Paparella: Volume III: Head and Neck

Section 2: Disorders of the Head and Neck

Part 2: The Oral Cavity

Chapter 15: Oral Ulcerative Diseases

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One of the most common complaints encountered in the practice of oral medicine is that of a painful or burning mouth attributable to some inflammatory or ulcerative process. Despite the relative frequency or this occurrence, however, the conditions that these findings or symptoms may represent present a most difficult challenge in both diagnosis and treatment.

This chapter is designed to discuss the most commonly encountered conditions that may present in the oral cavity in an inflammatory, ulcerative, erosive, or vesiculobullous fashion. Some occur primarily as a single, well-defined lesion, whereas others may typically be diffusely spread throughout the oral cavity, and still others may present in either manner.

Because of the variability with which an individual condition may present, as well as the fact that a variety of diseases may have a similar presentation within the oral cavity, the practitioner must approach the process of diagnosis and treatment in an orderly fashion. One means of accomplishing this is to develop an outline to systematically approach the clinical diagnosis. Once this is done, appropriate clinical questions coupled with a thorough oral examination will often make the diagnosis obvious. Occasionally, however, histopathologic or cytologic examination, as well as specific laboratory tests, must be performed.

In order to aid the reader in developing a systematic approach to the differential diagnosis of oral ulcerative disease, this chapter has been divided into sections according to the clinical presentation, that is, whether the process is acute, chronic, or generalized in nature.

The following outline is the author's approach to the differential diagnosis of the more common oral stomatitides.

An attempt will be made to delineate the diagnostic clinical features, appropriate diagnostic tests that may be performed, and preferred treatment modalities, along with the long-term prognosis for the various entities discussed in this chapter.

Acute Oral Ulcers

The lesions discussed in this section have in common the fact that they will all present as small ulcerative lesions of recent onset, whether single or multiple, and are characterized clinically as shallow lesions with their borders not raised above the mucosal surface. Although

these lesions are of short-term duration, they may frequently be recurrent.

I. Acute
   A. Trauma
   B. Recurrent aphthous stomatitis (RAS); Behçet's disease
   C. Recurrent labial and intraoral herpes
II. Chronic
   A. Trauma
   B. Infection
      1. Viral
      2. Bacterial
      3. Mycotic
   C. Neoplasm
      1. Epithelial
      2. Mesenchymal
III. Generalized
   A. Physical, chemical, drug induced
      1. Contact stomatitis
      2. Fixed drug eruption
      3. Radiation mucositis
      4. Cancer chemotherapy
   B. Infection
      1. Primary herpetic gingivostomatitis
      2. Candidiasis
   C. Dermatologic disorders
      1. Erythema multiforme
      2. Lichen planus
      3. Benign mucous membrane pemphigoid
      4. Bullous pemphigoid
      5. Pemphigus vulgaris
      6. Lupus erythematosus
   D. Systemic diseases
      1. Diabetes mellitus
      2. Uremia
      3. Crohn's disease
      4. Blood dyscrasias
         a. Leukemia
         b. Pancytopenia
         c. Agranulocytosis
         d. Cyclic neutropenia
         e. Sickle cell anemia.

Traumatic Ulcer

Trauma is certainly the most common cause of ulceration of the oral mucous membranes. Traumatic ulcers may be either factitial or iatrogenic in their origin and may result from physical, chemical, or thermal insults to the tissue. Diagnosis of a traumatic oral ulcer is often a matter of simple clinical problem solving. Common physical injuries to the oral cavity include biting the cheek or tongue, irritation from a sharp filling or broken tooth, denture irritation, a traumatic event involving a sharp foreign object, or even toothbrush trauma from overzealous brushing with a hard-bristled toothbrush. An example of an iatrogenic physical injury might be found in a patient who has bitten the cheek or tongue following dental anesthesia.

In its acute stage, a traumatic ulcer resulting from physical injury will typically present as a break in the mucosa with a shallow base and nonraised margins. It may be diffuse, as in the case of a cheek biting injury, or a localized, well-circumscribed ulcer if caused by a sharp filling or carious tooth. Acute oral ulcers such as this are usually at least mildly painful.

The most common example of a chemically induced ulcer in the oral cavity is the "aspirin burn" caused by holding aspirin against a painful carious tooth. This type of ulcer is characterized by a white slough that may partially rub off, revealing an ulcerated base. Direct mucosal contact with any number of drugs may cause a similar type of burn. Chemical burns can also be seen in patients who have used phenol or silver nitrate as a "treatment" for recurrent aphthous ulcers. Additionally, patients may find any number of noxious chemicals to introduce into the oral cavity, which may cause either localized or generalized oral ulcerations, often in the form of a generalized sloughing of the oral mucous membranes that produces a painful, raw, bleeding lesion.

Extremely hot foods or liquids may cause painful oral ulcerations, with one of the more common being the classic "pizza burn" from hot melted cheese contacting the palate, tongue, and lips. A less common example of thermal injury to the oral cavity may be noted in patients who make a habit of "reverse-smoking" materials such as marijuana.

Physical injuries are treated by removing the responsible irritant, after which healing is usually uneventful. Cleansing the tissues with a mild saline rinse or an oxidizing mouthwash (hydrogen peroxide USP 3 per cent diluted with an equal part of mouthwash or warm water) may speed healing. If doubt exists as to the diagnosis or if after removal of the presumed causative agent the ulcer does not resolve, a biopsy should be performed.

Chemical burns are often quite painful and may require analgesics during the healing period. Supportive therapy, including careful attention to oral hygiene and the use of cleansing mouth rinses as already described, is indicated. Local anesthetic rinses such as 2 per cent viscous lidocaine, diphenhydramine (elixir or Benadryl), and Kaopectate may be used but only after first rinsing the mouth with an oxidizing mouthwash. A mixture of equal parts of a tetracycline-nystatin-decadron elixir may also be useful. Topical corticosteroids (see Appendix) may be applied to the affected area following careful cleansing and drying of the tissues.

Although healing of thermal injuries is usually uneventful, supportive therapy, medications for pain, or topical corticosteroids, or all, may be indicated.

Recurrent Aphthous Stomatitis

Recurrent aphthous stomatitis (RAS), also known as canker sores or aphthous ulcers, is a common chronic disease characterized by the occurrence of periodic painful ulcers of the nonkeratinized oral mucosa. The most common form of RAS is minor aphthous stomatitis or ulceration. The ulcers in this form of the disease are usually well-defined, round to ovoid, 2- to 4-mm ulcers. They may be either single or multiple and preceded for up to 24 hours by vague symptoms. They are almost always painful, and usually heal in 7 to 14 days without scarring. They occur on the nonkeratinizing oral mucous membranes not overlying bone and appear as shallow ulcers with a yellowish gray necrotic center, slightly raised border, and an erythematous halo. Their frequency of occurrence may vary from only one or two attacks/year to the occasional individual who may go for extended periods of time without freedom from lesions. Lesions clinically identical to those seen in this form of RAS may be found in patients with Behçet's disease, Reiter's disease, Crohn's disease, and ulcerative colitis, as well as in leukopenias.

Another form of RAS that composes approximately 10 per cent of cases is known as major aphthous stomatitis, periadenitis mucosa necrotica recurrent (PMNR), Sutton's disease, or major scarring aphthae. Major aphthous stomatitis, the most severe form of RAS, often initially appears during childhood or adolescence and is characterized by large (usually greater than 1 cm in diameter), painful ulcers on the buccal and labial mucosa, tongue, soft palate, and tonsillar pillar areas. They occur at frequent intervals, singly or in groups, and as in RAS, patients may go for long periods without freedom from their disease. Clinically, they are often large, relatively deep-based ulcers with a yellow-gray necrotic center and raised rolled borders. Individual lesions may persist for weeks and often heal with scarring. When multiple attacks have occurred, prominent linear scar bands may be seen.

An additional 10 per cent of patients with RAS may present with a variant known as herpetiform aphthous stomatitis, so named because of its clinically similar appearance to herpetic stomatitis. They present as numerous discrete ulcers, usually less than 1 mm in diameter, which may coalesce to form large single ulcers.

Although the cause of RAS is unknown, it is theorized that either nonspecific factors, such as trauma or food allergy, or specific factors, such as bacterial or viral infection, may trigger a temporary imbalance in various immune cell subpopulations leading to an upset in immune regulation and local destruction of the oral epithelium with ulceration.

Although their onset may be noted during the first decade of life, they appear to occur most frequently between the ages of 10 and 40 years. Estimates of the prevalence of RAR vary. Although it is believed that approximately 20 per cent of the general population is affected by this disease at one time or another, one study of young adult armed forces recruits and students in the health professions in 21 countries revealed a 39 per cent incidence in men and a 50 per

cent incidence in women of two or more lifetime occurrences. In another study of a large group of professional students, an incidence rate of more than 55 per cent was noted. A retrospective study of this same population 12 years later indicated a net reduction in disease prevalence of 12 per cent. It was speculated that a reduction in general patterns of stress generated by academic achievement, stabilization of family and home life, and a decrease in occupational stress concomitant with the attainment of personal and financial goals may have attributed to this decrease.

Although proposed treatment regimens for RAS abound, most have proved to be of little or no value. In uncomplicated cases in which a single or even several small lesions are occasionally noted, supportive therapy alone may be indicated. An ulcer in the labial or buccal mucosa or buccal vestibule area, for instance, will often cause the patient to "favor" that area using uninvolved parts of the mouth when taking liquids or chewing a bolus of food, thus restricting the normal mechanical cleansing of tissues in the area of the ulcer. This, coupled with the normal desquamation of epithelial cells in the area, as well as the microbial flora normally present, will increase the chance of secondary bacterial infection within the ulcer bed, which only serves to increase the size of the ulcer and prolong healing time. In cases such as this, an oxidizing mouth rinse such as equal parts of hydrogen peroxide and warm water may prove useful in locally debriding the area and accelerating the healing time.

When the lesions of RAS become particularly painful, a topical steroid preparation (see Appendix) may be employed in the following manner. The mouth is first rinsed with an oxidizing mouthwash as described previously, after which the ulcer base is carefully cleaned and dried with a cotton swab or gauze sponge. Taking care to keep this area dry, a small amount of the topical steroid paste is applied over the ulcer base but not rubbed in. Dipping a finger in warm water and "tamping" the paste down will then help seal the preparation over the ulcerated area. This should be done after meals and at bedtime. A dab of Terra-Cortril topical ointment (oxytetracycline hydrochloride-hydrocortisone) may be applied to the ulcer just prior to applying the "seal" of triamcinolone acetonide (Kenalog) in Orabase. In those cases in which accessibility is difficult, a topical steroid aerosol may be used. In cases of generalized oral involvement, tetracycline mouth rinses (250 mg/5 mL water) or chlorhexidine gluconate, 0.12 per cent, are helpful. In one study of 38 patients, chlorhexidine mouthwash was noted to significantly reduce the total number of ulcer days and increase the number of ulcer-free days in patients with minor aphthous ulceration. Persistent lesions sa seen in the major aphthae may be treated by intralesional injection of triamcinolone acetonide (see Appendix). In extreme or protracted attaches, systemic corticosteroids and antibiotic therapy may be indicated. Table 1 shows the clinical characteristics that distinguish RAS from recurrent herpetic stomatitis.

Behçet's Syndrome

In 1937, Behçet described a symptom complex consisting of recurrent aphthous ulcers of the mouth, as well as recurrent painful ulcers of the eyes and genitals. Since that time, additional characteristic findings, such as neurologic, gastrointestinal, articular, and vascular involvement, have also been described. The diagnosis of Behçet's disease is made on the basis of the

clinicopathologic findings, which may be confused clinically with Stevens-Johnson syndrome and Reiter's disease.

Therapy for the oral lesions in Behçet's syndrome is the same as that discussed for aphthous ulcers.

Table 1. Comparison of the Clinical Features of Recurrent Herpetic Stomatitis and Recurrent Aphthous Stomatitis

	Recurrent Herpetic Stomatitis	Recurrent Aphthous Stomatitis
Location	Vermillion border of lips, heavily keratinized mucosa (ie, hard palate and attached gingiva)	Moist mucous membranes not bound to bone
Appearance	Fluid-filled vesicles that break to form a small red ulcer covered by a brownish crust (palate and gingival vesicles break to form small punctuate ulcers which may coalesce)	Initial erythema followed by shallow ulcers with yellowish gray necrotic centers and erythematous halos
Initiating	Sunshine, mechanical trauma, anxiety or emotional upset, fever, gastrointestinal upset, debilitating disease	Mechanical trauma, anxiety or emotional upset, fever, gastrointestinal upset, debilitating disease
Duration	10-14 days	10-14 days.

Herpesvirus Infection - Secondary or Recurrent Labial and Intraoral Herpes

Herpes simples (HSV) is an acute viral infection that may produce a wide variety of symptoms. Two distinct strains of herpesvirus hominis occur, HSV-1 and HSV-2. HSV-1 primarily infects the oropharynx, whereas HSV-2 most frequently infects the genitals. HSV-2, however, may infect the oropharynx just as HSV-1 may infect the genitals, and each may recur in that site. Infections with HSV are divided into two types: (1) primary and (2) secondary or recurrent infection, with the majority of primary infections of both HSV-1 and HSV-2 being clinically unapparent to the patient. Following primary infection, the HSV will remain latent in neural tissue, such as the trigeminal ganglia. Reactivation of latent virus then results in spread through centrifugal migration of infectious virions along peripheral sensory nerves to the mucosal surfaces, resulting in recurrent herpetic infection.

For many years, the incidence of individuals with neutralizing antibody to herpesvirus hominis has been quoted as 90 per cent of the population older than 15 years of age. With time, however, it has become apparent that the incidence of seropositivity varies with both age and the socioeconomic background of the population being studied. A study of medical students and nursing students at Oxford and Edinburgh showed an incidence of 36 to 48 per cent of neutralizing and complement-fixing antibodies to HSV, whereas the general population in that area demonstrated a 65 to 89 per cent positivity. A study of a middle class population in Seattle showed a variation in incidence between 20.1 per cent for individuals aged 5 to 9 years to 84 per cent for individuals in the 55- to 65-year age range. The incidence of complement-fixing antibody to HSV did not reach 50 per cent until 25 years of age.

Although the incidence of recurrence after primary oral HSV infection is not known, one prospective study showed orolabial recurrences in 5 of 12 patients with HSV-1 and in 1 of 27 patients with HSV-2. Shipp and co-workers reported an incidence of recurrent herpes labialis in an investigation of 1788 professional school students from the schools of medicine, veterinary medicine, dental medicine, nursing, and dental hygiene. It is interesting to note that a retrospective 12-year study of this population showed only 24 per cent of respondents still reporting recurrent herpes labialis. Recurrent intraoral HSV infections were reported to occur in 1 to 1.5 per cent of subjects.

The lesions of recurrent or secondary herpetic gingivostomatitis, commonly known as herpes labialis, "fever blisters", or "cold sores", are characterized by vesicular eruptions that localize around the mouth, most frequently on the vermilion border of the lips. Attacks of recurrent herpes labialis may be precipitated by many factors, such as exposure to sunlight, fatigue, emotional stress, fever, upper respiratory tract infection, gastrointestinal upset, menstruation, pregnancy, and immune deficiency states. A prodromal sensation of burning, itching, swelling, or slight soreness may be noticed at the site of the recurrent lesion just prior to vesicle formation. The vesicles, which are well localized, occur either singly or in clusters, and are each 1 to 2 mm in diameter, appear fluid-filled and quickly rupture, leaving a small red ulceration that soon becomes covered by a brownish crust.

The less common intraoral lesions occur on mucosa attached to or overlying bone, specifically the heavily keratinized mucosa of the hard palate and gingiva. As with their labial counterparts, they occur as intraepithelial vesicles that easily rupture, leaving punctate ulcerative lesions approximately 1.5 mm in diameter. Individual lesions, however, may coalesce to form a single, large, irregularly shaped ulcer, often with small satellite lesions that may help differentiate it from an ulcer of traumatic origin.

At present, there is no clear consensus as to the efficacy of specific therapy for recurrent orolabial herpesvirus infections. Topical therapy with either vidarabine cream or acyclovir ointment has not been found to be clinically effective in treating recurrent herpes labialis. In another study, however, application of vidarabine (ara-AMP) by iontophoresis on patients with vesicular orolabial herpes was compared with acyclovir and sodium chloride, each applied in the same fashion. It was shown that the ara-AMP significantly decreased the duration of virus

shedding as well as the time to a dry crust when compared with the other two agents. These authors also noted a trend toward decreased healing time after the ara-AMP treatment.

Acyclovir capsules (200 mg) taken at the earliest symptom of recurrent herpes labialis and continued at five capsules/day for 5 days have been noted to significantly decrease the duration of pain, the time to loss of crust, and the time to complete healing in some episodes of recurrent herpes labialis. These authors also pointed out that although patients taking acyclovir fared better in almost every category of clinical healing characteristics, these differences were not as pronounced as has been reported in similar trials of oral acyclovir in genital herpes.

Chronic Oral Ulcers

The differential diagnosis and clinical features of chronic oral ulcers are very different from the acute, short-term ulcers that have previously been described. Chronic oral ulcers share in common the fact that they are frequently well circumscribed with raised borders above the mucosal surface and an indurated, often crateriform base. Other times, they may present as a diffuse granulomatous-appearing lesion. They are further characterized by their nonresolution within 2 to 3 weeks as is seen with acute ulcerations (such as recurrent aphthous ulcers, recurrent herpetic lesions, or acute traumatic ulcers once the noxious stimulus has been removed). An acute ulcer will rarely persist as such for longer than 2 weeks but will begin to develop hyperplastic borders with enlargement of the ulcer base. In cases in which an ulcer that was initially thought to be acute or short term has persisted and begins to develop the clinical features of a more chronic process, the clinician should rethink the diagnosis - that is, does the trauma persist or is there another disease process present?

At this point, the clinician is often faced with a number of stumbling blocks to making a diagnosis. It is not uncommon for the clinical history of the lesion to be vague with regard to the length of time it has been present or to the circumstances regarding its initial appearance. This may be accounted for by the fact that chronic ulcers, unlike their acute counterparts, may be either painless or painful, often being painless until they become secondarily infected or enlarged to the point of causing dysfunction or involving peripheral nerves. Also, chronic ulcers typically do not demonstrate the site specificity seen in their acute counterparts.

Chronic oral ulcers typically fall into one of three broad categories: traumatic, infectious or neoplastic.

Traumatic Origin

Chronic oral ulcers of traumatic origin develop when the noxious stimulus that originally caused the lesion has persisted over time. Removal of the stimulus is often enough to promote healing; however, occasionally specific therapy, such as the use of topical or injected steroid preparations (see Appendix)) may be indicated. Performing an incisional biopsy as a diagnostic procedure may provide the stimulus for resolution of the ulcer. Although uncommon, it may be necessary to surgically excise the lesion if healing is not taking place.

Infectious Origin

Viral infection will seldom lead to development of a chronic oral ulcer. One instance in which this might be seen is in a severely immunocompromised HIV-positive patient when the recurrent herpes simplex virus infection persists and does not resolve in the usual time. Although nonspecific bacterial infection of chronic oral ulcers is common, specific bacterial infections are not. An example of a chronic ulcerative disease caused by a specific bacterial infection would include a gumma in tertiary syphilis, a tuberculous ulcer, or actinomycosis. Deep mycotic infections, such as histoplasmosis or blastomycosis, will typically cause chronic, deep-based ulcers that may be granulomatous and friable in appearance.

Neoplastic Origin

Various neoplastic processes may manifest as chronic oral ulcers, including squamous cell carcinoma, adenocarcinoma of minor salivary gland origin, and mesenchymal malignancies, including malignant lymphoma.

Generalized Oral Ulcers

The category of generalized oral ulcerative disease is a broad one encompassing a wide variety of causative agents or diseases. Allergic stomatitis, whether caused by contact with or ingestion of an allergen, is primarily a diagnostic challenge, whereas radiation mucositis and cancer chemotherapy, though generally obvious clinically, may produce a significant therapeutic challenge. Neither primary herpetic gingivostomatitis nor oral candidiasis are particularly challenging with regard to diagnosis or treatment, but are included here for the sake of completeness.

The mucocutaneous disorders, in contrast, not only have variable, often overlapping, clinical features but also present a difficult therapeutic challenge. Oral ulcers secondary to systemic disease are not discussed in depth here.

Physical, Chemical, and Drug-Induced Oral Ulcers

Contact Stomatitis (Stomatitis Venenata)

The local reaction resulting from sensitization of the oral tissues to contact with a drug or other substance is called stomatitis venenata. This sensitization or altered reactivity of the oral mucous membrane is the result of prior exposure of this area to a causative drug or material or to a chemically closely related substance. Subsequent contacts following stimulation of the body's immune system to produce antibodies against the sensitizing agent will cause the local tissue reaction to recur. Since the antibodies are in the sensitized mucosa rather than in the circulation, no severe anaphylactic reaction occurs.

An allergen is an antigen that provokes an undesirable clinical reaction in a predisposed individual. Substances may seem to act as allergens even when the responses they produce are not mediated by antibodies. Various classes of agents may elicit a contact reaction in susceptible individuals. These include, but are not limited to, dental prosthetic materials, such as the acrylic resin materials used to fabricate dentures; oral and cosmetic preparations used by the patient, such as dentifrices, denture powders, mouthwashes, and lipstick; topical medications used by the patient, such as antibiotic lozenges; topical anesthetics used by the dentist, such as procaine; and a host of other agents, including chewing gum, candy, cough drops, and so on. This local response may vary from a mild erythema to erosive or vesiculobullous lesions. In some cases, the gingiva may take on an erythematous, boggy, granular appearance, for example, in plasma cell gingivostomatitis.

Treatment consists of identifying and discontinuing all contact with the causative agent. Although the clinician should be on the lookout for new agents with which the patient may have recently come in contact, it should be kept in mind that substances that have been routinely used by a patient for many months to years may also be the cause of the allergic reaction. Although prompt patient healing usually occurs, antihistamines will speed resolution of the lesions.

Drug Allergy (Stomatitis Medicamentosa)

Stomatitis medicamentosa is an allergic reaction that arises from the systemic administration of a drug to which the patient has previously been sensitized. This allergic reaction may present with a clinical spectrum varying from erythema and edema to erosive, vesicular, or bullous lesions that are not in themselves pathognomonic clinically.

Features to look for in establishing a diagnosis of stomatitis medicamentosa include sudden appearance of lesions, involvement of skin or other mucosal sites, and appearance of lesions subsequent to ingestion of drugs or medications. A list of the more common drugs known to cause reactions in susceptible individuals includes antibiotics (such as penicillin, tetracycline, erythromycin, and sulfa drugs), barbiturates, salicylates, phenytoin, and phenolphthalein.

Treatment consists of immediately discontinuing use of the involved drug, with administration of an antihistamine if the symptoms are severe. The prompt use of corticosteroid drugs may be indicated, especially in severe cases.

Mucosal reactions to drug therapy may exhibit specific clinical features, such as in lichenoid drug eruptions, lupus erythematosus-like eruptions, pemphigus-like drug reactions, and erythema multiforme.

Radiation Mucositis

Radiation reactions arising from treatment of malignancies in the oral cavity and oropharynx may be quite severe. Radiation mucositis is an early and acute reaction usually beginning during the second week of radiation as erythema followed by a spotty mucositis. The

foci of spotty mucositis coalesce to form areas of ulceration covered by a yellow-white pseudomembrane with a bright erythematous border. The lips are often involved, with a tenacious pseudomembrane and crusting being noted in the areas of ulceration. Exquisite pain and burning may be present even at rest and are exacerbated by contact with coarse or highly seasoned foods. Healing usually begins with the cessation of therapy and is usually complete within 3 to 4 weeks.

The "healed" mucosa may remain an atrophic dusky red color for a few weeks or months to the lifetime of the patient, making comfortable placement of a dental prosthesis over the area difficult. All of this is only exacerbated by the xerostomia that is a predictable, and for the most part permanent, side effect of radiation therapy to this area.

Treatment during this time can be both supportive and therapeutic. Rinsing the mouth with an oxidizing mouth rinse consisting of equal parts hydrogen peroxide (USP 3 per cent) and warm water or mouthwash will help to break up the thick, ropelike saliva covering the mucous membranes. The use of such a rinse serves two purposes, the first being to superficially debride the mucosal ulceration and help to reduce the amount of secondary infection that may ensue. Second, by helping to remove the superficial layer of thick mucous saliva from the oral mucous membranes, other supportive or therapeutic medications will have greater effect, as they will gain more intimate contact with the oral mucous membranes. Local anesthetic rinses containing equal parts of 2 per cent viscous lidocaine, elixir of Benadryl, and Kaopectate will reduce some of the discomfort and are particularly useful before meals. The mixture of tetracycline, nystatin, and decadron elixir may also prove useful and may serve to help decrease secondary infection. Chlorhexidine, 0.12 per cent, is an effective topical prophylactic as well as therapeutic agent against oral infection in patients with radiation mucositis. Additionally, prostaglandin inhibitors, such as indomethacin, have been shown to delay the onset of significant radiation mucositis and reduce the severity of this complication as it occurs.

Cancer Chemotherapy

Antineoplastic agents are extremely powerful drugs that have as a side effect the potential for disruption or destruction of the oral tissues. Chemotherapy-induced stomatitis is a common side effect of many of the antineoplastic drugs and may present as an excruciatingly painful mucositis involving any of the oral mucous membranes either in a localized or generalized fashion. Additionally, the concomitant suppression of the immune system by these chemotherapeutic agents may make the patient unable to fight secondary opportunistic infections that may develop in areas in which the mucous membrane has become ulcerated.

The oral manifestations of cancer chemotherapy have their onset shortly after the beginning of therapy, peak within a week after its cessation, and slowly resolve unless otherwise complicated by infection, hemorrhage, or reinstitution of therapy.

Uncomplicated cases of drug-induced mucositis are treated palliatively with cleansing mouth rinses, such as equal parts of hydrogen peroxide (USP 3 per cent) and warm water or mouthwash; topical anesthetics, such a mixture of 2 per cent viscous lidocaine, elixir of Benadryl,

and Kaopectate; antimicrobial agents, such as tetracycline and nystatin elixir mixed with decadron (see Appendix), or with the use of analgesics. Because of the increased susceptibility of the oral mucous membranes to secondary infection, the prevention and control of opportunistic and nosocomial infections must be considered an integral part of the basic management of these patients. A chlorhexidine, 0.12 per cent, rinse may be effective when used prophylactically in preventing oral infection, as well as offering a therapeutic benefit in resolution of existing oral infections from cancer chemotherapy.

Infection

Primary Herpetic Gingivostomatitis

HSV is an acute viral infection that may occur in the oral cavity in either a primary or recurrent form and is caused by one of two distinct strains of herpesvirus hominis, HSV-1 or HSV-2. The reader is referred to the section discussing secondary or recurrent labial and intraoral herpes in this chapter for a more in-depth discussion of this disease. In the case of primary herpetic gingivostomatitis, there is often a several-day prodromal period of low-grade fever, general malaise, and often mild to moderate gastrointestinal upset with loss of appetite. The symptoms may be rather vague and non-specific. Following the onset of symptoms, a burning or tingling of the gingiva may be noted, often accompanied by a bright red marginal gingivitis, erythema, and edema of the attached gingiva. Pain upon swallowing and cervical lymphadenopathy may be noted.

Any area of the mucosa may be involved, with the lips, gingiva, tongue, and palate most often affected. Vesicles form, which rupture and leave small, well-circumscribed ulcers or erosions that usually heal in 10 to 14 days. New vesicles continue to appear for several days. Varying degrees of severity may be encountered. Lip involvement may vary from only a few small vesicular ulcerative lesions to diffuse ulceration of the upper and lower lips with severe pain, oozing, and crusting. As vesicles on the gingiva erupt and break, a white pseudomembrane forms. The tongue is often covered by a white coating in addition to the vesicles and ulcers that may be present. Buccal mucosa and palatal lesions generally consist of vesicles and ulcers that often coalesce and are covered by a gray pseudomembrane with an erythematous halo.

Uncommon serious sequelae of primary HSV-1 infections include Kaposi's varicelliform eruption (eczema herpeticum), meningoencephalitis, and disseminated visceral herpes simplex.

Specific antiviral therapy is usually not employed in uncomplicated cases of primary herpetic gingivostomatitis as it is in cases of ocular and genital herpes. It must be remembered, however, that primary herpetic gingivostomatitis is a systemic disease and must be treated with proper supportive therapy. Adequate food and fluid intake is of great importance, especially in young patients who are more prone to dehydration. Prophylactic antibiotic therapy may be instituted to reduce the possibility of secondary bacterial oral infection. Mouth care is important to decrease the chance of secondary bacterial infection, as well as to decrease discomfort and enhance healing. In severe cases, a warm saline mouth rinse is of use in helping to cleanse the

oral cavity. As tolerated, a mixture of equal parts of hydrogen peroxide (USP 3 per cent) and warm water or mouthwash is excellent to help clean the teeth and mucous membranes of debris. The use of local anesthetic agents (see Appendix) following either a saline or peroxide mouth rinse will greatly decrease discomfort during meals. An oxidizing mouth rinse, such as hydrogen peroxide and warm water, is first rinsed around the mouth to locally debride the painful areas, after which time the local anesthetic agent is rinsed around the mouth and expectorated. Toothbrush therapy, using a soft brush, should be instituted as early as possible.

Candidiasis (Candidosis, Moniliasis, Thrush)

Candidiasis is the most frequent type of fungal infection involving the oral mucous membranes. The causative organism, *Candida albicans,* is a common normal inhabitant of the mouth and is nonpathogenic under normal conditions. Oral candidiasis usually occurs only when there has been either a reduction in the competitive oral microflora or a decrease in resistance of the host tissue to infection. The former is most commonly a result of long-term broad-spectrum antibiotic therapy. In the case of the latter, some underlying predisposing factor is usually present and should be searched for, such as infancy, pregnancy, decreased salivary flow, dentures, poorly controlled diabetes mellitus; *Candida* endocrinopathy syndrome, hypoparathyroidism, hypoadrenocorticism (hypoparathyroidism may precede other endocrinopathies by 10 years or more); debilitation from stress, malnutrition or underlying malignancy; immunosuppression, including acquired immunodeficiency syndrome (AIDS); lymphoreticular disorders such as agranulocytosis, leukemia, lymphoma, and so on; and high-dose radiation therapy (present or past) to the head and neck.

Oral candidiasis is classified according to its primary clinical manifestation. Acute pseudomembranous candidiasis (thrush) presents with profuse creamy white plaques, described as being milk curd-like in appearance, which cover the oral mucous membranes. These white plaques, which may cover any portion of the mouth, rub off easily, leaving a bright red, raw, bleeding surface. In some cases it may present as a brightly erythematous mucosa with only scattered white plaques.

Acute atrophic candidiasis is characterized by an inflamed symptomatic mucosa that is not specifically underlying a denture base and is often found following topical or systemic antibiotic therapy.

Chronic atrophic candidiasis most commonly presents as a bright red superficial erosion under dentures that are either poorly fitting or improperly cleaned. It is sharply demarcated and may perfectly outline the offending prosthesis on the underlying mucosa.

Chronic hyperplastic candidiasis is the form of the disease that presents clinically as a leukoplakic lesion that does not rub off the underlying mucosa. A biopsy is necessary to differentiate this form of candidiasis from other forms of leukoplakia. This is not to be confused with hairy leukoplakia, which, although once considered an early sign of human immunodeficiency virus infection (HIV), is now considered to be a nonspecific sign in

immunosuppression per se, and frequently demonstrates a superficial infection with *Candida albicans.*

Candida may extend to or primarily involve the corners of the mouth in patients who have lost vertical dimension of the jaws and appears as cracking and bleeding of the lip commissures with adherent white plaques that are easily stripped away. This occurrence is referred to as perlèche.

Although the diagnosis may be made primarily on the clinical features alone, cytologic smears are helpful in confirming it. This may be easily done in the office by making a smear of the suspected lesion on a glass slide, adding a drop of 20 per cent potassium hydroxide and examining the slide for the typical hyphae. Another method is to spray a fixative on the smear and submit it for cytologic evaluation of the periodic acid-Schiff (PAS)-stained slide.

Treatment of candidiasis comes in several forms, including topical therapy with nystatin oral suspension (500.000 to 600.000 units) or nystatin oral troche (Mycostatin pastilles, 200.000 to 400.000 units) four times daily, or by dissolving a clotrimazole troche (10 mg) in the mouth five times daily. Before topical administration of any of these medications, the oral mucous membranes should first be debrided with an oxidizing mouth rinse, such as equal parts of hydrogen peroxide and warm water. When topical therapy is unsuccessful, systemic therapy with ketoconazole tablets (200 mg) may be instituted. When a severe systemic infection exists, intravenous amphotericin therapy may be employed.

Dermatologic Disorders

Erythema Multiforme

Erythema multiforme is an acute, often recurrent inflammatory mucocutaneous disorder with, as its name implies, multiform manifestations. Although generally though of as self-limiting in nature, severe attacks without treatment may become chronic, lasting from 2 to 24 weeks. Two clinical forms are currently recognized, erythema multiforme minor and erythema multiforme major. The lesions of erythema multiforme minor are limited to the mucous membranes and the skin, whereas erythema multiforme major (Stevens-Johnson syndrome) is characterized by the presence of both systemic and severe mucocutaneous involvement.

Oral mucous membrane involvement is seen in almost all cases of erythema multiforme and occasionally may occur without skin lesions. It is characterized by diffuse oral erythema followed by formation of fragile vesicles that rupture quickly to form confluent areas of pseudomembrane-covered ulcerations. Ulceration and crusting of the lips, which may be hemorrhagic, is also noted. Skin lesions may present as the so-called classic iris, bullseye, or target lesion, or as an irregular macular or papular eruption with erythema and scab formation that have a predilection for the hands and feet. In erythema multiforme major, ocular involvement may vary from injection of the conjunctiva and purulent conjunctivitis to complete blindness. Urogenital mucous membrane involvement includes nonspecific urethritis, balanitis, and

vulvovaginitis.

The differential diagnosis of erythema multiforme includes benign mucous membrane (cicatricial) pemphigoid, pemphigus vulgaris, erosive lichen planus, Behçet disease, Reiter's disease, aphthous stomatitis, and herpetic stomatitis. When the diagnosis is in doubt, an oral biopsy may be performed, which is diagnostic for this disease.

There is no known single causative factor for the development of erythema multiforme, with numerous conditions having been mentioned as possible underlying causes. They include viral, bacterial, and mycotic infections, reactions to drugs and vaccinations, autoimmune diseases, radiation therapy for internal malignancies, and severe emotional disturbances. Of these, HSV is said to be the single most common precipitator of erythema multiforme, with occurrence of lesions typically appearing 10 to 14 days after a recurrent herpes-virus infection, with both HSV-1 and HSV-2 being recognized as precipitating agents. Another infectious agent commonly associated as a precipitation factor in erythema multiforme is *Mycoplasma pneumoniae.*

Other than infections, the most common causative agents are ingestants, primarily drugs, although food additives and dyes have also been implicated. Table 2 is a listing of drugs that have been implicated in the etiology of erythema multiforme major.

The treatment of the oral lesions of erythema multiforme varies with the severity of involvement. In mild cases, symptomatic therapy consisting of cleansing oral rinses and analgesics (see Appendix) will suffice. Topical steroid preparations (see Appendix) may also be useful in some cases. In cases in which lesions persist, systemic corticosteroid therapy may be used and is the treatment of choice in severe cases. Antibiotic therapy should also be used prophylactically in severe cases to combat secondary infection.

Lichen planus

Lichen planus is a relatively common chronic inflammatory mucocutaneous disease of unknown cause. Although considered a disease of adulthood, children are occasionally affected. The oral lesions of lichen planus are generally categorized into one of three clinical variants: reticular; atrophic, erosive, or vesiculobullous; and hypertrophic. In the classic reticular form of the disease, threadlike white lines are noted overlying otherwise normal-appearing mucosa in a reteform or annular arrangement, often producing a lacy appearance. These lacy white lines, which often intersect, are known as striae of Wickham. Although this pattern is considered to be the most common, Silverman and Griffith suggest that the erosive form may be seen more often. Whether or not this is the case, the development of ulcerative erosive or vesicular bullous lesions is certainly not uncommon.

In atrophic lichen planus, the mucosa takes on a smooth, dusky red appearance, usually with peripheral striae evident. Since the epithelium is thin, and therefore more susceptible to trauma, areas of erosion may occur. As the name implies, the erosive form of the disease is characterized by the development of areas of ulceration, erosion, and occasionally vesicle and

bulla formation. Degeneration of the basal cell layer is seen with destruction of the epithelium, leaving a bright red, often granular, surface. A yellow-gray pseudomembrane is often noted covering the more severely affected areas. These lesions are usually quite painful and if generalized throughout the oral cavity may be of a debilitating nature. This pattern of the disease is usually accompanied by characteristic white, lacy striae. Histologic confirmation of this form of the disease is accomplished through biopsy of the keratotic rather than the erosive areas.

Table 2. Drugs Implicated in the Etiology of Stevens-Johnson Syndrome

Allopurinol	Diflunisal	Penicarbazides
Amithiozone	Digitalis	Phenolphthalein
Antipurine	Furosemide	Phenothiazine
Antitoxins	Griseofulvine	Phenylbutazone
Antidiabetic agents	Gold salts	Phenytoin
Arsenic	Hydralazine	Proparacaine HCL
Barbiturates*	Ibuprofen	Rifampin
Belladonna	Iodides	Quinine
Bromides	Isoniazid	Salicilates
Carbamazepine	Meprobamate	Succinimide
Cephalexine	Mercurials	Sulfacetimide Na
Chloroquine	Minoxidil	Sulfonamides*
Chlorpropamide	Nitrogen mustard	Sulindac
Cimetidine	Oral contraceptives	Tetracycline
Clindamycin	Paramethadione	Thiouracil
Codeine	Penicillins*	Trimethadione
Co-trimoxazole	Phenacetin	Thiazides.

The oral lesions of lichen planus present most commonly in the buccal mucosa (80 per cent), almost always bilaterally, followed by the tongue (50 per cent), lips (22 per cent), palate (15 per cent), and gums (10 per cent), with the erosive form of this disease occurring at any of these locations.

Treatment of oral lichen planus is indicated only in the atrophic, erosive, or vesiculobullous form of the disease when pain is noted. Topical corticosteroid therapy (see Appendix) will facilitate healing in many cases in which the areas of erosion are localized. Chronic areas of ulceration that do not respond to topical corticosteroid therapy may be treated by intralesional injection with triamcinolone acetonide (see Appendix). In more generalized cases, however, systemic corticosteroid therapy may be necessary to effect symptomatic relief. Alternative therapy for severe oral erosive lichen planus may include griseofulvin, 250 to 1000 mg/day, alone or in combination with topical corticosteroid therapy. Although synthetic retinoids have been advocated in the treatment of chronic atrophic/erosive lichen planus, side effects are common and may outweigh the degree of improvement obtained. Additionally, though one study showed that topical vitamin A acid produced rapid resolution of the lesions of oral lichen planus, this improvement was often temporary, with recurrence quickly following cessation of therapy.

The periodic use of cleansing mouth rinses followed by a topical anesthetic rinse (see Appendix) may serve to decrease discomfort, especially during meals. Also, it should be remembered that prior to applying topical corticosteroid to the oral mucosa, an oxidizing mouth rinse consisting of equal parts of hydrogen peroxide (USP 3 per cent) and warm water should first be used to remove the adherent layer of mucous saliva.

Probably the least common and least typical form of the disease is the hypertrophic variety, which may be diagnosed on histopathologic examination of a lesion that was otherwise clinically leukoplakia.

Benign Mucous Membrane Pemphigoid (Cicatricial Pemphigoid)

Benign mucous membrane pemphigoid (BMMP) is a relatively uncommon benign, chronic, vesiculobullous disorder of mucosal tissues primarily involving the oral cavity and eyes, but also occasionally involving the genitals, urethra, vagina, rectum, nasal mucosa, pharynx, larynx, esophagus, and skin. It occurs most frequently during the sixth and seventh decades of life and demonstrates a predilection for women. The onset is usually mild with one or several localized lesions. Only rarely will multiple lesions involving many sites be seen in the initial phase. The oral mucosa is involved in all cases and may be the only site affected for many years. Areas of irritation, such as the gingiva, edentulous alveolar ridges, palate, buccal mucosa, and mucobuccal fold, are most frequently affected. Gingival involvement is characterized by a diffuse or patchy erythema and edema of both the attached and marginal gingivae, leading to a desquamative form of gingivitis. Tense subepithelial vesicles and bulla form and may be present for 24 to 48 hours before rupturing to leave a gray-white necrotic slough overlying a raw, red, bleeding ulcer. As the gingival lesions heal, a persistent erythema often becomes evident, which may persist for many months. Lesions in other areas of the oral cavity are primarily vesiculobullous in nature and are often surrounded by a wide zone of erythema. The vesicles and bullae collapse to leave an irregular area of ulceration, which occasionally heals with scar formation. After the gingiva, the buccal mucosa and palate are the most common sites of intraoral involvement, followed by the alveolar ridges, tongue, and lower lip.

The oral lesions in BMMP differ from those of other vesiculobullous diseases in their pattern of appearance, gradual onset, relatively slower healing, and occasional scar formation. The disease may be present for many years with intermittent periods of exacerbation and remission. The most serious sequela of this disease results from ocular involvement, which may eventually occur in as many as 60 to 75 per cent of cases and can lead to blindness. The diagnosis of BMMP is often made on the basis of the clinical findings and history alone.

Although the histologic findings are nonspecific and serve only to rule out other disorders, direct immunofluorescent studies of an intact mucosal specimen demonstrate antibodies fixed to the basement membrane zone, which are diagnostic of this disorder.

There is no single specific mode of therapy for treating BMMP. Because areas of irritation are frequently affected, reducing local inflammation in frequently involved areas, such as the

gingiva, is extremely important. A strict oral hygiene program consisting of proper brushing and flossing of the teeth, thorough periodic cleaning of the teeth in a dentist's office, and periodontal therapy as indicated will serve to keep gingival inflammation at a minimum. Partial or complete dentures must be checked for proper fit, as trauma from the ill-fitting prosthesis can cause vesicles and bullae to form. The use of a tissue conditioner in the denture may be helpful. Cleansing mouth rinses such as equal parts of hydrogen peroxide (USP 3 per cent) and water or mouthwash will also serve to locally debride the tissues and reduce inflammation. A topical anesthetic mouth rinse (see Appendix) may be needed to provide temporary relief of pain, especially at mealtime. Topical corticosteroid preparations (see Appendix) may be useful in some cases. Following the use of a cleansing mouth rinse, the area in question should be cleaned and dried with a cotton swab or gauze. A small amount of steroid paste is then dabbed on. Dipping a finger in warm water and "tamping" the paste down will help set the preparation over the affected area. Systemic corticosteroid therapy provides the most effective means of controlling this disorder, especially in severe cases. The treatment regimen must be tailored to the patient according to sites of involvement and severity of disease, minimizing side effects by making every effort to use the least amount of drug possible.

Bullous Pemphigoid

Bullous pemphigoid is an uncommon chronic mucocutaneous bullous disease of the skin that may also involve the oral cavity. Although bullous pemphigoid involves the skin in 100 per cent of cases, occasional cases are noted in which oral lesions precede skin involvement. Estimates of the frequency of oral lesions vary. Shklar and co-workers report oral mucous membrane involvement in bullous pemphigoid as being rare, whereas Laskaris and associates reported involvement of the oral mucous membranes in more than 39 per cent of cases.

Oral lesions in bullous pemphigoid occur most commonly in the buccal mucosa, palate, and tongue, followed by the lower lip, gingiva, upper lip, and floor of the mouth. The oral lesions are indistinguishable from those described in the previous section for BMMP, with the exception of intraoral distribution. Unlike BMMP, gingival involvement is a relatively uncommon intraoral finding in patients with bullous pemphigoid.

The histopathologic, as well as the immunopathologic, findings in both BMMP and bullous pemphigoid are similar and suggest that these two diseases are in all likelihood variants of the same entity.

The treatment for bullous pemphigoid is the same as that previously described for BMMP.

Pemphigus Vulgaris

Pemphigus is an intraepithelial vesiculobullous disorder involving the skin and mucous membranes that was almost invariably fatal prior to the advent of corticosteroid therapy. There are four clinically recognized variants of this disease; however, only pemphigus vulgaris will be discussed here.

Although primarily a disease of adulthood, with the majority of cases occurring in the 40- to 70-year-old age group, a juvenile counterpart is known to exist. Females are involved more often than are males, and the Jewish population shows a definite predilection for the development of pemphigus vulgaris. Oral lesions are almost invariably present in this condition and are the initial presenting symptom in the majority of cases. In one study, pemphigus vulgaris was confined to the oral mucosa in 45 per cent of the 157 cases reported. In a detailed description of the clinical findings in 28 cases of pemphigus vulgaris, all patients presented initially with mouth or throat lesions, or both, with two thirds of the respondents claiming to have had a sore throat related to their pemphigus vulgaris lesions. The gingiva, palate, and buccal mucosa were most frequently involved, followed less often by the lips, tongue, and floor of the mouth.

Lesions characteristically present as multiple, fragile, intraepithelial bullae that quickly collapse to form irregularly shaped erosions or ulcers covered by a gray-white necrotic slough. Intact bullae are seldom seen within the oral cavity. The gingiva may have a desquamative type of appearance with accompanying areas of erythema and erosion. The average duration between onset of oral symptoms and diagnosis has been reported to be between 7 and nearly 12 months. Several techniques may be used to diagnose pemphigus vulgaris: hematoxylin and eosin-stained tissue biopsy, tissue smear examination (Tzanck's test), or immunofluorescence studies. Direct immunofluorescence tests on biopsy material are the most accurate diagnostic approach. Indirect immunofluorescent examination of a patient's serum can be used both for diagnosis and for evaluation of the degree of disease control.

As already mentioned, prior to the introduction of corticosteroid therapy, pemphigus vulgaris was a uniformly fatal disease. Systemic corticosteroid therapy is still the treatment of choice, producing complete remissions in many cases. Topical and intralesional corticosteroids may also be used. Additionally, immunosuppressive agents, such as cyclophosphamide (Cytoxin), azathioprine (Imuran), and dapsone may be used adjunctively with prednisone to enhance the effect of the corticosteroid and reduce its usage. Secondary infection is often a complicating factor, and systemic antibiotic therapy may be indicated.

Lupus Erythematosus

Lupus erythematosus (LE) is a relatively common multisystem disorder that is included in the classification of connective tissue diseases. Oral lesions are found in both discoid lupus erythematous (DLE), the chronic cutaneous variety of LE, and in systemic lupus erythematosus (SLE).

Oral lesions occur in about 20 per cent of patients with DLE. Early lesions are often characterized by erythema without striae. The classic well-developed discoid lesions are characterized by a central zone of erythema with white spots and a 2- to 5-mm-wide border of white striae radiating from the center. Occasional lesions appear as white plaques and may be confused with leukoplakia. The buccal mucosa and lip lesions are commonly involved. Symptoms such as oral discomfort, a burning sensation from hot spicy food, tenderness (especially on toothbrushing), and a feeling of tightness and dry mouth are common complaints.

Oral mucosal lesions may also be found in SLE, the acute systemic form of this disease, which may appear discoid in nature or may be relatively nonspecific oral mucosal lesions that are a reflection on the patient's overall general disease state.

The histologic findings in oral discoid lesions are fairly characteristic but not pathognomonic. Direct immunofluorescence of the biopsy specimen is of diagnostic value. Laboratory tests useful in diagnosing SLE are the LE test, the fluorescent technique for antinuclear antibody (ANA), and immunofluorescent skin tests.

Intraoral therapy for LE may be largely facilitated by treatment of the patient's general systemic disease. Intraoral supportive therapy includes the use of oxidizing mouth rinses to cleanse the involved mucous membranes, followed by the use of anesthetic mouth rinses (see Appendix) to relieve the burning sensation that is often present. Application of topical steroids, as well as intralesional steroid injections (see Appendix), may also be helpful.

Systemic Diseases

Although a number of systemic diseases are known to present as erosive, ulcerative or hemorrhagic, generally painful, lesions in the oral cavity, none occurs with sufficient frequency to warrant a separate section in this chapter. Stomatitis secondary to systemic disease most often occurs in uncontrolled diabetes mellitus, uremia, Crohn's disease, and blood dyscrasias, such as leukemia, pancytopenia, agranulocytosis, cyclic neutropenia, and sickle cell anemia. The oral lesions in these disorders may be confused clinically with those found in many of the diseases already discussed and therefore should at least be considered in the differential diagnosis. It is in cases such as these that a thorough clinical history, in addition to a clinical examination, becomes especially important.

Stomatitis secondary to systemic disease is treated primarily by control of the disease process itself. Many of the local supportive measures previously described in this chapter (cleansing mouth rinses, topical anesthetic rinses, promotion of good oral hygiene, and local periodontal therapy), consistent with the patient's medical status, may be useful in decreasing both the patient's discomfort and the chance of more generalized involvement than may already be present. The use of antibiotics or antimycotic therapy presents a difficult problem in that although control of local infection may be achieved, this treatment may result in a superinfection that is quite difficult to control. In severely debilitated patients, the occurrence of a diffuse gangrenous stomatitis must be watched for as a secondary complication of the oral lesions already present.

Appendix. General Principles of Treatment

I. *Removal of Known Causative Factors or Agents.* A prerequisite to initiation of the healing process.

II. *Careful Attention to Oral Hygiene.* Meticulous attention to oral hygiene will speed healing by improving the overall health of the oral mucous membranes and by decreasing the chances of secondary infection.

III. *Cleansing Mouth Rinses.* A mild oxidizing mouthwash consisting of hydrogen peroxide (USP 3 per cent) diluted to a 1:1 or 1:2 solution with warm water or Cepacol (cetylpyridinium chloride) can be used as often as every 2 to 3 hours. A mouthwash such as this should also be used prior to the use of anesthetic and antibiotic rinses, antifungal agents, and topical corticosteroids.

IV. *Anesthetic Mouth Rinses.*

A. Antibiotic rinses - a mouthwash of tetracycline for oral suspension containing uncoated tetracycline crystals (250 mg/teaspoon, 5 mL) is held in the mouth over the area of the lesions and is rinsed in a flushing motion for a period of 2 to 5 minutes prior to expectoration.

B. Antifungal agents.

1. Nystatin oral suspension, 4 to 6 mL (400.000 to 600.000 units), dispersed to both sides of the mouth with a measured dropper may be used. This solution should be rinsed around the mouth at least 5 minutes before swallowing. Mycostatin pastilles, an oral troche (200.000 units), may be dissolved in the mouth, one to two troches four times a day.

2. Clotrimazole troches (Mycelex Troches), one troche five times a day for 14 consecutive days. Used in the treatment of oropharyngeal candidiasis. Safety for use in children less than 3 years of age has not been established.

C. Antiviral agents.

1. Idoxuridine (Stoxil) ophthalmic ointment applied every 4 hours during prodrome and very early vesicle stage only of recurrent herpes labialis.

2. Acyclovir (Zovirax) ointment 5 per cent applied every 3 hours starting with the earliest prodrome and during the vesicle stage of

recurrent herpes labialis.

D. Multiple-agent therapy.

1. In some instances, a combination of a local anesthetic with an antibiotic and antifungal agent may be indicated. A mixture of elixir of diphenhydramine, tetracycline, and nystatin may be effective in these cases.

2. A mixture of dexamethasone, nystatin, and tetracycline may be useful as palliative therapy for burning or geographic tongue.

E. Topical corticosteroids - triamcinolone acetonide 0.1 per cent (Kenalog in Orabase) and fluocinonide 0.05 per cent (Lidex gel or equal parts Lidex ointment and Orabase) have been shown to be effective topical steroid agents when used properly in a stepwise fashion as follows:

1. The mouth should first be thoroughly rinsed with a cleansing mouth rinse as previously described. This will serve to rid the oral mucous membranes of the layer of adherent mucous saliva and other debris.

2. The area to be treated should then be thoroughly dried with a 2x2 gauze sponge.

3. Taking great care to keep this area dry, the corticosteroid paste should be dabbed on (not rubbed in) the ulcerated mucous membrane.

4. The patient then dips a finger in warm water and tamps the newly applied corticosteroid paste onto the mucous membrane to "seal" the medication in place. The topical corticosteroid may be applied four times a day, preferably following meals and at bedtime.

F. Injectable corticosteroids - triamcinolone acetonide (10 mg/mL) may be injected submucosally in amounts of no more than 1 mL/cm.

V. *Systemic Therapy.*

A. Antibiotic therapy - in some instances, such as a severe case of primary herpetic gingivostomatitis with subsequent secondary bacterial infection that restricts the patient's ability to take fluids or food by mouth, it may be necessary to institute intravenous antibiotic therapy. In cases such as this in which the infection is limited to the oral cavity, penicillin is the

antibiotic of choice.

B. Antifungal agents - resistant cases of severe oral candidiasis may be treated with ketoconazole (Nizoral) as a single daily administration of 200 mg (one tablet) which may be increased to 400 mg once daily in the case of very serious infections, or if clinical response is insufficient within the expected time. Although the minimum treatment time for candidiasis is usually 1 to 2 weeks, patients with chronic mucocutaneous candidiasis may require maintenance therapy.

C. Corticosteroids - oral and intramuscular corticosteroid therapy may be indicated in treating severe generalized cases of stomatitis, especially the mucocutaneous disorders. The type and dosage of medication used must be individualized according to the diagnosis and severity of the disease state present.