Oral manifestations of Tropical Infectious Diseases of Central and South America. Part I: Protozoal and Helminthic Infections; Part II: Bacterial and Mycotic Infections.

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Oral manifestations of tropical infectious diseases are seldom discussed extensively in most current textbooks of oral diagnosis or oral pathology. This paper is the result of a survey of literature in which the oral manifestations of infectious diseases of particular significance to Latin America have been described. In addition to emphasizing the oral manifestations, the major clinical and therapeutic aspects of each disease are also discussed in this two-part paper. Part I features protozoal and helminthic diseases and Part II features bacterial and mycotic infections.
Oral Manifestations of Tropical Infectious Diseases of Central and South America

Part II: Bacterial and Mycotic Infections

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INTRODUCTION

Knowledge of the oral manifestations of tropical diseases has not been well documented. Recognition of such signs or symptoms which may be present during oral examination would certainly enhance overall patient management. It is hoped that this paper may augment the clinician's awareness and knowledge of this facet of a frequently overlooked group of diseases.

BACTERIAL INFECTIONS

1. Treponematoses.

   Syphilis. One group of particular interest is the treponematoses. The spirochetal infection, syphilis, caused by *Treponema pallidum,* is probably of greatest interest to the oral diagnostician. Syphilis is a highly infectious venereal disease of great morbidity when not treated. Although 90% of primary infections involve the genitalia, more than 75% of extra-genital primary lesions occur in and about the mouth.6 Although syphilis is not really considered a tropical disease *per se,* the World Health Organization reported more than 80,000 cases throughout Latin America in 1975.27 Because the general clinical and oral manifestations of syphilis have been thoroughly described in most text books of pathology or diagnosis, discussion of clinical features will not be included within this paper.

   Yaws. The other treponematoses are generally considered to be of a nonvenereal nature. *Treponema pertenue* is a spirochete which is both morphologically and immunologically identical to *T. pallidum.* *T. pertenue*
is the etiologic agent which causes both yaws and bejel, the latter being limited geographically to the Middle East, eastern Europe and Africa. Only yaws has been considered to be within the scope of this discussion.

Although *T. pertenue* is morphologically indistinguishable from *T. pallidum*, the clinical features of yaws are rather distinct from those of syphilis. Epidemiologically, yaws is most prevalent among rural populations of humid tropical regions, particularly Mexico, Panama, and northern South America. The disease occurs most frequently before the age of ten years and is rarely congenital as infants are usually immune for up to 18 months after birth. Yaws is a highly contagious disease which is transmitted from man to man by direct skin contact; however, the organisms cannot penetrate intact skin.

The primary lesion, colloquially called the "mother yaw" is a cutaneous lesion occurring three to six weeks after exposure and usually at the site of primary infection. It is an erythematous, granulomatous papule which may or may not become ulcerated, and may attain a size of two inches in diameter. It is usually painless, unless secondarily infected, and may persist for several weeks. The primary lesion is highly infective, and *T. pertenue* are readily demonstrated by darkfield microscopy.

Secondary lesions usually occur weeks to months after the appearance of the primary lesion. These are granulomatous verrucoid lesions which are smaller, more numerous, and occur in crops, particularly around the mucocutaneous borders of the mouth and anogenital areas.
These lesions are also infectious and heal within weeks to months with no scar. Secondary cutaneous lesions also may be accompanied by multiple punched-out radiolucent lesions of the long bones as well as periosteal proliferations. These changes usually disappear with the healing of skin lesions; however, the extremities involved may remain deformed.

Tertiary yaws occurs in untreated or improperly treated patients, most often during adolescence, and several years after the earliest signs appear. These lesions consist of gummatous granulomata of the skin and subcutaneous tissues, producing destructive changes in the deeper tissues including the underlying bone. In advanced cases, a characteristic facial deformity called "gangosa" results from destructive involvement of the maxillary nasal processes and hard palate and heals with heavy scarring. The lesions of tertiary yaws are rarely infectious and are essentially free of organisms.

Like syphilis, yaws is readily treated and controlled with penicillin therapy.

2. Lymphogranuloma Venereum

Lymphogranuloma venereum (LGV) is a venereal disease caused by infection with microorganisms once designated as a virus of the Bedsonia or Miyagawaniella, and which are now classified morphologically as bacteria of the genus Chlamydia. Still, many consider the exact nature of the organism to be undetermined. LGV may be contracted by contact with either an infected individual or from an asymptomatic carrier. Although the disease occurs in temperate climates, there is a high incidence
throughout tropical regions.

Clinical manifestations are characterized as primary lesions (which occur at the site of contamination), secondary reticuloendothelial involvement with prominent regional lymphadenopathy, and tertiary or late stage manifestations of generalized dissemination.

Primary lesions usually present as anogenital or oral vesiculo-ulcerations. The primary oral lesion has been described as a nonpainful vesicle on the dorsum of the tongue. The vesicle enlarges and ruptures, becoming a painful ulcer up to 1 cm in diameter, having a raised border and a shallow gray base. Ulcers heal with scarring and retraction of tissues.²

Late stage changes include atrophy of the lingual papillae, formation of granulomatous papules on the dorsal surface of the tongue and painful sensitivity to salty or sour foods.

One to five weeks after initial lesions appear, a painful suppurative regional lymphadenitis occurs. Lymphadenopathy may be accompanied by other nonspecific features including fever, headache, sweats, nausea, malaise, weight loss, polyarthritis, and splenomegaly.

Diagnosis is more reliably confirmed by the use of complement fixation techniques than by the intradermal Frei test.

Antibiotic treatment of lymphogranuloma venereum has consisted primarily of sulfonamides, tetracycline, and chloramphenicol, which have all had variable effectiveness.

3. Leprosy

Leprosy is a chronic granulomatous disease caused by the acid-fast bacillus Mycobacterium leprae. Although man has been afflicted with the
disease since before the Christian Era, leprosy is still a prominent problem. An estimated eleven million people are affected around the world, with prevalence in the tropical and subtropical regions and endemicity in much of Central and South America.\textsuperscript{26} During the period from 1940-1968, 46 U. S. military personnel contracted leprosy while serving in countries where leprosy is endemic.\textsuperscript{6}

Manifestations of the disease present a spectrum of degrees of involvement which is determined primarily by individual host resistance to \textit{M. leprae}. Leprosy may occur at any age, although most cases are diagnosed during the first three decades. Transmission may occur by direct contact with skin or through the secretions of nasal and oral mucous membranes; however, only the lepromatous form is considered to be contagious. Dermal lesions of this form of leprosy are characterized as large granulomatous nodules (lepromas) which initially involve subcutaneous tissues of the face. Dermal adnexal structures including facial hair, eyebrows, and eyelashes are replaced by the granulomatous infiltrations. The other forms generally have minimal bacteriological activity.

Oral manifestations, although rare in tuberculoid or dimorphous leprosy, have been reported in 20-60\% of lepromatous cases.\textsuperscript{19} Oral lesions occur most often as a result of extension from involvement of nasal mucous membranes.\textsuperscript{17} Mucosal involvement of both nasal and oral cavities is characterized by early stages of invasion and proliferation and later stages of resolution and fibrosis. Early nodules produce symptoms of nasal stuffiness, coryza, and epistaxis. Ulceration with
extension to subjacent supportive structures leads to the typical
nasal collapse. Saddle-nose deformities and palatal perforations
occur in 25% of lepromatous patients due to destruction and resorption
of the nasal cartilage and nasomaxillary complex. Oral lesions are
characterized as yellow-red or brownish-red hemorrhagic sessile nodules
occurring most frequently on the maxillary incisive papilla, lips,
tongue, soft palate, uvula, and glossopharyngeal arches. The
sequelae of ulceration, necrosis, and subsequent fibrosis, in later
stages frequently result in microstomia, uvular atrophy, and fixation
of the soft palate. Lepromata on the dorsum of the tongue have been
reported in 25% of all cases, and chronic gingivitis and periodontitis
are common. In addition to oral soft tissue involvement, reported
changes affecting the dentition commonly include loosening of teeth,
morphologic anomalies — primarily of a hypoplastic nature, and myco-
bacterial pulp necrosis. Dental involvement is most common in the
maxillary anterior teeth.

In addition to peripheral nerve involvement, hypesthesia, hyper-
esthesia, and paralysis may result from extension to the trigeminal,
facial, and glossopharyngeal nerves. However, neural involvement is
much more frequent in tuberculoid leprosy than in the lepromatous form.

Lesions of leprosy must be differentiated from those of neurofibroma-
tosis, leishmaniasis, mycoses, and lupus vulgaris. Diagnosis is con-
firmed by histologic demonstration of acid-fast bacilli and the Mitsuda
skin test. Current therapy consists of administration of sulfone com-
pounds. Diaminodiphenylsulfone is the drug of choice. Patients are
usually treated for four to five years or longer to prevent relapse.

4. **Gonorrhea**

Gonorrhea is a highly contagious venereal disease caused by the gram-negative diplococcus, *Neisseria gonorrhoeae*. The disease has a world-wide occurrence with approximately 137,000 cases reported throughout Latin America in 1975. Gonorrhea is a disease of increasing significance to the oral clinician. The incidence of gonorrhea has been increasing around the world since the early 1970's, being particularly associated with an increasing number of penicillin-resistant strains of the bacterium. Oral sexual practices have contributed to an increased prevalence of oral manifestations. These are of particular significance to the dental practitioner because an estimated 75-80% of female patients and 15-20% of male patients may be clinically asymptomatic. These patients may, therefore, be a reservoir for transmission to the dentist, his auxiliaries, and even to other patients if proper sterilization techniques are not utilized. Furthermore, such complications as oral gonococcal osteomyelitis could result from surgical manipulation of affected oral tissues.

Oral lesions may occur either directly, through oral sexual practices, or indirectly, through dissemination of the infection. Although the tonsils and oropharynx are the most frequently involved oral areas, virtually all of the oral mucous membranes have been reported to be affected.

Earliest oral symptoms may be the sensation of burning, dryness,
or itching of the mucosa, with acute pain following in a few days. Salivary flow may be increased or decreased and may be distasteful, indicating sialadenitis. Fétor oris is common, and symptomatic patients usually have a pyrexia of 102°F or greater. Primary lesions may manifest as an acute ulcerative inflammation of the lips, tongue, buccal mucosa, soft palate, uvula, and pharynx. In some patients, a diffuse painful stomatitis occurs in which all oral membranes become fiery red and edematous. Speech, swallowing, and simple mouth movements become extremely painful. The gingiva may present a diffuse spongy erythema with necrosis of the interdental papillae. Also, acute suppurative parotitis and cervical and submandibular lymphadenitis have been reported.

Chue has emphasized both the difficulty in attempting to clinically diagnose oral gonorrhea due to its varied manifestations and the high level of suspicion which is necessary in light of these features. Diagnosis may be verified by bacterial culturing as well as by fluorescent antibody techniques. During periods of acute oral gonococcal infections, surgical procedures should be avoided and only emergency dental procedures are recommended.

Gonorrhea is best treated with procaine penicillin, ampicillin, or tetracycline. In the case of infection by penicillin-resistant strains, augmentation of antibiotic therapy with probenecid has been effectively used to ensure high blood levels of the antibiotic. However, van Overbeek has stressed that oropharyngeal gonorrhea requires more therapy for longer durations than urogenital infections.
FUNGAL DISEASES

Paracoccidioidomycosis. Paracoccidioidomycosis (South American Blastomycosis) is a chronic granulomatous disease caused by infection with the fungus Paracoccidioides brasiliensis. The disease is endemic throughout Latin America with particularly high incidence in Brazil, Venezuela, and Colombia. Approximately 90% of all cases have been reported in male patients 30-50 years of age.\textsuperscript{7,18} Infection most commonly occurs through inhalation of spores resulting in a pulmonary infection which may or may not become disseminated. Not uncommonly, however, a primary focal mucocutaneous infection may occur due to traumatic inoculation of organisms while sucking on a blade of grass or chewing a piece of unprocessed wood as a toothpick. Interhuman transmission occurs rarely, only following prolonged intimate contact.

Three clinical forms of the disease have been described. A subclinical form has been reported in which approximately 10% of the normal rural population in endemic areas develop a positive skin test to paracoccidioidin antigen. The primary pulmonary form may clinically resemble pulmonary tuberculosis, in which 8% of the patients develop oral or pharyngeal lesions. In patients with disseminated paracoccidioidomycosis, 60-90% have pulmonary infection which may be clinically inapparent.\textsuperscript{7} However, lesions of the oral mucosa occur most often in disseminated infections. Cutaneous lesions, which often occur as an extension of mucosal involvement, have been described as erythematous papules, pustules, and desquamations, as well as vegetative ulcers resembling leishmaniasis.
Dissemination of the fungus may also produce lesions of the gastrointestinal canal, hepatobiliary system, central nervous system, bones, and adrenal gland.

Oral manifestations most commonly include erythematous proliferative granulomata which become ulcerative and ultimately heal with fibrosis and cicatrization. Lesions usually involve the lips, labial and buccal mucosa, tongue, floor of the mouth, palate, and pharynx. Hemorrhagic gingivitis and loosening of the teeth may be an early sign of infection and hyperpigmentation of the mucosa is a frequently observed indication of adrenal gland involvement. Other features described include regional lymphadenopathy and sialorrhea which may be so severe as to interrupt the patient's sleep.

Diagnosis of paracoccidioidomycosis is verified by histological examination of biopsied tissue, mycological examination of cultured material and immunological testing. The infection is usually effectively treated with sulfonamide drugs or Amphotericin B.

Histoplasmosis. There are two forms of histoplasmosis infection in humans: a. The "classical" form is caused by the intracellular fungus *Histoplasma capsulatum* which has a predominant distribution in the western hemisphere, particularly in the Ohio–Mississippi River Valley of the United States and throughout Central and South America; and b. African histoplasmosis, caused by *Histoplasma duboisii*, occurs almost exclusively in Africa and, therefore, will not be discussed in this context.
Classical histoplasmosis was first described in the Panama Canal Zone in 1906. It has been estimated that 20-25% of new arrivals to that area develop a positive histoplasmin antibody titer within six months. The fungus is believed to grow primarily in soil enriched by bird excrement, and infection occurs by inhalation of spores with contaminated dust. The disease is basically a mycosis of the reticulo-endothelial system; however, it may present as a benign primary pulmonary form, a mucosal form (with or without cutaneous involvement) or a disseminated form with widespread involvement. Disseminated disease may first manifest clinically with oral lesions, but gradually progresses to produce lymphadenopathy, splenomegaly, hepatomegaly, digestive disturbances, and lesions of the adrenal glands, bone, kidneys, heart, and central nervous system. Also, tuberculoid pulmonary lesions (histoplasmosomas), which frequently heal by calcification, may be a prominent feature of disseminated histoplasmosis. General signs of infection may include low grade fever, cough, recurrent epistaxis, idiopathic weight loss, and lymphadenopathy. Granulomatous lesions of the bone may be so severe that approximately 75% of all disseminated cases develop anemia and 50% are leukopenic. Leukocytosis is extremely uncommon, particularly in advanced histoplasmosis.

Lesions of the oral mucosa are found in 30-50% of the disseminated cases. Oral lesions have been described as vegetative or nodular granulomas or fungating ulcerous lesions with an indurated border around a proliferating fleshy center. Lesions may involve the lips, tongue, gingiva, and palate. Buccal mucosa is most often involved by an
ulcerous process which spreads over the adjacent gingiva and is covered by a pseudomembrane. Furthermore, patients who have pharyngeal or laryngeal involvement frequently complain of soreness, dysphagia, and dysphonia.\textsuperscript{16}

Diagnosis of histoplasmosis may be verified by histologic identification of the yeasts in multinucleated giant cells of biopsied tissue, histoplasmin skin testing, and mycological isolation of the organisms.

Amphotericin B is the drug of choice for the treatment of histoplasmosis; however, Saramycetin and Bactrim have also been used effectively.

\textbf{Rhinosporidiosis.} Rhinosporidiosis, caused by the aquatic fungus \textit{Rhinosporidium seeberi}, is a chronic granulomatous infection of mucous membranes, and less often of skin. Although 90\% of all infections are reported from India and Ceylon,\textsuperscript{5} there is a world-wide distribution with Latin American incidence being highest in Mexico, Cuba, Brazil, Argentina, and Paraguay. At least 36 cases have been reported from the United States. The disease is not contagious, however, infection is associated with extended exposure to natural waters.\textsuperscript{10}

Primary lesions occur most often on nasal mucosa with symptoms of itching and mucinous discharge. Seventy-five percent of those infected present with exuberant granulomatous lesions of the nasal mucosa, oropharynx, or soft palate.\textsuperscript{10} Lesions may also occur on the conjunctiva, lacrimal sac, larynx, penis, vagina, rectum, and skin. Systemic dissemination is very rare.

Diagnosis of rhinosporidiosis is verified by histologic identification
of sporangia which may reach 350 μ in diameter within the granulomatous proliferations. Culturing, animal inoculation, and immunological testing have been unsuccessful and the actual classification of R. seeberi as a fungus or as a parasite of aquatic plants is still uncertain.

Chemotherapeutic management of this disease has been ineffective and current treatment has consisted of surgical excision.\(^\text{11}\) However, recurrences are not uncommon.

**Differential Diagnosis**

Many of the diseases discussed in this paper have clinical features which may be quite similar. Obviously, the diagnosis becomes reliant upon the results of special laboratory tests, many of which have been specified. However, if the clinician is able to develop a differential diagnosis, from which certain diseases may be excluded, his task is made much easier. The following tables not only summarize the outstanding clinical features of the diseases included in this paper, but may also aid in the formulation of a clinical differential diagnosis. It must be emphasized that the following lists are not to be in exclusion of, but in addition to, those entities of infectious, neoplastic, immunological, nutritional, etc. etiology which the clinician might ordinarily consider.

1. **Diseases Presenting Cutaneous and Mucosal Nodules**
   - Leprosy
   - Post kala-azar dermal leishmaniasis
   - Cysticercosis
   - Trypanosomiasis
2. **Diseases Causing Mucocutaneous Ulcers**
   - Mucocutaneous leishmaniasis
   - Lymphogranuloma venereum
   - Histoplasmosis
   - Paracoccidioidomycosis
   - Malaria

3. **Diseases Causing Proliferative Granulomatous Mucosal Masses**
   - Paracoccidioidomycosis
   - Histoplasmosis
   - Rhinosporidiosis

4. **Diseases Causing Severe Destruction of Orofacial Tissues**
   - Espundia (latent mucocutaneous leishmaniasis)
   - Malaria
   - Yaws
   - Leprosy

5. **Diseases Causing Hemorrhagic or Erythematous Inflammatory Reactions in Oral Mucosa**
   - Kala-azar
   - Gonorrhea
   - Taeniasis

6. **Diseases Producing Diffuse Mucosal Edema**
   - Filariasis

7. **Diseases Producing Oral Signs of Anemia**
   - Malaria
   - Hookworm
The opinions or assertions contained herein are the private views of the authors and are not to be construed as reflecting the views of the Department of the Army or the Department of Defense.

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