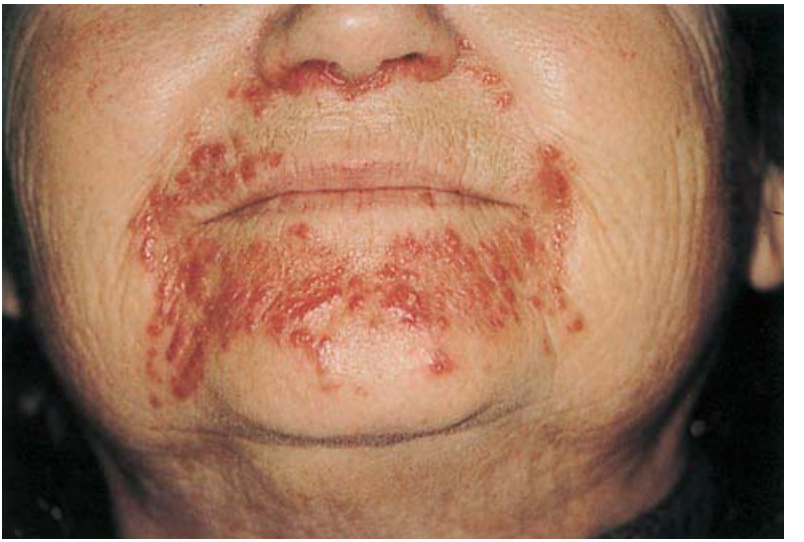


Fig. 332 Sarcoidosis: multiple lesions on the perioral skin.

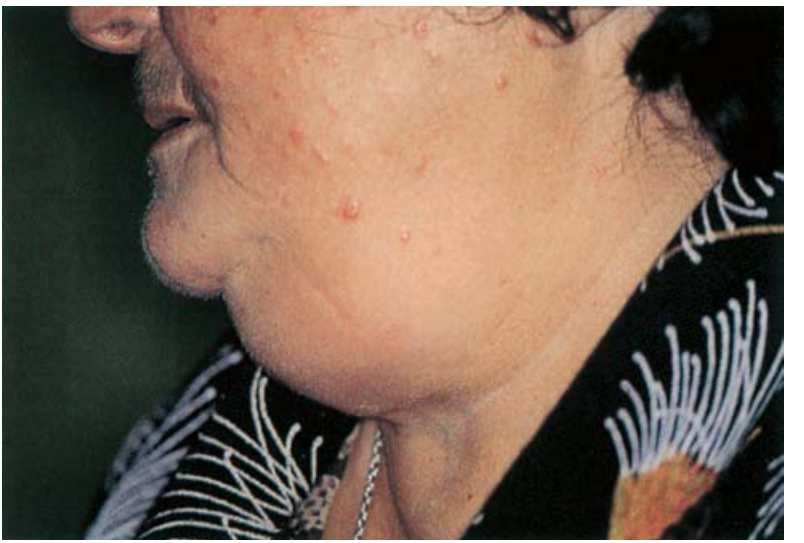


Fig. 333 Heerfordt syndrome: swelling of the major salivary glands.

Sjögren Syndrome

Definition Sjögren syndrome is a chronic autoimmune disease of the exocrine glands.

Etiology Unknown.

Clinical features Two forms of the disease are recognized: *primary* and *secondary*, when it is associated with collagen diseases. The cardinal clinical manifestations include a recurrent enlargement of the parotid, submandibular (Fig. **334**) and lacrimal glands, lymphadenopathy, purpura, Raynaud phenomenon, myositis, and renal and pulmonary manifestations. Keratoconjunctivitis sicca, xerostomia, cheilitis, dental caries, and candidiasis are common manifestations (Fig. **335**, **336**). The disease most frequently affects women between 40 and 60 years of age.

Laboratory tests Histopathological examination, serological tests—antinuclear antibodies (ANA), anti-SSA (Ro), SS-B (La) antibodies.

Differential diagnosis Heerfordt syndrome, Mikulicz syndrome, collagen diseases, graft-versus–host disease.

Treatment Steroids and immunosuppressive drugs. Artificial saliva and tears.

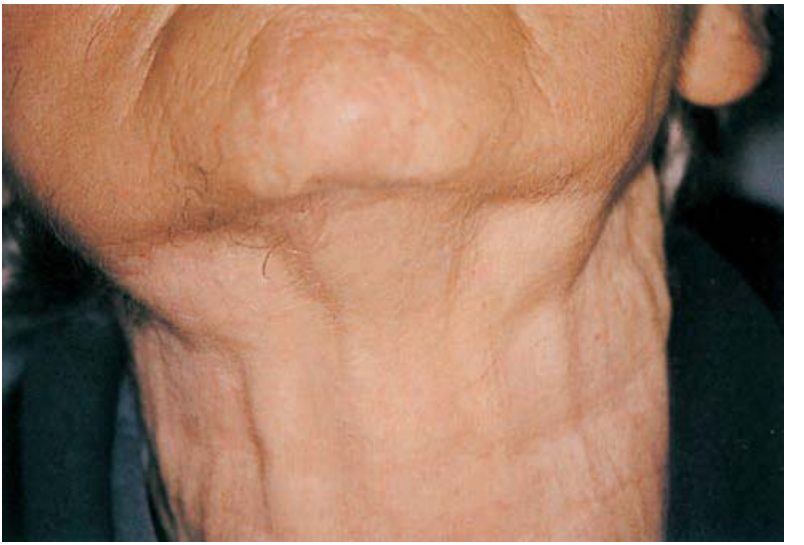


Fig. 334 Sjögren syndrome: bilateral enlargement of the submandibular glands.

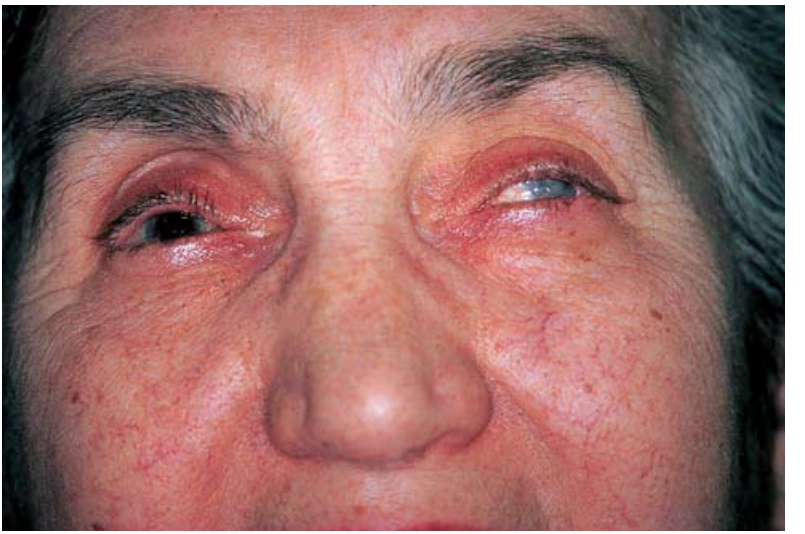


Fig. 335 Sjögren syndrome, severe ocular lesions.

Hodgkin Disease

Definition Hodgkin disease is a malignant disease of the mononuclear cell system.

Etiology Unknown.

Clinical features Painless and persistent swelling, usually of the cervical and supraclavicular lymph nodes or other lymph-node groups, is the common presenting sign (Fig. **337**). In the early stages the lymph nodes are often movable, and later they become fixed to the surrounding tissues. Anorexia, weight loss, fever, night sweats, and pruritus may accompany lymphadenopathy. Oral ulceration may also occur.

Laboratory tests Histopathological examination, immunological markers.

Differential diagnosis Non-Hodgkin lymphoma, tuberculosis, infectious mononucleosis.

Treatment Chemotherapy, radiotherapy.

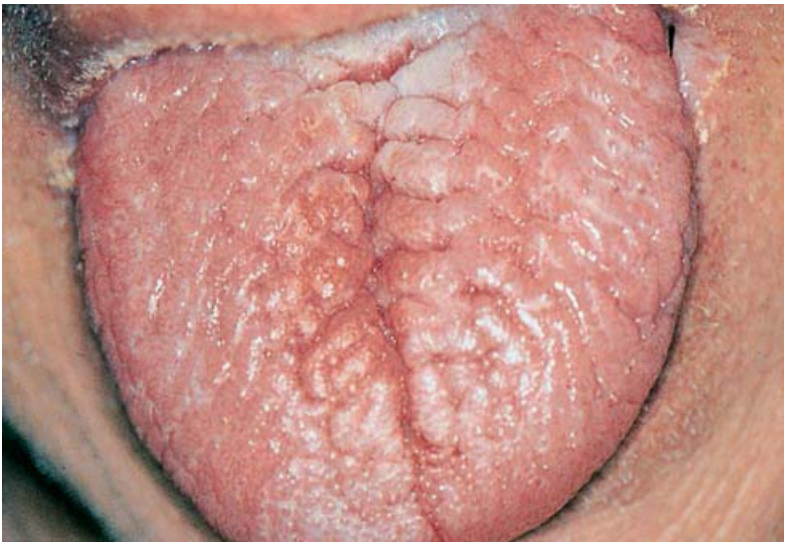


Fig. 336 Sjögren syndrome: dry and lobulated tongue.

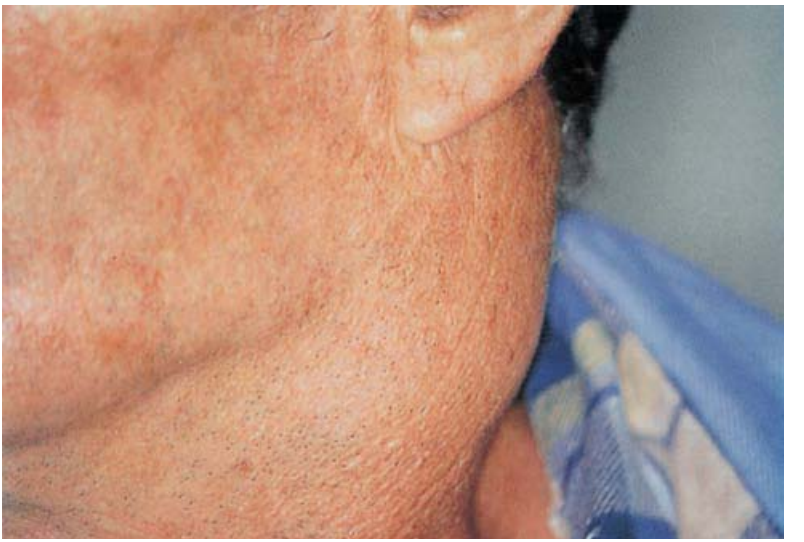


Fig. 337 Hodgkin disease: swelling of the cervical lymph nodes.

Metastatic Carcinoma in the Lymph Nodes

Metastases of oral squamous-cell carcinoma are a relatively common phenomenon and mainly occur in the regional cervical lymph nodes, via the lymphatic vessels. It has been estimated that approximately 30–50% of patients with oral carcinoma present at diagnosis with cervical metastases. The submandibular and jugular nodes are more frequently affected. Clinically, the metastases are not tender, and are usually firm, fixed, and swelling (Fig. **338**). The metastatic deposits are usually lateral, and rarely bilateral.

Differential diagnosis Submandibular sialadenitis, Hodgkin disease, leukemia, tuberculosis, syphilis, infectious mononucleosis.

Treatment See squamous-cell carcinoma, p. 172.

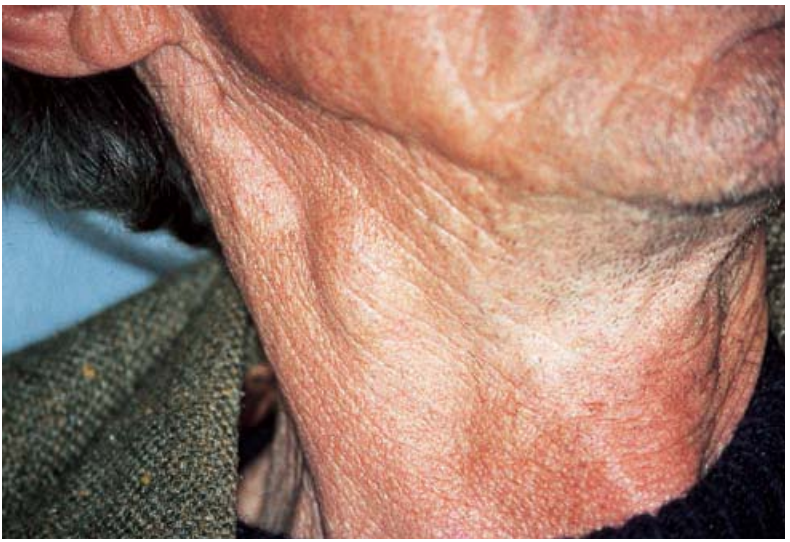
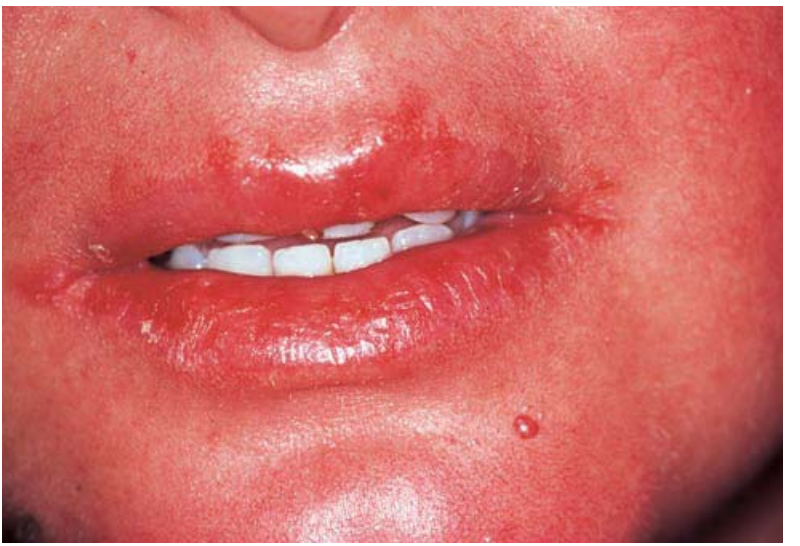


Fig. 338 Metastatic cervical lymph-node swelling from a posterior lateral squamous-cell carcinoma of the tongue.

12 Lip Lesions

Disorders that exclusively affect the lips, systemic diseases that produce characteristic lip lesions, and some other entities are included in this group. In some of them, the diagnosis should be made on the basis of clinical criteria, but histopathological confirmation of the diagnosis is always necessary.

- Cheilitis glandularis
- Cheilitis granulomatosa
- Melkersson–Rosenthal syndrome
- Exfoliative cheilitis
- Contact cheilitis
- Actinic cheilitis
- Angular cheilitis
- Lip-licking dermatitis
- Median lip fissure
- Angioneurotic edema
- Lymphedema due to radiation
- Systemic diseases (Crohn disease, sarcoidosis, tuberculosis, cystic fibrosis)



Cheilitis Glandularis

Definition Cheilitis glandularis is an uncommon chronic inflammatory condition of the minor salivary glands, characteristically affecting the lower lip.

Etiology Unknown.

Clinical features It presents as a swelling of the lower lip due to hyperplasia and inflammation of the glands (Fig. **339**). Characteristically, the orifices of the salivary glands are dilated, and pressure on the lip may produce mucous or mucopustular fluid from the ductal openings. Crusting and erosions may also occur.

Laboratory tests Histopathological examination.

Differential diagnosis Cheilitis granulomatosa, Melkersson–Rosenthal syndrome, Crohn disease, sarcoidosis, cystic fibrosis.

Treatment Supportive. Vermilionectomy only in severe cases.

Cheilitis Granulomatosa

Definition Cheilitis granulomatosa is a rare chronic disorder of the lips.

Etiology Unknown.

Clinical features It presents as a painless, persistent, and diffuse swelling of one or both lips (Fig. **340**). Small vesicles, erosions, and scaling may occur. It is thought that cheilitis granulomatosa is a monosymptomatic form of Melkersson–Rosenthal syndrome.

Laboratory tests Histopathological examination.

Differential diagnosis Cheilitis glandularis, Crohn disease, sarcoidosis, cystic fibrosis, lymphangioma, angioneurotic edema.

Treatment Topical or systemic steroids, tetracyclines. Plastic surgery in severe cases.

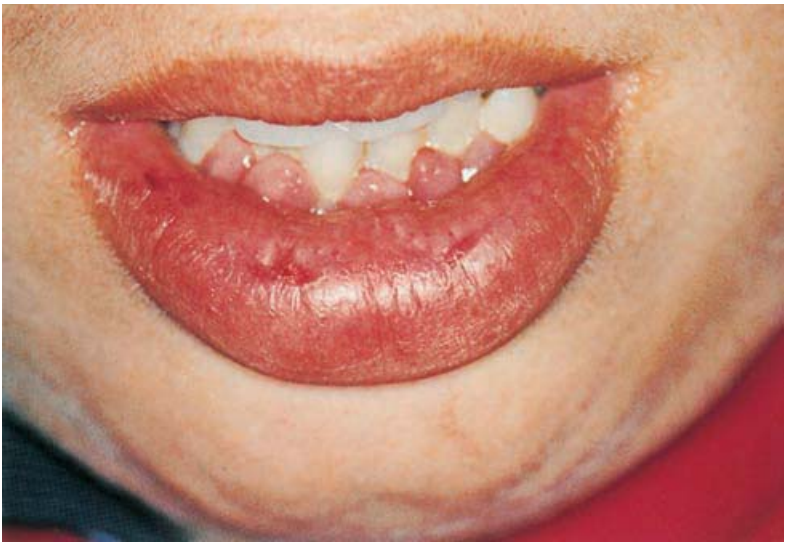


Fig. 339 Cheilitis glandularis.

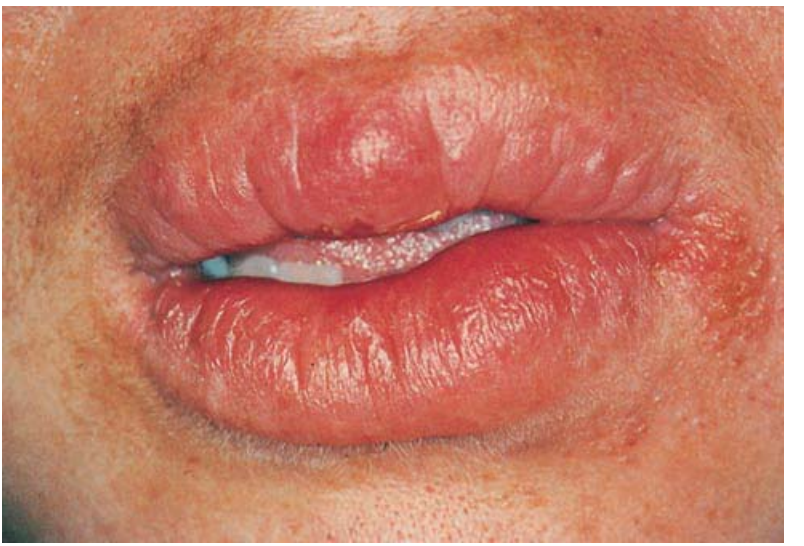


Fig. 340 Cheilitis granulomatosa.

Melkersson–Rosenthal Syndrome

Melkersson–Rosenthal syndrome is a rare disorder characterized by cheilitis granulomatosa, facial paralysis, fissured tongue, and less often intraoral and facial edema (Fig. **341**). The term "orofacial granulomatosis" has recently been proposed to include conditions and diseases characterized by granulomatous inflammation in the oral and facial area (cheilitis granulomatosa, Melkersson–Rosenthal syndrome, Crohn disease, sarcoidosis). The differential diagnosis and treatment are identical to those of cheilitis granulomatosa.

Exfoliative Cheilitis

Definition Exfoliative cheilitis is a chronic inflammatory disorder of the lips.

Etiology Unknown.

Clinical features It is characterized by scaling, crusting, and erythema of the vermilion border of the lips. This pattern is repetitive, resulting in yellowish, hyperkeratotic thickening, crusting, and fissuring (Fig. **342**). The lesions are more common in young women, usually persist with variable severity for months or years, and may cause cosmetic problems. The diagnosis is based on the clinical findings.

Differential diagnosis Contact cheilitis, actinic cheilitis.

Treatment Symptomatic. Topical moistening agents and steroids may be helpful. Topical ointment of tacrolimus 0.1% may be helpful.

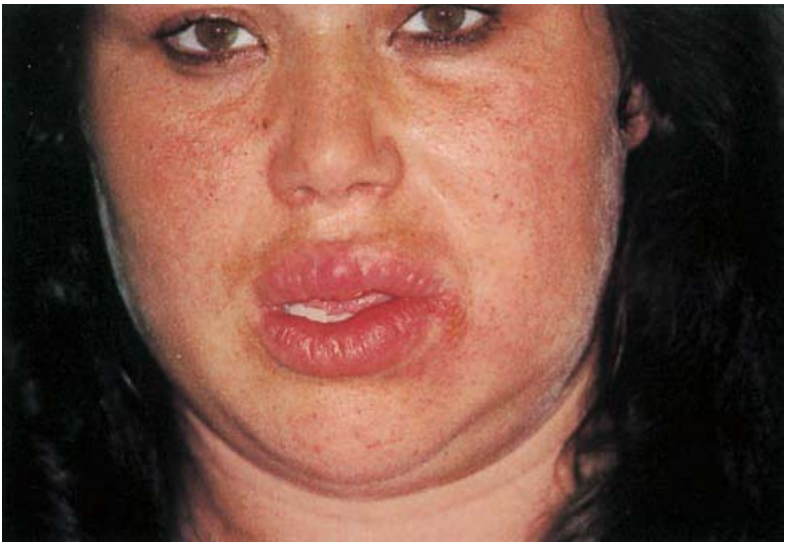


Fig. 341 Melkersson–Rosenthal syndrome: swelling of the lips and face.

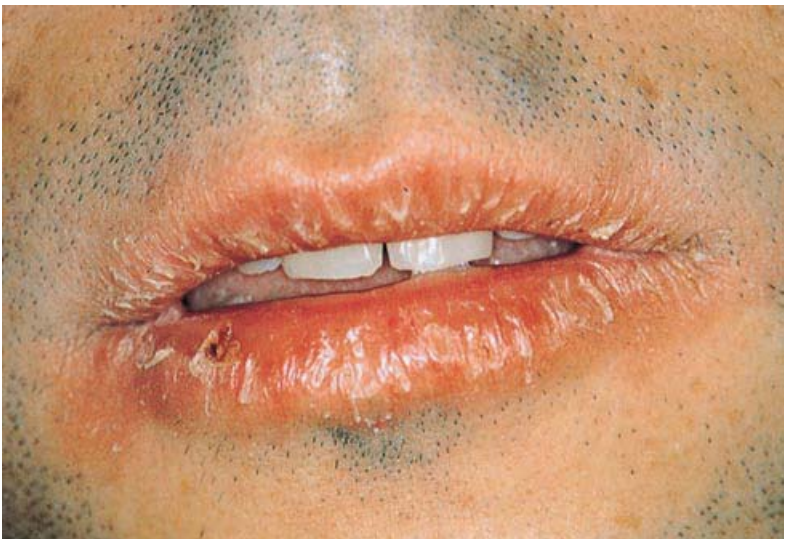


Fig. 342 Exfoliative cheilitis.

Contact Cheilitis

Definition Contact cheilitis is an acute inflammatory disorder of the lips.

Etiology Topical contact with various chemical agents.

Clinical features It is characterized by mild edema and erythema, followed by irritation and thick scaling (Fig. **343**). It is usually confined to the vermilion border of both lips. The diagnosis is based on clinical criteria and a skin patch test.

Differential diagnosis Exfoliative cheilitis, plasma-cell cheilitis.

Treatment Discontinuation of contact with chemicals; topical steroids.

Actinic Cheilitis

Definition Actinic cheilitis is a chronic degenerative disorder of the lower lip.

Etiology Long-term exposure to sunlight.

Clinical features In the early stage, mild erythema and edema followed by dryness and fine scaling of the lower lip vermilion border are the presenting signs. As the lesion progresses, the epithelium becomes thin and smooth, with small whitish-gray areas intermingled with red regions and scaly formations (Fig. **344**). Erosions and tiny nodules may develop. The lesion is premalignant, and usually occurs in men over 50 years of age.

Laboratory tests Histopathological examination.

Differential diagnosis Leukoplakia, lichen planus, lupus erythematosus, early squamous-cell carcinoma, cheilitis due to radiation.

Treatment Protection of lips from sunlight. Vermilionectomy in severe cases.

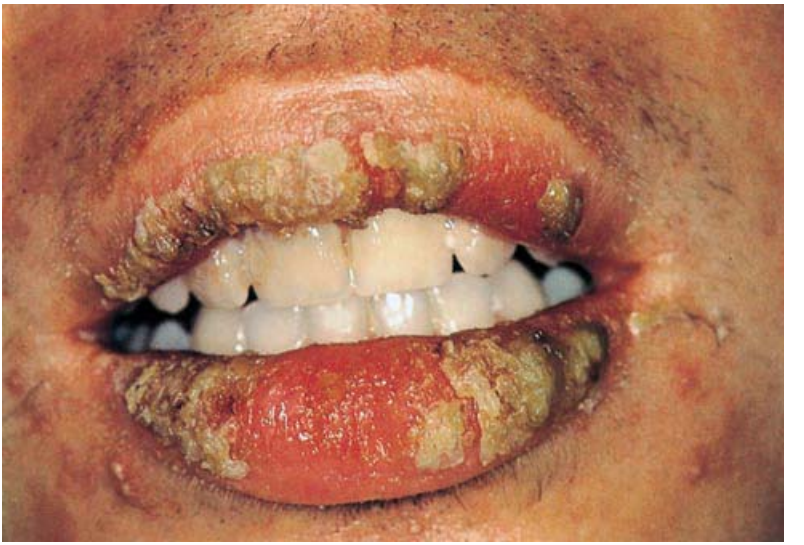


Fig. 343 Contact cheilitis.

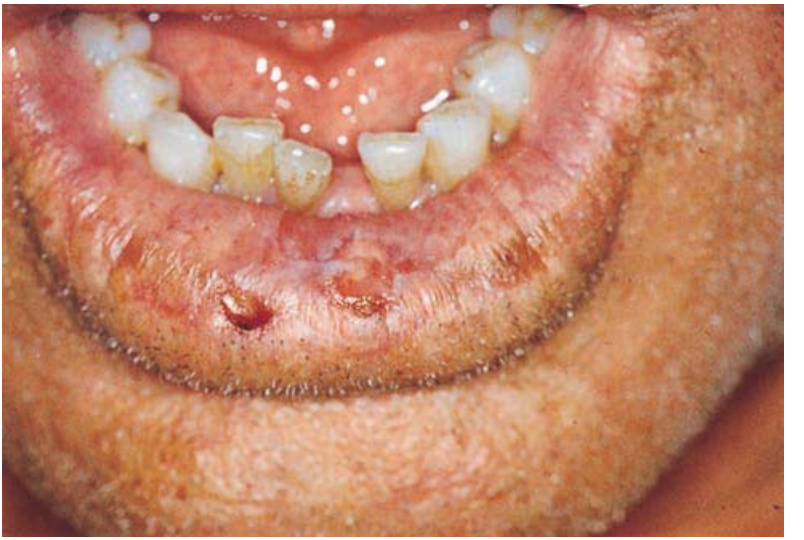


Fig. 344 Actinic cheilitis.

Angular Cheilitis

Definition Angular cheilitis, or perlèche, is a common disorder of the angles of the mouth.

Etiology Reduced vertical dimension, mechanical trauma, *Candida albicans*, *staphylococci*, *streptococci*, iron-deficiency anemia, riboflavin deficiency.

Clinical features The condition is characterized by erythema, maceration, fissuring, erosions, and crusting at the commissures (Figs. **345**, **346**, **347**). Classically, the lesions do not extend beyond the mucocutaneous border. A burning sensation and a feeling of dryness may occur. Remissions and exacerbations are common. The diagnosis is based on the clinical findings.

Treatment Correction of the occlusal vertical dimension, topical steroids, and antifungal ointments.

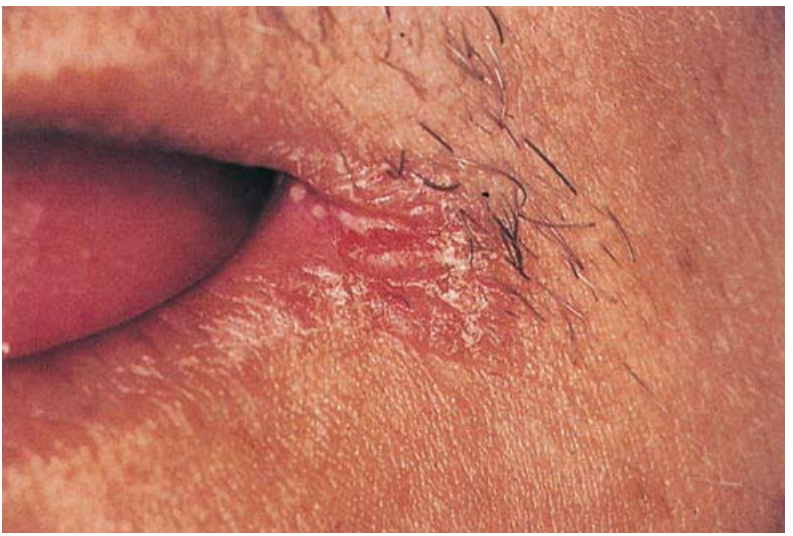


Fig. 345 Angular cheilitis.

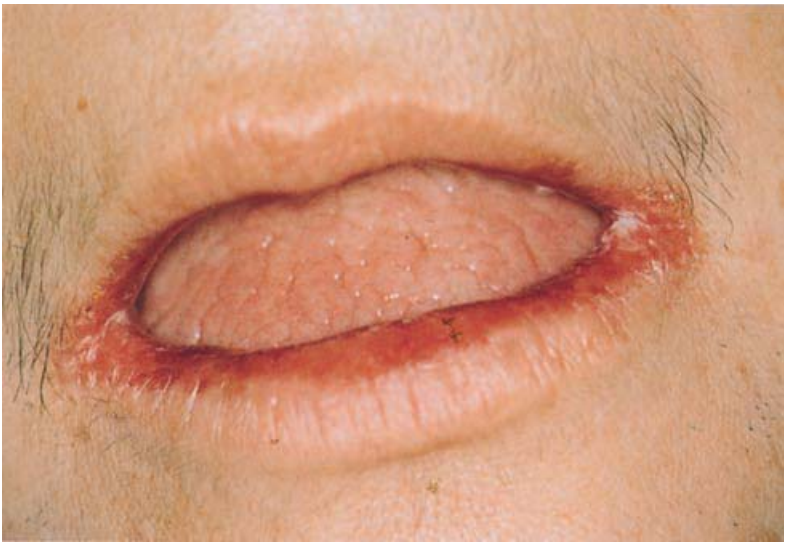


Fig. 346 Angular cheilitis.

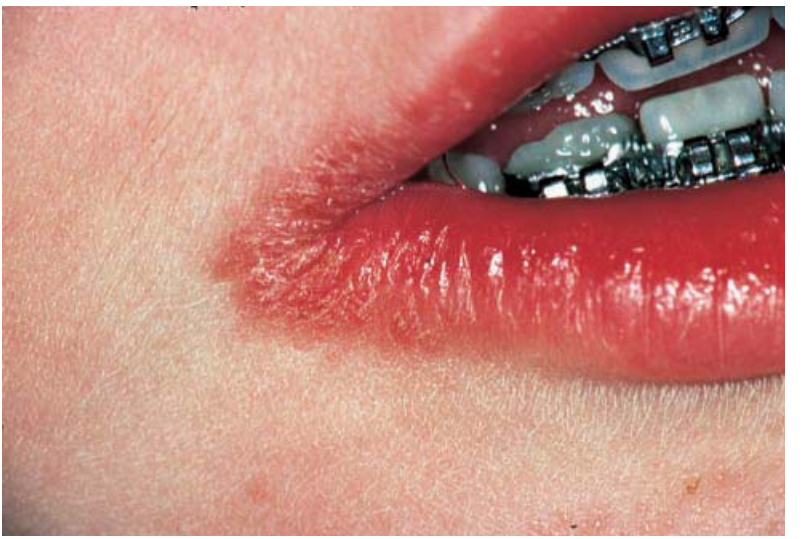


Fig. 347 Angular cheilitis.

Lip-Licking Dermatitis

Definition Lip-licking dermatitis is an irritant contact condition that most commonly occurs in children.

Etiology Chronic licking.

Clinical features The lips and the perioral skin are erythematous, associated with scaling, crusting, and fissuring of variable severity (Fig. **348**). A burning sensation is a common symptom. The diagnosis is based on the clinical findings.

Differential diagnosis Perioral dermatitis, contact cheilitis, and dermatitis.

Treatment Elimination of licking. Topical steroids and tacrolimus ointment.

Median Lip Fissure

Definition Median lip fissure is a relatively rare disorder that may appear in the lower or upper lip.

Etiology Unclear.

Clinical features It presents as a deep, inflammatory, persistent vertical fissure at the middle of the lip, usually infected by *Candida albicans* and bacteria (Fig. **349**). Spontaneous bleeding, discomfort, and pain are common. The diagnosis is based on the clinical findings.

Treatment Topical steroids with or without antifungal agents and antibiotics. Plastic reconstruction in severe cases.

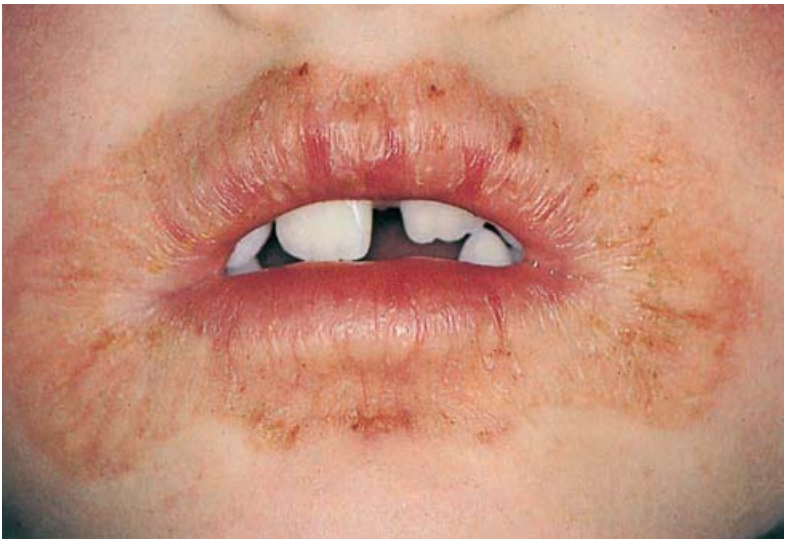


Fig. 348 Lip-licking dermatitis: erythema associated with scaling, crusting, and fissuring.

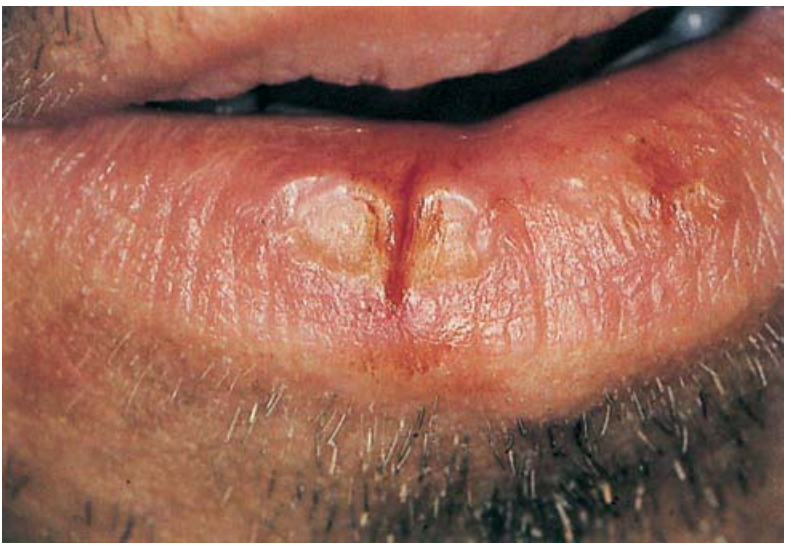


Fig. 349 Median deep vertical fissure of the lower lip.

Angioneurotic Edema

Definition Angioneurotic edema is a relatively common allergic disorder.

Etiology Inherited or acquired (food allergy, chemicals, infections, stress).

Clinical features It characteristically has a sudden onset, and lasts for 24–48 hours. The lesion presents as a painless, smooth swelling of the lips (Fig. **350**). Other intraoral regions and the glottis may also be involved. The diagnosis is usually based on the clinical findings.

Differential diagnosis Cheilitis granulomatosa, emphysema, cellulitis.

Treatment Antihistamines, systemic steroids.

Lymphedema due to Radiation

Radiation therapy for oral and other head and neck malignancies is common. The side effects on the oral mucosa after radiation mainly depend on the dose and duration of the treatment. Lymphedema of the lips may occur. It presents clinically as a painless, erythematous swelling (Fig. **351**).

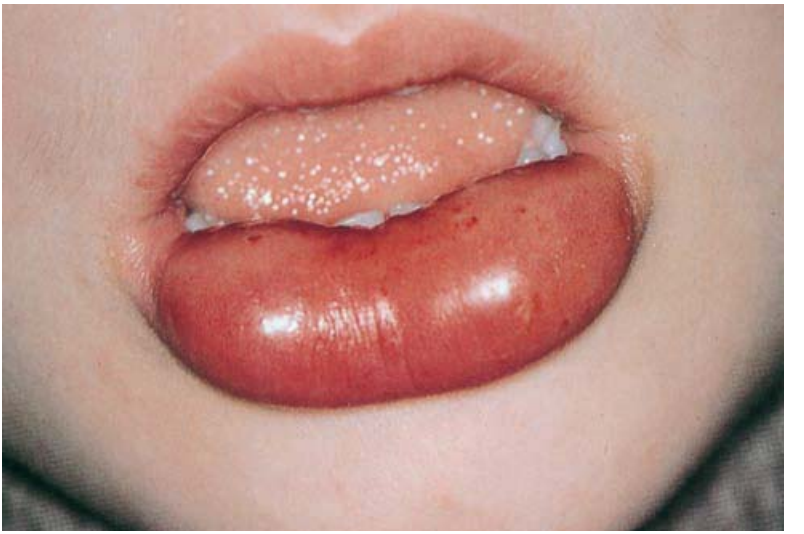


Fig. 350 Angioneurotic edema: swelling of the lower lip.

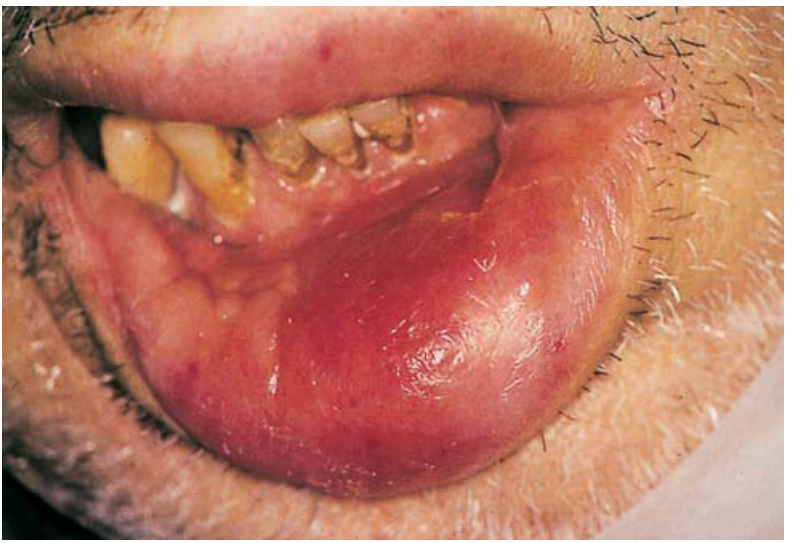


Fig. 351 Lymphedema of the lower lip after radiotherapy.

Systemic Diseases

Some systemic diseases with oral manifestations may produce lip swelling. Crohn disease, sarcoidosis, tuberculosis, and cystic fibrosis are the more common conditions in this group.

Crohn disease is a chronic inflammatory, probably immunologically mediated, condition primarily involving the ileum and other parts of the gastrointestinal tract. Lip swelling is one of the most common oral manifestations of the disease (Figs. **352**, **353**). Nodular or diffuse soft swelling, a cobblestone appearance of the mucosa, mucosal tag lesions, ulcers, angular cheilitis, and aphthouslike ulcerations may also occur.

Sarcoidosis is a systemic granulomatous disease affecting the lungs, lymph nodes, spleen, liver, central nervous system, bones, oral mucosa, and salivary glands (see also p. 332). The mouth is rarely involved. Lip swelling may occur (Fig. **354**). Red oral mucosal nodules, with or without ulceration, may also be seen.

Tuberculosis (see p. 154) may rarely produce inflammatory lip swelling.

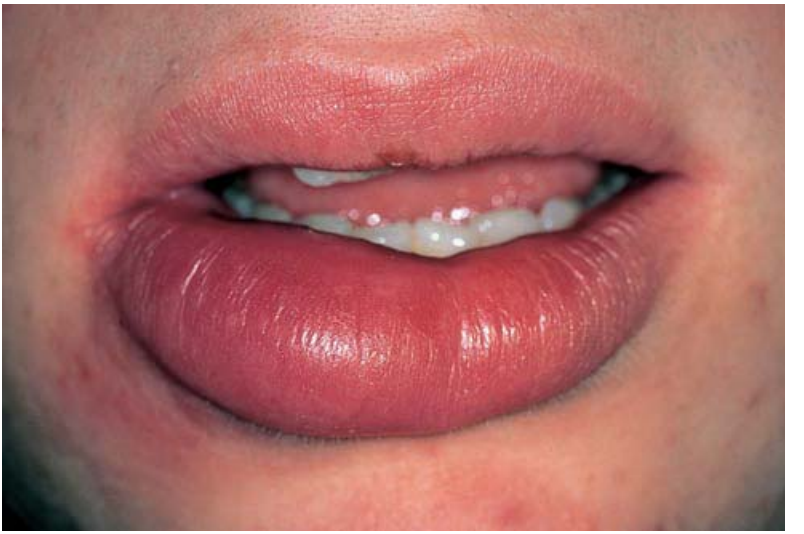


Fig. 352 Crohn disease, lip swelling.

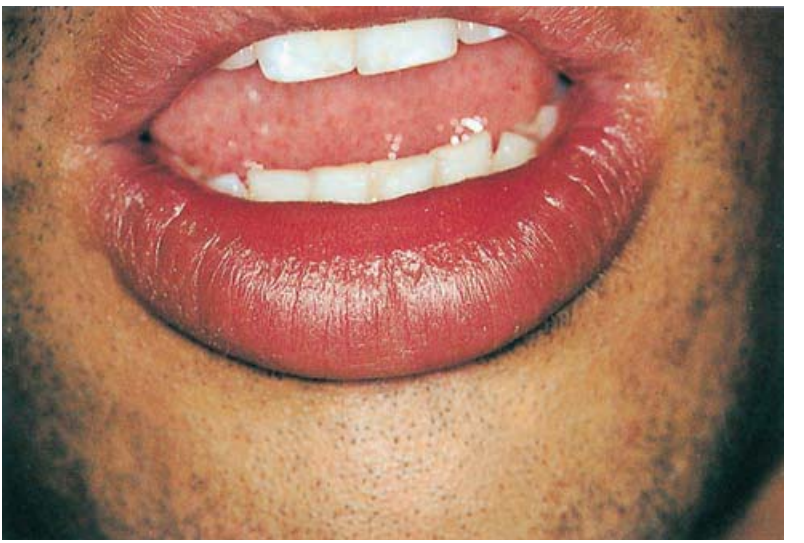


Fig. 353 Crohn disease: lip swelling.

Cystic fibrosis is a relatively common multisystemic, life-threatening, inherited disorder (one in 2000 births) caused by a defective gene on chromosome 7. The disease is characterized by dysfunction of the exocrine glands (pancreas, branchial, tracheal, gastrointestinal tract, and sweat glands). The salivary glands may also be affected. Lip swelling, gingivitis, and dryness are the more frequent oral findings (Fig. **355**). The principal manifestations are chronic pulmonary infections, pancreatic insufficiency, cirrhosis, malabsorption, abdominal pain, skeletal disorders, skin wrinkling, and sweating with characteristic salty taste. The clinical diagnosis should be confirmed by laboratory tests.

Laboratory tests Increased chloride and sodium ion levels in sweat, absence of pancreatic enzymes in the intestinal fluid, chest radiography, and histopathological examination of the minor salivary glands.

Differential diagnosis Lipoid proteinosis, mucopolysaccharidosis, cheilitis granulomatosa, cheilitis glandularis.

Treatment Treatment should be left to the specialist pediatrician.

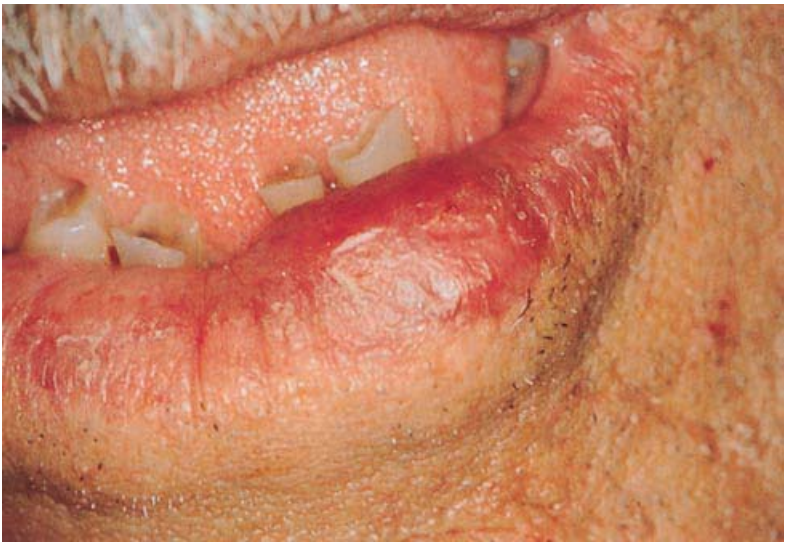


Fig. 354 Sarcoidosis: large red nodule on the lower lip.

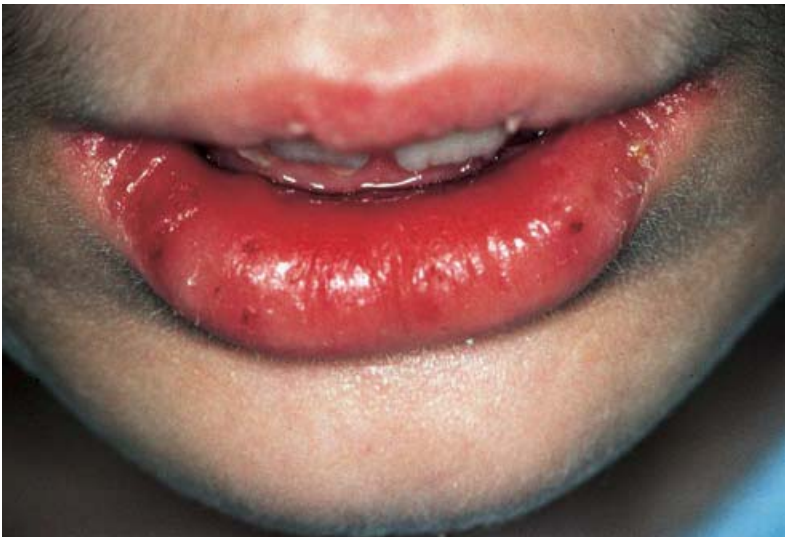


Fig. 355 Lower lip swelling in a 12-year-old girl with cystic fibrosis.

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