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EROSIVE AND ULCERATIVE LESIONS OF ORAL MUCOSA

Minsk BSMU 2021

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
2-я КАФЕДРА ТЕРАПЕВТИЧЕСКОЙ СТОМАТОЛОГИИ

Л. Н. Полянская, И. А. Захарова

ЭРОЗИВНО-ЯЗВЕННЫЕ ПОРАЖЕНИЯ СЛИЗИСТОЙ ОБОЛОЧКИ ПОЛОСТИ РТА

EROSIVE AND ULCERATIVE LESIONS OF ORAL MUCOSA

Учебно-методическое пособие

Минск БГМУ 2021

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Рассмотрены клинические проявления, подходы к дифференциальной диагностике и лечению эрозивно-язвенных поражений слизистой оболочки полости рта.

Предназначено для студентов 5-го курса медицинского факультета иностранных учащихся, обучающихся на английском языке по специальности «Стоматология».

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MOTIVATIONAL CHARACTERISTIC OF THE THEME

Total time: 70–90 minutes (seminar).

Erosive and ulcerative lesions of the oral cavity are common. Assessment of the nature of oral ulcers requires a thorough history of the present illness. Certain ulcerations occur in multiples, and many are recurrent. Signs and symptoms relative to general health with review of organ systems will point to a diagnosis of certain systematic problems that can manifest oral ulceration.

The purpose of the seminar: to integrate knowledge about the basic principles of diagnosis and treatment of erosive and ulcerative lesions of oral mucosa.

The tasks of the seminar. The student should know:

1. The scheme of the clinical examination of the patient with oral mucosa disease.
2. Description sequence and characteristic features of oral mucosa lesions.
3. Additional methods of examination and laboratory diagnosis of oral mucosa diseases.
4. Principles of differential diagnosis of erosive and ulcerative lesions of oral mucosa.
5. Basic principles and methods of treatment of patients with the diseases of oral mucosa. Groups of medicines.

Requirements for the initial level of knowledge. For full understanding of the topic the student must revise:

– human anatomy: anatomical features of oral mucosa;

– histology, cytology, embryology: morphological structure of oral mucosa;

– therapeutic dentistry: dental examination, basic and additional methods, types of oral mucosa lesions.

Control questions from related disciplines:

1. Anatomical and histological structure of oral mucosa.
2. Classification and characteristics of oral mucosal lesions.
3. Cytological, histological, microbiological, allergic, biochemical methods of examination.

Control questions for the seminar:

1. Classification of oral mucosa diseases (WHO).
2. Methods of examination in patients with oral mucosa diseases.
3. Diagnosis and clinical features of erosive and ulcerative lesions of oral mucosa.
4. Differential diagnosis of erosive and ulcerative lesions.
5. Contemporary principles of treatment of erosive and ulcerative lesions of oral mucosa.

EROSIVE AND ULCERATIVE LESIONS

It is prudent to distinguish an ulcer from an erosion. An *erosion* is the superficial destruction of the epithelial covering of the mucosa by inflammation or trauma. In contrast, an *ulcer* is a break in the skin or the mucous membrane with loss of surface tissue, and disintegration of epithelial tissue. These are well-circumscribed, sometimes depressed lesions with an epithelial defect that is covered by a fibrin clot, resulting in a yellow-white appearance. The nature of the ulcer itself is vitally important when a definitive diagnosis is pursued. One should always remember that oral vesiculobullous diseases are subject to trauma, with loss of the characteristic vesicular nature of the lesions clinically. For this reason, the patient should be questioned concerning the nature of the lesions at their outset, and attempts should be made to search for an intact vesicle. If the ulcerations prove to be, or to have been, vesiculobullous, refer the patient for discussion of vesiculobullous diseases. In this section, only diseases that begin as ulcers are considered.

Here is a **fragment of the International Classification of Diseases (ICD-DA 1995, WHO)**, which are manifested by erosive and ulcerative lesions:

Section I. Certain infectious or parasitic diseases

Tuberculosis (A 18–22)

A 18 Tuberculosis of other organs

A 18.8 Tuberculosis of other specified organs

A 18.8X Mouth

Infections with a predominantly sexual mode of transmission (A 50–58)

A 51 Early syphilis

A 51.2 Primary syphilis of other sites

A 51.2X Oral manifestations

A 51.3 Secondary syphilis of skin and mucous membranes

A 51.3X Oral manifestations

Other spirochaetal diseases (A 65–69)

A 69 Other spirochaetal infections

A 69.0 Necrotizing ulcerative stomatitis

A 69.1 Other Vincent's infections

A 69.10 Acute necrotizing ulcerative gingivitis [fusospirochaetal gingivitis] [Vincent's gingivitis]

A 69.11 Vincent's angina

Section II Neoplasms

Malignant neoplasms of lymphoid, haematopoietic and related tissue (C 81–96)

C 91–95 Leukaemia. Oral manifestations

Malignant neoplasms of lip, oral cavity and pharynx (C 00–14)

Section XI. Diseases of the digestive system

Stomatitis and related lesions (K 12)

K12.0 Recurrent oral aphthae

K12.00 Recurrent (minor) aphthae [Aphthous stomatitis; Canker sore; Mikulicz' aphthae; Minor aphthae; Recurrent aphthous ulcer]

K12.01 Periadenitis mucosa necrotica recurrens [Cicatrizing aphthous stomatitis; Major aphthae; Sutton's aphthae]

K12.02 Stomatitis herpetiformis [herpetiform eruption]
Excludes: dermatitis herpetiformis (L 13.OX)
herpesviral gingivostomatitis (B00.2X)

K12.03 Bednar's aphthae

K12.04 Traumatic ulcer
Excludes: traumatic ulcer of tongue (K 14.01)
ulcers of tongue NOS (K 14.09)

K12.08 Other specified recurrent oral aphthae

K12.09 Recurrent oral aphthae, unspecified

APHTHOUS ULCERS

Definition. Recurrent aphthous stomatitis (RAS) is a common disorder characterized by recurring ulcers confined to the oral mucosa in patients with no other signs of systemic disease. Of all the types of nontraumatic ulceration that affect oral mucosa, aphthous ulcers (canker sores) are probably the most common. The incidence ranges from 20 % to 60 %, depending on the population studied. Prevalence tends to be higher in professional, or white collar, individuals, upper socioeconomic groups, and nonsmokers.

Etiology. Although the cause of aphthous ulcerations is unknown, several possibilities have been postulated.

There have been theories suggesting a link between RAS and a number of microbial agents but there are presently no conclusive data linking RAS to a specific microorganism.

There is considerable evidence that aphthous ulcers are related to a focal immune dysfunction in which T lymphocytes play a significant role. The nature of the initiating stimulus remains a mystery. The causative agent could be endogenous (autoimmune) antigen or exogenous (hyperimmune) antigen, or it could be a nonspecific factor, such as trauma in which chemical mediators may be involved.

Deficiencies of vitamin B_{12}, folic acid, and iron as measured in serum have been found only in a small percentage of patients with aphthous ulcers.

Other causes of aphthous ulcers that have been investigated include hormonal alterations, stress, trauma, and food allergies. None of these is seriously regarded as being important in the primary causation of aphthous ulcers, although any of them may have a modifying or triggering role.

The best documented factor is heredity. Over 40 % of affected patients have a first-degree relative who is also affected by aphthous ulcers. A 90 % degree of risk is present when both parents are affected.

Clinical features. Three forms of aphthous ulcers have been recognized: minor, major, and herpetiform aphthous ulcers (Table 1). All are believed to be a part of the same disease spectrum, and all are believed to have a common etiology. Differences are essentially clinical and correspond to the degree of severity. All forms present as painful recurrent ulcers. Patients occasionally have prodromal symptoms of tingling or burning before the appearance of lesions. The ulcers are not preceded by vesicles and characteristically appear on the vestibular and buccal mucosa, tongue, soft palate, fauces, and floor of the mouth.

Table 1

Aphthous Ulcers: Clinical Features

Feature	Minor aphthae	Major aphthae	Herpetiform aphthae
Size	< 1 cm	> 1 cm	0.5–2 mm
Shape	oval, well demarcated	ragged oval, crateriform	round and well-defined; may coalesce to form an irregular outline
Color	yellow/gray base with thin erythematous border	yellow/gray base	yellow with marked periulcer erythema
Number	1–5	1–3	10–100
Location	nonkeratinized mucosa	nonkeratinized mucosa	any intraoral site
Healing	no scarring	heal with scarring	no scarring
Treatment	topical corticosteroids, tetracycline mouth rinse	topical/systemic/intralesional corticosteroids, immunosuppressives	topical/systemic corticosteroids, tetracycline mouth rinse

MINOR APHTHOUS ULCERS

Minor aphthous ulcers are the most commonly encountered form. This type usually appears as a single, painful, oval ulcer that is less than 1 cm in diameter, covered by a yellow fibrinous membrane and surrounded by an erythematous halo (Fig. 1, 2).

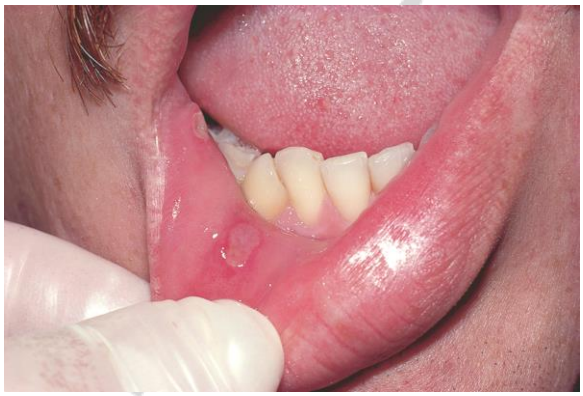

Figure 1. Minor aphthous ulcer of the lip

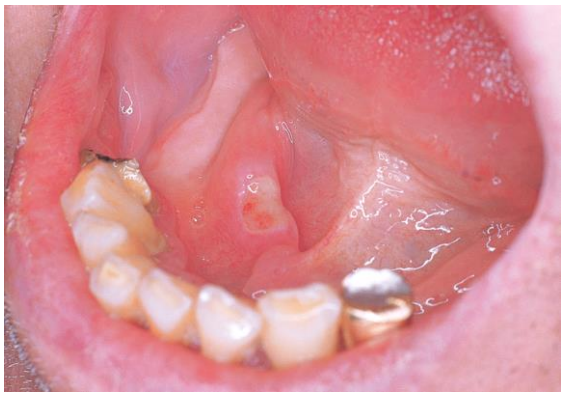

Figure 2. Minor aphthous ulcer of the floor of the mouth

These ulcers can cause considerable pain and may interfere with eating, speaking and swallowing. The individual lesions are shallow, but no tissue tags are present from ruptured vesicles, which helps distinguish RAS from diseases that start as vesicles. Healing without scarring is spontaneous and usually complete in 10–14 days. Recurrences vary from one individual to another.

MAJOR APHTHOUS ULCERS

Major aphthous ulcers were previously thought to be a separate entity, and this form was referred to as periadenitis mucosa necrotica recurrens or Sutton's disease. It is now regarded as the most severe expression of aphthous stomatitis. Lesions are larger (> 1 cm) and more painful and persist longer than minor aphthae (Fig. 3). Because of the depth of inflammation, major aphthous ulcers clinically appear crateriform and heal with scar formation that may result in decreased mobility of the uvula and tongue. Lesions may take as long as 6 weeks to heal, and as soon as one ulcer disappears, another one starts. In patients who experience an unremitting course with significant pain and discomfort, systemic health may be compromised because of difficulty in eating and psychological stress.

HERPETIFORM APHTHOUS ULCERS

Herpetiform aphthous ulcers present clinically as recurrent crops of small ulcers (Fig. 4). Although movable mucosa is predominantly affected, palatal and gingival mucosa may also be involved. Pain may be considerable, and healing generally occurs in 1 to 2 weeks. Unlike herpes infection, herpetiform aphthous ulcers are not preceded by vesicles and exhibit no virus-infected cells.

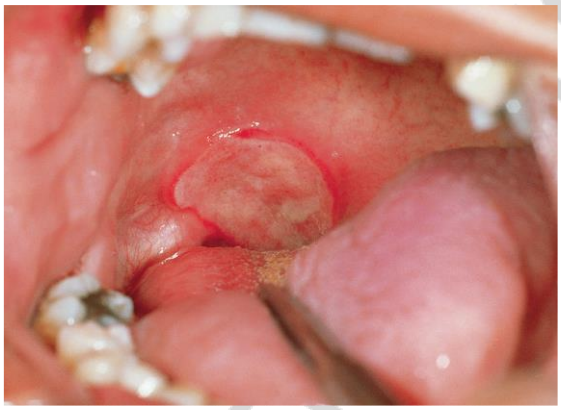

Figure 3. Major aphthous ulcer of the lip

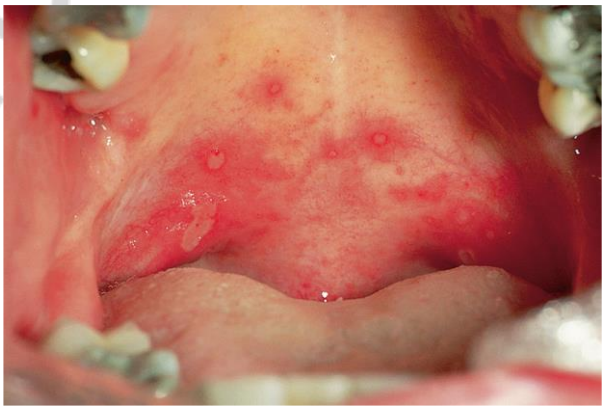

Figure 4. Herpetiform aphthous ulcers

Diagnosis. Diagnosis of aphthous ulcers is generally based on the history and clinical appearance. Because the diagnosis of these ulcers is usually evident clinically, biopsies usually are unnecessary and therefore are only indicated for exclusion of other diseases. Aphthous ulcers have nonspecific microscopic findings, and no histologic features are diagnostic.

Differential diagnosis. Lesions of secondary (recurrent) oral herpes are often confused with, but usually can be distinguished from, aphthous ulcers (Table 2). A history of vesicles preceding ulcers, location on the attached gingiva and hard palate, and crops of lesions indicate herpetic rather than aphthous ulcers.

Table 2

Aphthous Ulcers vs. Secondary Herpes Simplex Infection

Feature	Aphthous ulcers	Herpes infection
Cause	Immune dysfunction	HSV1
Triggers	Stress, trauma, diet, hormones, depressed immunity	Stress, trauma, ultraviolet light, depressed immunity
Prodrome	Little prodrome	Prodromal symptoms
Appearance	Nonspecific microscopy	Viral cytopathic changes
	No vesicles	Vesicles precede ulcers
	Single, oval ulcer	Multiple, confluent ulcers
Sites	Nonkeratinized mucosa	Keratinized mucosa
Treatment	Corticosteroids, tetracycline	Antiviral treatment

Other painful oral ulcerative conditions that may simulate the various forms of aphthous ulcers include trauma, pemphigus vulgaris, mucous membrane pemphigoid, and neutropenia.

In some patients with recalcitrant aphthae, a diagnosis of Crohn's disease may be considered. This granulomatous disease may affect the gastrointestinal tract from mouth to anus. Oral manifestations include mucosal fissures and small, multiple, hyperplastic nodules on the buccal mucosa, producing a cobblestone appearance. Biopsy findings of these mucosal nodules show small, noncaseating granulomas characteristic of Crohn's disease.

Behçet's syndrome should also be investigated because oral lesions in that disease are indistinguishable from aphthae. Behçet's is a form of vasculitis that includes genital ulceration, ocular lesions, artritis, erythema nodosum (painful purplish nodules with peripheral halo) and skin rashes.

Patients with severe minor aphthae or major aphthous ulcers should be investigated for systemic disorders, including connective tissue diseases and hematologic abnormalities, such as reduced levels of serum iron, folate, vitamin B12 and ferritin.

Treatment. In patients with occasional or few minor aphthous ulcers, usually no treatment is needed apart from a bland mouth rinse such as sodium bicarbonate in warm water to keep the mouth clean. In mild cases with two or three small lesions, use of a protective emollient such as Orabase™ often alleviates pain and facilitates healing. Pain relief of minor lesions can be effected with a topical anesthetic agent such as benzocaine or lidocaine.

In more severe cases, the use of a high-potency topical steroid preparation, such as fluocinonide, betamethasone, or clobetasol, placed directly on the lesion,

shortens healing time and reduces the size of the ulcers. The steroid gel should be applied directly to the lesion after meals and at bedtime two to three times a day or mixed with an adhesive such as Orabase™ prior to application. Larger lesions can be treated by placing a gauze sponge containing the topical steroid on the ulcer and leaving it in place for 15–30 minutes to allow for longer contact of the medication.

Tetracycline or doxycycline suspensions, used topically, often produce excellent results. In addition to their antibacterial effect of keeping the mouth clean, tetracyclines speed resolution of the ulcers. A typical regimen for treating aphthous ulcers consists of emptying a 250-mg capsule of tetracycline into 30 ml of warm water and then rinsing the mouth for several minutes. This is repeated up to 4 times a day for 4 days. Results are best if this mouth rinse is used on the first day that the ulcers appear, or when they are in a prodromal stage.

When patients with major aphthae or severe cases of multiple minor aphthae do not improve sufficiently with topical therapy, use of systemic therapy should be considered. Systemic steroids and immunosuppressive drugs may be used.

TRAUMATIC ULCERATIONS

Definition. Traumatic ulceration is an acute or chronic lesion caused by direct physical/mechanical, thermal, or chemical trauma when a cause-and-effect relationship is usually obvious.

Etiology. Acute bite injuries, an example of direct physical/mechanical trauma, occur often in regions that are readily trapped or abraded between the teeth, such as the lower lip, tongue, and buccal mucosa. They may be particularly severe if this occurs when the mucosa is numb after local anesthesia has been given for dental procedures. Traumatic injuries may also result from malocclusion, ill-fitting dental prostheses, overzealous toothbrushing and flossing, self-injurious habits, and oral piercings. Traumatic oral ulcers may also be iatrogenic, inadvertently induced by a health care practitioner during a diagnostic, surgical, or medical procedure.

Thermal injuries including electrical burns are infrequently seen in children who inadvertently chew on electrical wiring. More commonly, thermal burns occur on the palatal mucosa from ingesting hot foods and beverages. An iatrogenic cause of thermal injury is from a heated dental instrument inadvertently contacting the mucosa.

Chemicals may also cause oral ulcers because of their acidity or alkalinity, their ability to act as local irritants, or as contact allergens. These may be patient induced or iatrogenic. Aspirin burns are still seen, although they are increasingly less common. Many over-the-counter medications for toothache, aphthous ulcers, and denture-related injuries have the ability to damage the oral mucosa if used injudiciously. Dental cavity medications, especially those containing phenol, may cause iatrogenic oral ulcers. Acidic tooth-etching agents have been

associated with chemical burns of the mucosa. Endodontic and vital bleaching procedures, which use strong oxidizing agents such as 30 % hydrogen peroxide, have also produced burns.

Clinical features. Acute reactive ulcers of oral mucous membranes exhibit the clinical signs and symptoms of acute inflammation, including variable degrees of pain, redness, and swelling (Fig. 5, 6). The ulcers are covered by a yellow-white fibrinous exudate and are surrounded by an erythematous halo.

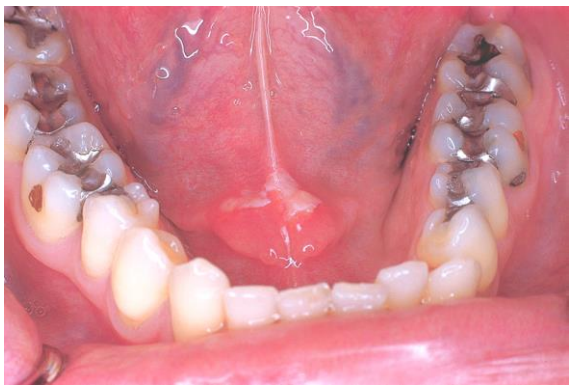

Figure 5. Acute ulcer of the floor of the mouth (saliva ejector injury)

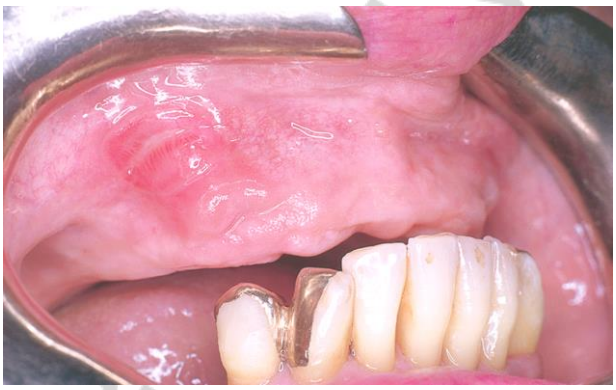

Figure 6. Ulcers and erythema caused by a denture flange

Chronic reactive ulcers may cause little or no pain. They are covered by a yellow membrane and are surrounded by elevated margins that may show hyperkeratosis (Fig. 7). Induration, often associated with these lesions, is due to the scar formation and chronic inflammatory cell infiltration.

Traumatic ulcers of the soft palate in the region of the pterygoid hamulus in infants have been referred to as Bednar's aphthae.

A particularly ominous-appearing, but benign chronic ulcer known as traumatic granuloma may be seen in association with a deep mucosal injury (Fig. 8). This crateriform ulcer may measure 1 to 2 cm in diameter, and healing may take several weeks to a few months. It is usually found in the tongue with an associated inflammatory infiltrate rich in eosinophils, histiocytes, and myofibroblasts.

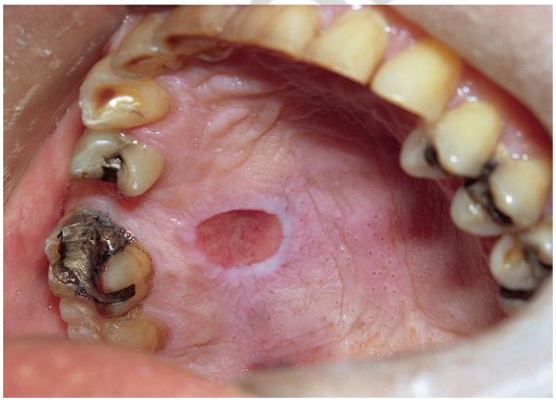

Figure 7. Chronic ulcer of the palate

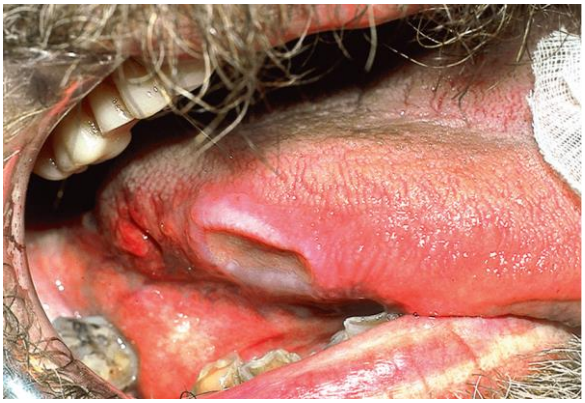

Figure 8. Traumatic granuloma of the tongue

Diagnosis. With acute reactive ulcers, the cause-and-effect relationship is usually apparent from the clinical examination and history. None is required if there is a clear history of injury to the site.

The cause of chronic reactive ulcers may not be as readily apparent. In some cases it can be determined by examining for flange overextension on dentures using pressure-indicating paste, or by checking for jagged or malposed cusps and restorations. Culture may be needed if the areas do not heal well or if suppuration develops, suggesting a secondary bacterial infection. A biopsy should be performed if the ulcer does not heal within a few weeks.

Differential diagnosis. Traumatic ulcers may be extensive and associated with tumefaction. In these patients, carcinoma, specific granulomatous inflammation, traumatic granuloma, and atypical histiocytic granuloma must be ruled out by biopsy. Infections (syphilis, tuberculosis, deep fungal infection) must also be considered.

Treatment. Avoidance of reinjury is important. Initially, most reactive ulcers may be observed, and having the patient use a bland mucolytic mouth rinse such as sodium bicarbonate in warm water, will help to keep the ulcer clean. Smaller lesions caused by less severe thermal or chemical injury heal on their own once the irritant is removed. Pain control can be achieved with topical anesthetics. If pain is considerable, topical treatment may be beneficial, like a topical corticosteroid. Healing of traumatic granuloma is spontaneous, but topical and intralesional steroids can accelerate healing and reduce symptoms. If the ulcer does not heal within a 2-week period, biopsy should be performed to establish the diagnosis and exclude neoplasia or infection.

NECROTIZING ULCERATIVE GINGIVITIS

Definition. Necrotizing ulcerative gingivitis (NUG) is an acute ulcerative-inflammatory condition of the gingiva that is associated with polymicrobial infection.

During World War I, NUG was dubbed “trench mouth” since it was frequent among the soldiers in the trenches.

Etiology. The infectious microorganisms associated with ANUG are anaerobic fusiform and spirochetal bacteria. The more important and constant of the microbes involved include *Treponema* species, *Prevotella intermedia*, *Fusobacterium nucleatum*, *Peptostreptococcus micros*, *Porphyromonas gingivalis*, *Selenomonas* species, and *Campylobacter*. In patients with HIV, candida and herpesvirus are also commonly present. Since some of these fusospirochetal organisms are common in the periodontal tissues, many believe that it is the permissive environment of an immunocompromised host that allows these microbes to proliferate. NUG has strong associations with immune suppression (especially AIDS), debilitation, smoking, stress, poor oral hygiene,

local trauma, and contaminated food supply. Diabetes may also be a risk factor. The tissue destruction is most probably a result of the production of endotoxins and/or immunologic activation and subsequent destruction of the gingiva and adjacent tissues. If there is underlying systemic illness, NUG can spread rapidly from the gingiva to the periodontium and into the soft tissues.

Clinical features. NUG may or may not be associated with fever and malaise, although submandibular lymphadenopathy is usually present. NUG has a rapid and acute onset. The first symptoms include excessive salivation, a metallic taste, and sensitivity of the gingiva. This rapidly develops into extremely painful and erythematous gingiva with scattered punched-out ulcerations, usually on the interdental papillae. The papillae are blunted, with necrotic craters showing a marginal zone of erythema (Fig. 9), although any part of the marginal gingiva may be affected. There is accompanying malodor, and there may be gingival bleeding. Because of the pain associated with the gingivitis, there is usually abundant buildup of dental plaque around the teeth because it may be too painful to perform effective oral hygiene. Uncommonly, ulcerations extend beyond the gingiva to include the palate and mucobuccal fold, where they may be extensive (Fig. 10).

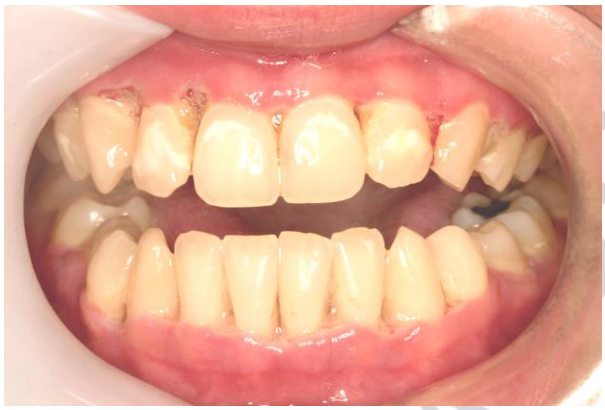

Figure 9. Necrotizing ulcerative gingivitis with typical punched out, necrotic and ulcerated interdental papillae

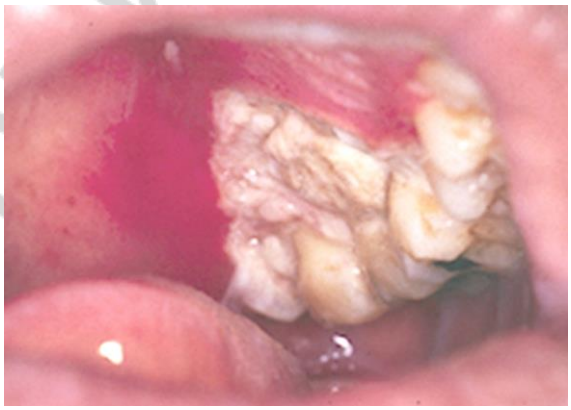

Figure 10. Necrotizing ulcerative periodontitis with osteonecrosis in a patient with AIDS

Diagnosis. Diagnosis is based on clinical features and microbiological examination. Smears and dark-field scrapings disclose the presence of fusiform and mobile spirochete bacterial forms. A biopsy is usually not helpful in making a diagnosis, although biopsies may be performed to rule out some other conditions that may have a similar clinical presentation. Tissue sections show nonspecific ulceration with superficial necrosis and a subacute inflammatory cell infiltrate.

Differential diagnosis. The acute onset of erythematous and ulcerated gingiva of NUG may suggest a diagnosis of primary herpetic gingivostomatitis, and this is readily ruled out with a culture. Desquamative gingivitis (caused by

lichen planus, mucous membrane pemphigoid, pemphigus vulgaris, and hypersensitivity reactions) may present primarily on the gingiva, with no skin findings. However, these conditions are not of acute onset but rather chronic and/or progressive over months and years and are characterized by inflammation rather than necrosis.

Neutropenic ulcers in patients on cancer chemotherapy may appear similar, leading to extensive ulceration and necrosis of the marginal gingiva and other mucosal surfaces.

Single large necrotic ulcers of noma suggest deep fungal infections or infections with the herpes family of viruses, especially in immunocompromised patients. Squamous cell carcinoma is also a consideration in this group of patients.

Treatment. This is directed towards supportive care and pain control, definitive treatment, and identification of underlying predisposing factors. Definitive treatment of NUG consists of gentle debridement to remove as much of the debris and plaque as possible; this is best accomplished with topical anesthesia during the first few visits. The use of chlorhexidine bigluconate mouthrinse leads to resolution in > 90 % of cases. Hydrogen peroxide rinses are also indicated. Patients with more extensive disease and/or systemic symptoms may require antibiotics active against gram-negative anaerobes, such as β-lactams. Interestingly, metronidazole, which has little activity against spirochetes, also is effective, suggesting that resolution can occur without treatment of the entire microbial complex. Once the acutely painful episodes have resolved, scaling and root planing to completely remove all residual plaque and calculus are indicated. Periodontal surgery may be necessary to correct gingival and periodontal defects.

SYPHILIS

Definition. Syphilis is a relatively common sexually transmitted disease caused by *Treponema pallidum.*

Etiology. *Treponema pallidum* is the spirochete bacteria. It is acquired by sexual contact with a partner with active lesions, by transfusion of infected blood, or by transplacental inoculation of the fetus by an infected mother (congenital syphilis).

Clinical features. When the disease is spread through direct contact, a hard ulcer, or chancre, forms at the site of spirochete entry, usually three weeks after the infection. Oral chancre appears in about 5–15 % of cases, and clinically presents as a painless ulcer with a smooth red, brown, or purple surface, rolled margins, raised borders, and an indurated base, firm to palpation (Fig. 11, 12). The lesion does not produce an exudate. Regional lymphadenopathy, typified by firm, painless, nonsuppurative swelling, is also a part of the clinical picture. The chancre heals spontaneously after several weeks without treatment, leaving the patient with no apparent signs of the disease.

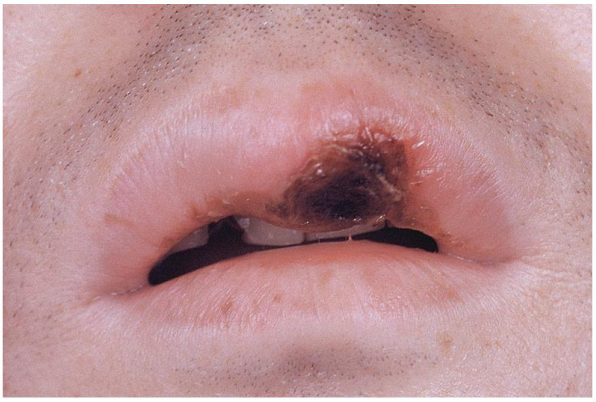

Figure 11. Primary syphilis (chancre) on the upper lip

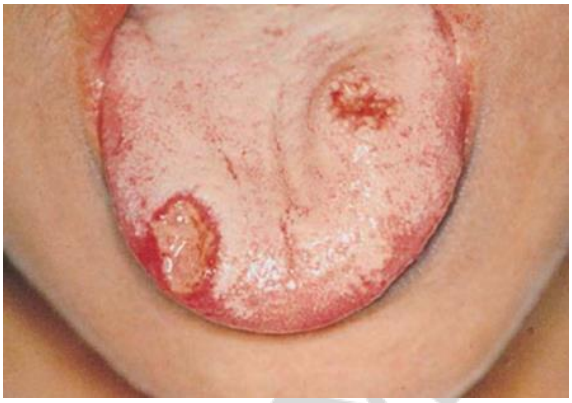

Figure 12. Two chancres on the tongue

After a latent period (6–8 weeks after the chancre appearance) secondary syphilis develops (patients infected via transfusion bypass the primary stage and begin with secondary syphilis). This stage lasts for 2–10 weeks and is marked by a spirochetemia with wide dissemination. Fever, flulike symptoms, mucocutaneous lesions, and lymphadenopathy are typical. The disease manifests as a reddish brown maculopapular cutaneous rash and mucosal ulcers affecting not only the area of inoculation but also other parts of the body. In secondary disease, oral lesions are rarely deeply ulcerated, but rather show mucoid exudate (mucous patches). Commonly affected sites include the tongue, lip, buccal mucosa, and palate (Fig. 13). Elevated broad-based verrucal plaques, known as condylomata lata, may appear on the skin and mucosal surfaces (Fig. 14). Inflammatory lesions may occur in any organ during secondary syphilis.

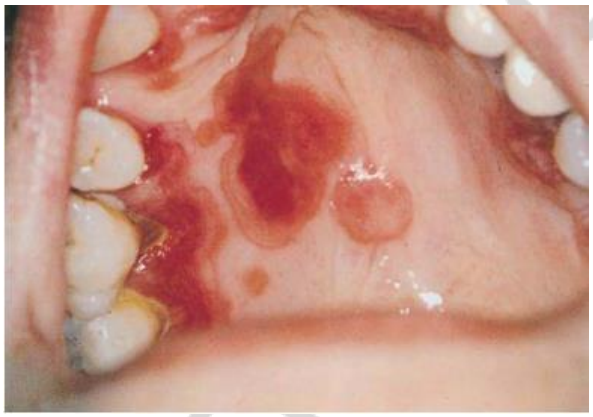

Figure 13. Mucous patches on the palate and gingiva in secondary syphilis

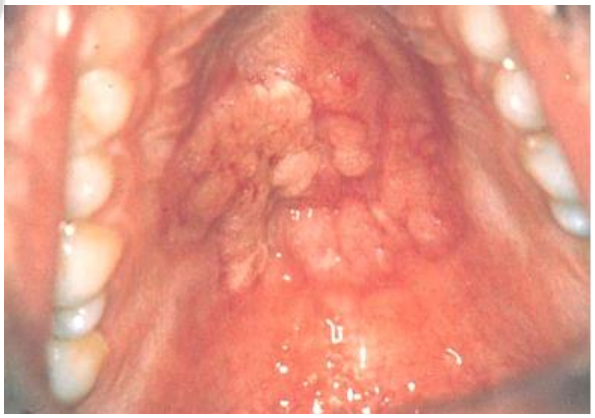

Figure 14. Condylomata lata on the palate

Diagnosis. Definitive diagnosis of syphilis is based on laboratory test confirmation of the clinical impression. The diagnosis of syphilis is best performed by using darkfield microscopy examination of scrapings or exudate from active lesions. There are several screening serologic blood tests that are

positive to antibody formation to the Treponema. These include the nonspecific Venereal Disease Research Laboratory test (VDRL) and the more specific fluorescent treponemal antibody absorption test.

Differential diagnosis. Clinically, as well as microscopically, syphilis is said to be the great imitator or mimicker because of its resemblance to many other unrelated conditions. When it presents within the mouth, the chancre may be confused with, and must be differentiated from, squamous cell carcinoma, chronic traumatic lesions, and other infectious diseases, such as tuberculosis and histoplasmosis. A history of venereal transmission with rapid onset and growth should arouse suspicion of primary syphilis. The differential diagnosis of secondary syphilis would include many infectious and noninfectious conditions marked by a mucocutaneous eruption.

Treatment. The drug of choice for treating all stages of syphilis is penicillin. Through the years, *T. pallidum* has remained sensitive to penicillin, as well as to other antibiotics such as erythromycin, doxycycline, and tetracycline. A single dose of oral azithromycin is an alternative choice. The patient can be referred to a dermatologist or general physician for treatment.

TUBERCULOSIS

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

Etiology. TB is caused by the aerobic, non–spore-forming bacillus *Mycobacterium tuberculosis.* The organism is usually acquired by airborne transmission and grows in the pulmonary alveoli and macrophages with a local inflammatory response. In most cases, T helper cells activate macrophages through the secretion of cytokines and gamma interferon (IFN), and the infection is suppressed permanently or may remain latent to reactivate months or years later. If the immune response is compromised and cannot prevent replication of the bacteria, active disease begins.

The Centers for Disease Control and Prevention (CDC) estimates that worldwide, over 8 million people will develop active tuberculosis annually, resulting in over 1 million deaths. The potential for human to human transmission of tuberculosis through the respiratory route is extremely high.

Clinical features. Unless the primary infection becomes progressive, an infected patient will probably exhibit no symptoms. In the reactivated disease low-grade signs and symptoms of fever, night sweats, malaise, and weight loss may appear. With progression, cough, hemoptysis, and chest pain (pleural involvement) occur. Occasionally, TB can spread to other parts of the body by the lymph and blood systems. Miliary (blood infection) and meningeal TB are the most serious forms of the disease and area associated with high mortality rates.

Oral lesions may occur in up to 3 % of patients with a long-term active TB. Oral manifestations that usually follow implantation of *M. tuberculosis* from infected sputum may appear on any mucosal surface. The tongue and the palate are favored locations. The typical lesion is an indurated, chronic, nonhealing ulcer that is usually painful. Clinically, the ulcer is irregular, with a thin undermined border and a vegetating surface, usually covered by a gray-yellowish exudate (Fig. 15, 16).

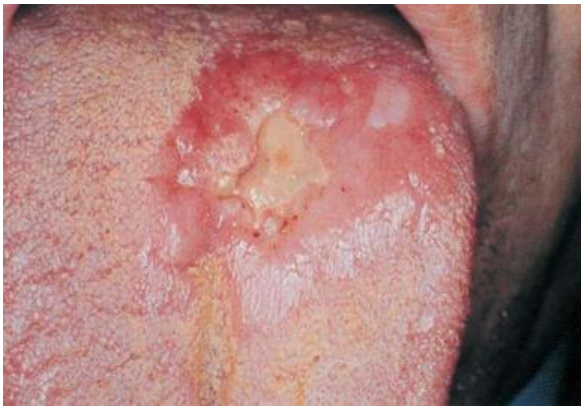

Figure 15. Tuberculosis of the tongue

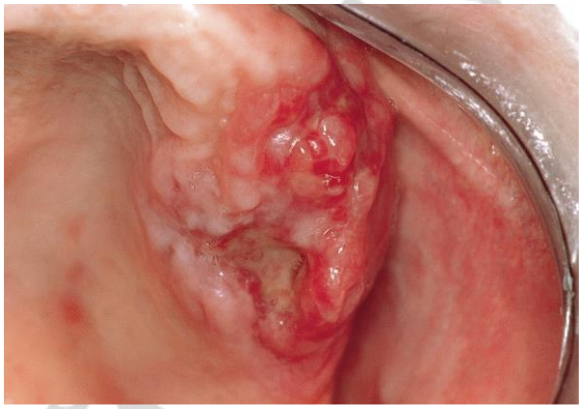

Figure 16. Tuberculosis of the maxillary alveolar ridge

Lesions may also occur in the neck lymph nodes. The latter is termed scrofula. Bony involvement of the maxilla and mandible may produce tuberculous osteomyelitis. This most likely follows hematogenous spread of the organism. Pharyngeal involvement results in painful ulcers, which may cause dysphagia, odynophagia, and voice changes.

Diagnosis. Sputum culture, tuberculin skin test (TST), histopathological examination and chest radiography are used. The basic microscopic lesion of TB is granulomatous inflammation, in which granulomas show central caseous necrosis.

To identify healthcare workers (HCWs) who have been exposed to TB, many hospitals require personnel to be skin tested annually. This appears to be a reasonable practice in settings with a significant high-risk population.

Differential diagnosis. On the basis of clinical signs and symptoms alone, oral TB cannot be differentiated from several other conditions. A chronic indurated ulcer should prompt the clinician to consider primary syphilis and oral manifestations of deep fungal diseases. Noninfectious processes that should be considered clinically are foreign body reaction, sarcoidosis, Crohn's disease, orofacial granulomatosis, squamous cell carcinoma, and chronic traumatic ulcer. Major aphthae might be included, although a history of recurrent disease should help separate this condition from the others.

Treatment. Because oral granulomatous lesions are associated with pulmonary disease, referral to an internist is indicated. Patients with active TB

are isolated during initial therapy, and dental treatment should be deferred until the patient is no longer considered infectious. First-line drugs likely to be used for treatment of TB include isoniazid, rifampin, pyrazinamide, and ethambutol. Patients are no longer considered infectious if they have two consecutive negative sputum cultures or have received tuberculosis treatment for at least two weeks. Oral lesions would be expected to resolve with treatment of the patient's systemic disease. Unfortunately, infection with multidrug-resistant organisms is a serious clinical problem that appears to be on the increase. Development and testing new classes of drugs are necessary to meet the challenge of resistant organisms.

Infected HCWs identified through screening are medically evaluated and considered for up to nine months of isoniazid (INH) therapy.

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.

The term leukemia, from the greek leukos "clear, white" and haima "blood", encompasses a wide group of neoplasms involving the body's blood-forming tissues, including the bone marrow and the lymphatic system with a final result of formation of abnormal white blood cells called "blasts". The excessive number of abnormal cells can also interfere with the level of other cells, causing further harmful imbalance in the blood count.

Didactically, leukemia is classified into four major categories: acute lymphoblastic leukemia (ALL) in adults and children, acute myelogenous leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myelogenous leukemia (CML).

Etiology. Various causes have been attributed to the development of specific forms of leukemia, including genetic factors such as specific chromosome translocations, environmental agents such as benzene, ionizing radiation, and viruses such as human T-cell lymphotrophic virus type 1 (HTLV-1).

Clinical features. Leukemias are classified as acute and chronic, depending on the clinical course, and myeloid or lymphocytic, according to the hystogenetic 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. Fever and fatigue/malaise are the most common presenting symptoms in patients with all types of leukemia. All forms of leukemia can have oral manifestations. Acute forms of the leukemias are more likely than chronic forms to be associated with oral lesions.

The most common oral lesions are ulcerations (Fig. 17, 18). Several studies reported well circumscribed, single or multiple ovoid-shaped oral ulcers resembling either aphthous stomatitis or herpetic lesions located mostly on nonkeratinized mucosa. Spontaneous gingival hemorrhage, petechiae, ecchymoses, tooth loosening, and delayed wound healing are also typical findings. Leukemic infiltration of the gingivae has been associated with monocytic variants of AML. Candidiasis and herpetic infections are relatively common oral complications of leukemia.

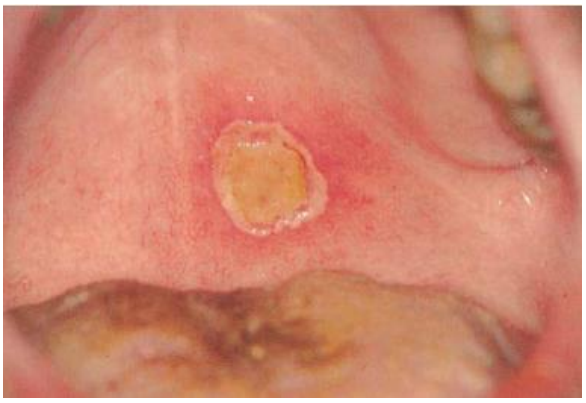

Figure 17. Chronic lymphocytic leukemia, ulcer on the palate

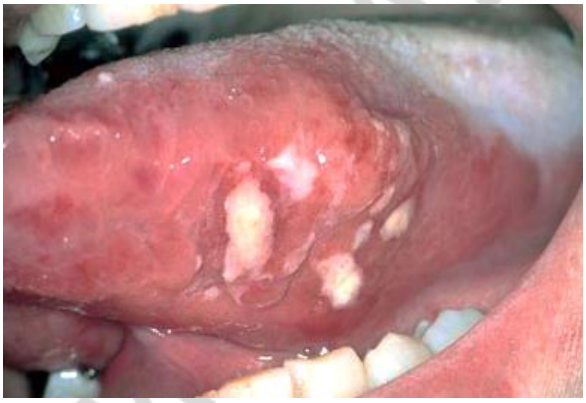

Figure 18. Acute myelocytic leukemia, ulcers on the tongue

Diagnosis. Diagnosis involves a baseline blood test showing an abnormal white cell count and a consequent bone marrow biopsy may confirm and identify the specific type of leukemia (leukemic cells, DNA markers, and chromosome changes).

Differential diagnosis. Agranulocytosis, cyclic neutropenia, myelic aplasia, thrombocytopenic purpura, acute necrotizing ulcerative gingivitis, idiopathic gingival fibromatosis, gingival overgrowth due to drugs (ciclosporin, phenytoin, calciumchannel blocking agents), aphthous stomatitis or herpetic lesions.

Treatment. Chemotherapy, bone-marrow transplantation, supportive therapy drugs. The treatment and prognosis for leukemia depend on the type of the blood cells affected and whether the leukemia is acute or chronic.

SQUAMOUS CELL CARCINOMA

Definition. Squamous cell carcinoma is the most common intraoral malignancy. *Any oral ulcer without a readily apparent cause should be considered carcinoma until proven otherwise, particularly if the lesion has persisted longer than 2 weeks.*

Etiology. Carcinomatous ulcers may arise in preexisting leukoplakia or erythroplasia, but there may be no history of a precedent precancerous lesion. Of all factors believed to contribute to the etiology of oral cancer, tobacco is

regarded as the most important. The patients usually give a history of smoking and show a proclivity for overimbibing alcoholic beverages. Elderly adults, mostly men are affected.

Clinical features. The most common presenting sign of oral cancer is the focal nonhealing ulceration with indurated margins. The lesion occasionally may widely infiltrate the soft tissues. The lateral border of the tongue (Fig. 19), floor of the mouth (Fig. 20), alveolar ridge, and the lower lip are the sites of predilection; however, oral cancer can develop in any location. The ulcer is often, yet not always, painless. In later stages, as deep invasion occurs, pain or dysphagia may be a prominent patient complaint. The growth rate is variable but usually progresses relatively rapidly. The larger the tumefactive ulceration, the more likely the chance for nodal metastasis. Oral cancer spreads first to the submandibular and cervical lymph nodes. Regional metastatic disease in the neck, like the primary lesion, is indurated and fixed to adjacent tissues.

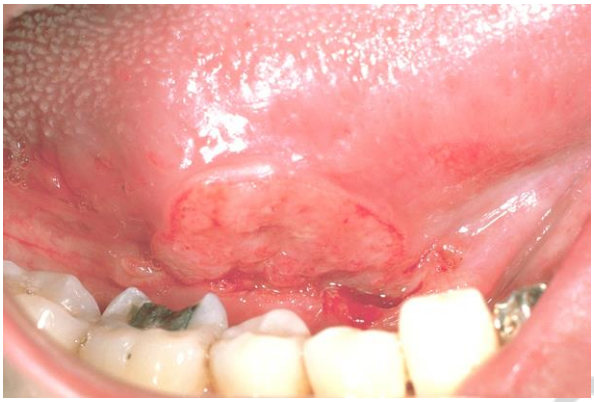

Figure 19. Squamous cell carcinoma of the lateral tongue

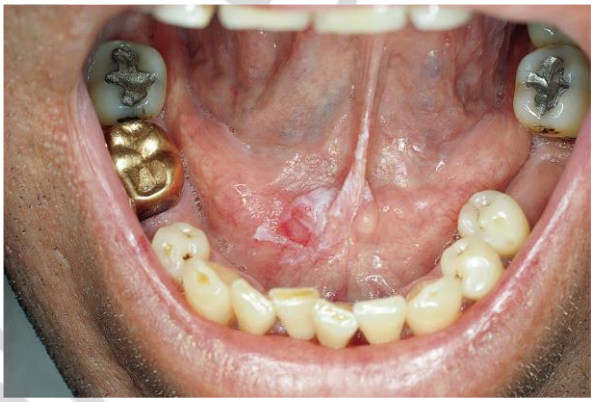

Figure 20. Early squamous cell carcinoma of the floor of the mouth

Diagnosis. Careful history taking is especially important, and biopsy findings confirm the diagnosis. Subjacent and lateral to the zone of ulceration are invasive islands, cords, and nests of malignant epithelial cells that demonstrate varying degrees of pleomorphism, hyperchromatism, and increased mitoses, many of which are bizarre.

Differential diagnosis. Carcinoma appearing as an oral ulcer may be clinically indistinguishable from traumatic ulcer, chancre, or one of the specific granulomatous infections. Certainly, any ulcer without a cause, or one that fails to heal when a suspected cause is removed, requires microscopic examination.

Treatment. Cancer should be managed by an oncologist. Surgery, radiotherapy, or a combination of the two are the treatment methods of choice.

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CONTENTS

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