Diagnosis and Treatment of Commonly Occurring Oral Mucosal Lesions

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RECURRENT APHTHOUS STOMATITIS AND HERPETIC ULCERS

An aphthous lesion (canker sore) is a shallow mucosal ulcer with flat, fairly even borders surrounded by erythema (Fig. 1, A). The ulcer may or may not be covered with a pseudomembrane composed of epithelial cells, fibrin, and debris. One or more ulcers may be present, and they tend to be recurrent. They are often painful. It has never been demonstrated that this lesion is due to a virus or to any other specific chemical, physical or microbial agent. The evidence against a viral etiology is based on the following: Viruses have never been isolated from these lesions; there is no rise in herpes antibody titer during their presence; virus-induced cellular changes cannot be demonstrated histologically; typical cytopathologic viral effects cannot be observed following tissue culture inoculations. In one study, a microorganism, Streptococcus sanguis, has been demonstrated in over 90 per cent of aphthous lesions reported. However, it is also found in 50 per cent of nonaphthous patients. Therefore, a specific relationship cannot be concluded.

It has been estimated that aphthous lesions occur in one quarter to one third of the American population, with a preponderance of females over males of approximately two to one. They can occur on any oral mucous membrane. A familial tendency has been suggested but not documented. As for other associations, there is no evidence to indicate that any gastrointestinal problem, such as hyperacidity, predisposes to aphthous lesions. Emotional problems, which may occur in some patients, have not been documented reliably as significant etiologic factors. There appears to be an increased incidence in patients who have allergic conditions, suggesting a built-in predisposition. The evidence is convincing

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that certain types of foods, such as citrus fruits, chocolate, and walnuts, or trauma will serve as cofactors in the occurrence of these lesions; but avoiding these types of irritants does not guarantee a cure. Although there are suggested hormonal influences in individual patients who have aphthous outbreaks at certain reproducible times in their menstrual cycles, a relationship cannot be shown on group studies.

The diagnosis depends mainly on ruling out similar but more readily identifiable diseases, the history of recurrence, and inspection of the ulcer. Cytology and biopsy are nonspecific for this condition.

As for treatment, some of these lesions bother patients so little that they require no formal therapy. Therefore, since there is no single effective treatment, management depends on patient symptoms. Bland mouth rinses and hydrocortisone ointments in an adhesive base may reduce pain and encourage healing. Since there are bacterial contaminants, tetracycline mouth rinses (250 mg./5 ml.) held in the mouth for two minutes four times daily and then swallowed may reduce symptoms. Analgetics, either as local troches or systemically, may be required in the more painful cases. Sedatives and vitamins may help indirectly.

In the painful, persistent, chronically recurring multiple aphthous stomatitis, systemic corticoids in dosages equivalent of 80 to 120 mg. hydrocortisone daily up to five days appear to control the symptoms
and encourage remissions in many patients. This may possibly be explained on an immunologic etiologic basis. This hypothesis is supported by recent studies which have indicated alterations in serum gamma globulins, antigen-antibody phenomena, and a suggestive white cell tissue infiltrate. Smallpox vaccinations and gamma globulin injections have not proved significantly beneficial; neither have numerous other preparations, such as autogenous vaccines, lactobacilli powders, and numerous other proprietary agents. Although caustics relieve pain by cauterizing fine nerve endings, they also cause necrosis and scar tissue, which delay healing and often prepare the site for chronic recurrences. Since certain types of foods or trauma in some patients seem to encourage the occurrence of these lesions, they should be avoided.

Each patient seems to have his own specific course for these lesions. Healing usually occurs in one to three weeks and may be only slightly accelerated with treatment.

**Periadenitis mucosa necrotica recurrens** is an accentuated form of the recurrent aphthous lesion in which the ulceration is large and may persist for months (Fig. 1, B). The etiology is unknown, and treatment is similar to that of the aphthous lesion. Therefore, the main difference is in the size and persistence of the lesion. Sometimes when they heal, they will leave residual scar tissue.

**Herpetic stomatitis** is a condition that usually occurs in children. It is estimated that over 90 per cent of the population is exposed to the herpes virus during the first three years of life. Only a small number of these children exhibit clinical manifestations of this infection. Young adults in whom exposure is delayed are usually very ill. They have intraoral aphthous-like lesions, fever, lymphadenopathy, and malaise for up to three weeks.

The diagnosis is established by the clinical features (Fig. 1, C, D) and ruling out other conditions, such as infections, mononucleosis, leukemia, and various hypersensitivity reactions. Cytologic smears from the oral ulcerations will reveal typical pseudogiant cells which are pathognomonic for this condition (Fig. 1, E). Laboratory results will reveal a normal white count with elevated lymphocytes, and increased sedimentation rate, and an increase of the herpes antibody titer.

Treatment is supportive by administering sedatives, analgetics, mouth rinses and fluids as necessary. Patients develop antibodies which cure the disease and render future immunity.

**Herpes labialis** (cold sore) is an ulceration of the vermilion border of the lip due to the herpes simplex virus. This is demonstrated by virus isolation techniques. The lesion begins as an erythematous, burning lesions, followed by a vesicular stage and then scabs. Sometimes they are quite painful and may persist for as long as three weeks. Although these lesions can occur spontaneously, they are often in response to trauma, cold, stress, illness, or fever. They tend to be recurrent.
The most effective treatment has been protecting predisposed sites prior to eruption or immediately after eruption with various ointments or creams. Topical cortisone has been effective in minimizing the symptoms and encouraging healing. Antiviral preparations (iododeoxyuridine) or local subcutaneous gamma globulin injections have not been regularly helpful. There are no other uniformly effective preventive or therapeutic measures.

LEUKOPLAKIA

The term leukoplakia is used to designate a clinical white patch or plaque on the oral mucous membranes that cannot be removed by scraping and cannot be classified clinically or microscopically as another disease entity. Most of these lesions are reflections of benign hyperkeratosis. Although pipe and cigarette smoking, snuff, or trauma may induce hyperkeratosis, causes for the occurrence of many leukoplakias are unknown. Leukoplakia occurs mostly in persons over 40, a similar age range as that of oral cancer. Although there are no adequate epidemiologic studies on the incidence of oral leukoplakia, it probably is present in less than 2 per cent of the adult population.

For many years leukoplakia has been recognized as an important precancerous condition of the oral cavity. Malignant transformation of these lesions may be estimated in either of two ways: 1. Indirectly by (a) establishing the number of leukoplakias associated with oral carcinoma in large series of patients or, (b) by determining the number of carcinomas found in a series of histologic specimens which had been clinically classified as leukoplakias; 2. Directly by following a number of leukoplakias over a period of time and determining the incidence of malignant transformation. Studies on groups of patients with oral carcinoma reveal associated leukoplakia ranging from 11 to 60 per cent, which is much larger than that expected in the general population. From biopsy studies, the percentage of malignancies and premalignant changes occurring in lesions clinically diagnosed as leukoplakia varies from 10 to 20 per cent, indicating that carcinomas masquerade as leukoplakias and are associated with hyperkeratosis. Although there are no reliable statistics on the percentage of leukoplakias which will convert into malignancies, transformation has been reported and documented by many reports, substantiating the premalignant potential of a hyperkeratotic lesion.

Leukoplakia is usually asymptomatic. It is often discovered upon routine examination or by patients feeling roughness in their mouths. There are no consistent and reliable clinical signs and symptoms associated with oral leukoplakia which allow differentiation or prediction of a premalignant or early malignant change (Fig. 2, A, B, C). However, one type of leukoplakia that clinically has a speckled appearance (white
plaques or nodules on an erythematous mucosa) is associated frequently with microscopic changes of carcinoma, carcinoma in situ, or epithelial atypia (Fig. 2, D). Because of the simultaneous occurrences of leukoplakia and carcinoma and the lack of an established prognostic clinical guide, all white lesions characterized as leukoplakia must be microscopically diagnosed, removed, or followed with care.

A biopsy is the only definitive way of establishing the exact nature of oral leukoplakias. However, because of the extensiveness of some intraoral leukoplakias, as well as the need for frequent observations, cytologic smears from the surface are helpful in supplementing both clinical and biopsy information. Even prior to ulceration, scrapings will yield representative cells. This is based on the following known facts:

1. Because of a relatively fast renewal time (probably less than two weeks), hyperkeratotic surface cells will demonstrate representative nuclear morphology.

2. Leukoplakias that appear histologically as hyperorthokeratotic (surface appears as an amorphous mass of keratin without evidence of nuclei) in effect contain many tightly packed but intact cells, some of which contain nuclei.

3. Carcinoma usually occurs under surface cells which contain nuclei.

4. Carcinomas in leukoplakias most often develop in areas of atrophy and erythema and not in the areas of greatest cornification.

The first step in treatment consists of removing all irritants (e.g., tobacco, ill-fitting dentures). If the leukoplakia is not reversible, excision

Figure 2. A, Leukoplakia, floor of mouth. B, Carcinoma, lower anterior labial reflex, appearing as leukoplakia. C, Leukoplakia, buccal mucosa, and associated carcinoma (arrow). D, Speckled leukoplakia, palate, and alveolar mucosa.
should be performed when feasible. However, since some leukoplakias occur so diffusely that complete excision often is impractical, careful clinical examination and follow-up are essential. It must be remembered that the diagnosis must be reaffirmed periodically since a leukoplakia may unpredictably transform into a malignancy. Electrodesiccation, vitamin A, and proteolytic enzymes have not given predictably favorable results.

**LICHEN PLANUS**

The etiology of lichen planus is unknown. This lesion occurs on mucous membranes and skin, either independently or simultaneously. In the mouth lichen planus can take three forms (Fig. 3): 1. A reticular
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or lace-like pattern; 2. An erosive or bullous pattern in which the keratotic changes are interspersed with an erythematous mucosa, pseudomembranes, and erosions; 3. The plaque type, which sometimes can be confused with leukoplakia.

The diagnosis is based on clinical appearance and biopsy. There are no other diagnostic tests which will support the diagnosis.

Since most patients with lichen planus are asymptomatic, no specific treatment is necessary. The patient should be reassured of the benign but persistent nature of the disease. A very small percentage of these cases have been reported to be associated with a carcinoma; therefore, although it cannot be strictly considered a premalignant lesion, periodic observations are indicated. In the few cases where carcinoma has occurred in areas of lichen planus, half of these were found on the buccal mucosa, and the majority were associated with the erosive type of lichen planus.

The oral lesions are usually chronic, with slight remissions and flares. The course may run for months or years, but spontaneous cures occur. Excision is contraindicated since most of these lesions are extensive, recur in the site of the surgical area, and frequently will become symptomatic. When symptoms occur with lichen planus, only supportive therapy, such as avoiding foods which irritate the lesion, sedatives, and analgesics are indicated. Topical ointments, hydrocortisone, antibiotics, and tranquilizers have not been uniformly effective in aiding these patients.

PIGMENTATIONS

Pigmentation of the oral mucosa is most commonly due to a racially controlled melanin deposition in the epithelium. This occurrence is most prevalent in non-Caucasian peoples. The color varies from brown to black, and the involvement may be in isolated patches or a diffuse speckling.

Amalgam fragments which become embedded in the mucosa during dental care are most common (Fig. 4, A). These areas will appear as brown, blue, or black spots. Other causes of pigmentation include epithelial or dermal nevi, and drug reactions from bismuth, arsenic, or mercury ingestion. Similar lesions may also appear during the menopause or in Addison's disease, intestinal polyposis, neurofibromatosis, and several other disorders associated with generalized pigmentations.

The diagnosis is established by information obtained from a complete history and biopsy. The most important disease to consider in the differential diagnosis is malignant melanoma (Fig. 4, B). These lesions often show growth, ulceration and induration. Fortunately they are uncommon.

The most important part of treatment is definitively establishing the diagnosis. Cytology is of no value in these lesions. Genetic pigmentations require no further treatment. Amalgam fragments require removal only if there is associated infection or symptoms. Since it is not established that nevi are premalignant, excision is not indicated unless biopsy of
Oral candidiasis (moniliasis, thrush) is due to overgrowth of a fungus, *Candida albicans*. It is characterized by creamy-white, curdlike patches which may occur on any mucosal surface of the mouth (Fig. 5). The adjacent mucosa is usually erythematous, and scraping the lesions usually uncovers a raw bleeding surface. Pain is common, with fever and lymphadenopathy sometimes being present also. Although this fungus occurs in about one-third of normal appearing mouths, overgrowth and pathogenicity do not occur unless the “balance” of oral flora is disturbed, e.g., by debilitating or acute illnesses or as a result of anti-infective therapy. Concomitant candidiasis of the gastrointestinal tract may occur.

The diagnosis is based on the rather typical clinical picture, and may be confirmed by cultures made from oral scrapings.

Treatment is not uniformly successful; and the infection usually will persist in spite of treatment as long as the causative factors are
present. The patient should have a nutritious diet with vitamin supplementation, and should receive sufficient rest. Saline solution mouth rinses every two hours may give local relief and promote healing. Specific antifungal therapy consists of nystatin (Mycostatin) mouth rinses, 500,000 units t.i.d. (100,000 units/ml. in a flavored vehicle), held in the mouth for two minutes and then swallowed; Mycostatin troches (100,000 units) to be dissolved orally q.i.d.; and 1 per cent aqueous gentian violet solution painted on affected areas t.i.d.

In some instances, primarily under dentures, a candidal lesion may appear as a slightly granular or irregularly eroded erythematous patch.

Figure 5. A, Candidiasis, gingiva.  
B, Candidiasis, commissure.  
C, Candidiasis, tongue.  
D, Candidiasis, palate.  
E, Leukoplakia of tongue.  
F, Same leukoplakia of tongue (Fig. 5, E), showing spontaneous dekeratinization during a candidal flare.
In these cases, a diagnosis can be established by a heavy overgrowth of *Candida albicans* in culture or a biopsy revealing hyphae of candida invading epithelium (PAS stain). Mycostatin powder, 100,000 units/gm., applied four times daily for several weeks, is frequently effective in reversing signs and symptoms.

**DENTURE IRRITATION LESIONS**

Many patients who have objectively or subjectively ill-fitting dentures do not develop any oral lesions. However, when patients do form lesions from denture trauma, the manifestations vary. These changes most often are manifested by a palatal papillary hyperplasia, erythema, fibrous hyperplasia (epulis fissuratum) and ulceration.

Although many carcinomas appear to stem from an area covered by a prosthetic appliance, studies have not conclusively demonstrated whether there is a coincidental or a cause and effect relationship. However, elimination of irritation and careful follow-up are indicated; and, in case of doubt, periodic cytology and occasional biopsy are advised. Complete removal is sometimes difficult because of the widespread nature of the lesion. Reversal by altering the appliance may help, but has not been uniformly successful.

**GLOSSITIS**

Inflammation of the tongue is usually associated with partial or complete loss of filiform papillae, which creates a red, smooth appearance (Fig. 6, A). This may be secondary to a variety of diseases such as anemia, nutritional deficiency or malabsorption, drug reactions, systemic infection, and physical or chemical irritations. The tongue may also present fissures, a rather common developmental anomaly, sometimes with superimposed infection. (Fig. 6, B). Treatment is based on identifying and correcting the primary cause, if possible, and palliating the tongue symptoms as required.

Geographic tongue (erythema migrans or wandering rash) is a benign condition of unknown etiology in which smooth erythematous patches with discrete borders appear on the dorsum or lateral borders of the tongue (Fig. 6, C). They most frequently will change position, simulating movement, and after a period of time disappear—only to recur again. The remainder of the tongue may be unaffected or have the appearance of a coating, which in either case accentuates the denuded areas. Histologically the process usually is superficial and consists of desquamation of the filiform papillae and associated inflammation. Some surveys have indicated an incidence of about 1 to 2 per cent of our
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population. This condition is usually asymptomatic and requires no treatment.

Median rhomboid glossitis is manifested by a permanently depapillated area anterior to the circumvallate papillae on the tongue dorsum. The area is often irregularly shaped and may be smooth, raised, or furrowed. This is a developmental irregularity in the formation of the tongue and inflammation is not prominent. It is usually asymptomatic; but because it is noticed later in life, concern is aroused as to some other etiologic factor. No treatment is necessary.

Occasionally elongations of filiform papillae occur, giving a clinical picture of a hairy tongue (Fig. 6, D). It may appear as a variety of colors, creamy yellow to black, depending on food habits, tobacco usage, drugs, or oral microorganisms. Although in some cases a cause cannot be ascertained, frequently it is due to the intake of drugs (antibiotics), fever, or some other type of illness. The most effective treatment is correcting the etiologic factor and improving oral health. This often can be helped by brushing the tongue, which will desquamate the elongated filiform papillae. Hydrogen peroxide 3 per cent may be helpful. In some stubborn cases of unknown etiology, the use of a keratinolytic agent, Podophyllin (10 to 15 per cent solution in equal parts of acetone and alcohol), has been effective. It must be applied very cautiously with a

Figure 6. A, Depapillated tongue, secondary to pernicious anemia. B, Fissured tongue. C, Geographic tongue. D, Black hairy tongue, following penicillin ingestion.
cotton-tipped applicator once a day for three to five days. Caution should be used, since overusage will lead to soreness and possibly to ulceration.

Burning and pain which might involve part or the entire tongue may occur with or without glossitis. This may be associated with hypochromic or pernicious anemia, nutritional disturbances, diabetes mellitus, or other general disorders in which tongue complaints may be the presenting symptoms. In those cases due to diabetes, the two-hour glucose tolerance test is often positive when the screening urinalysis is negative. Allergens (dentifrices) are rare causes of tongue pain. Certain foods may cause flare-ups, but are not the primary causes. Dentures, poor oral hygiene, and dental infections are usually of no etiologic significance.

Although most cases occur in postmenopausal women, these disorders are not restricted to this group. In most cases a primary cause cannot be identified. Cultures are of no value. Many clinicians believe that these symptoms occur on a primarily functional basis.

Treatment is mainly empiric when an associated disease cannot be ascertained. Antihistamines, sedatives and tranquilizers, and vitamins are occasionally of value. The injection of hydrocortisone in an oil base directly into the tongue has been of some help in puzzling cases. Local anesthetic injections and placebo injections or tablets are of value in differentiating functional and organic disease. Ointments and mouth rinses are of no value.
Partial xerostomia occasionally contributes to the symptoms. This may be remedied by sucking on nonmedicated troches or by the administration of pilocarpine, 10 to 20 mg. (½ to ¾ grain), daily in divided doses. Estrogen supplementation in the postmenopausal patient is sometimes helpful.

SOFT TISSUE SWELLINGS

Growth in the mouth may be due to a proliferation of any epithelial or connective tissues (Fig. 7). True neoplasms may be benign or malignant. The much more common chronic inflammatory hyperplasias, such as the gingival pyogenic granuloma, and denture injury hyperplasias and cysts must be considered in the differential diagnosis. The diagnosis of these lesions depends on clinical characteristics and biopsy.