**Oral Manifestations of Tropical Infectious Diseases of Central and South America.**

**I. Protozoal & Helminthic Infections; Part II. Bacterial and Mycotic Infections**

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**Abstract:**
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 I: Protozoan and Helminthic Infections

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INTRODUCTION

The key to proper treatment and good patient management is proper diagnosis. While oral diagnosis is strongly emphasized in most current American dental curricula, there is decidedly little emphasis placed on those conditions, e.g. tropical diseases, which are uncommon in the United States, but which are of a much greater significance in other areas of the world. Furthermore, few of the currently available texts of oral diagnosis or oral medicine contain any depth of information about oral manifestations of tropical diseases. Thus, there are limited references available to the practitioner who may have the interest or the need for such a resource. The many presently existing and potential overseas assignments for the military practitioner, Peace Corps healthworker, etc. similarly require familiarization with manifestations of such diseases which may be either specific to, or endemic, in a particular duty locale.

The purpose of this paper is to broaden the clinician's awareness of the nature and presentation of a group of diseases which are frequently overlooked. It is hoped that this paper may serve as a concise, yet comprehensive, diagnostic reference for the student, teacher, and practitioner in the study of these diseases.

The 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. Although the oral manifestations of the most prevalent diseases are emphasized, the major clinical and therapeutic aspects are also discussed in this two-part paper. Part One
features protozoal and helminthic diseases and Part Two features bacterial and mycotic infections. The most significant clinical features of each disease are summarized in Table I at the conclusion of Part Two.

PROTOZOAN INFECTIONS

The unicellular parasites which infect man have been grouped into four basic classes based on the organisms' means of locomotion. These include Rhizopoda (which move by pseudopodia), the Sporozoa (which are nonmotile), Mastigophora (flagellates), and Ciliata.

1. Rhizopoda

The class Rhizopoda include primarily the amoebae of the alimentary canal. *Entamoeba gingivalis*, the first parasitic amoeba to be discovered, is commonly found in the oral cavity. It is most often found in the dental plaque of patients suffering from moderate to severe periodontitis, and although often implicated, its role as an oral pathogen has not been substantiated. Since *E. gingivalis* has been isolated occasionally from the normal healthy mouth, it is now considered an opportunist rather than a pathogen.

**Amoebiasis.** Of the class Rhizopoda, only *Entamoeba histolytica*, the cause of amoebic dysentery, is a known pathogen. Amoebiasis is a highly infectious intestinal disease which is most prevalent in areas where poor sanitation exists. The parasites are transmitted through fecal contamination of food, water, and other articles of daily life. In 1975 an estimated 75% of the rural population of Latin America and
at least 20% of the urban population had inadequate sewage facilities. Consequently, amoebiasis is a serious problem in many countries of Latin America, accounting for as much as two deaths per 1000 population. Amoebiasis may be characterized by an insidious onset with mild to moderate diarrhea, or may be fulminating with abdominal cramps, vomiting, nausea, pyrexia, severe diarrhea, and melena. Oral manifestations are not a prominent feature and have been described as a moist, furred tongue. Diagnosis is usually confirmed by demonstration of parasites in the stool.

2. Sporozoa

The second major class of infectious protozoans is the class Sporozoa, the members of which have a sexual phase of their life-cycle in an arthropod vector and an asexual phase in man. Within this class is the genus Plasmodium, four species of which cause human malaria.

Malaria. Malaria is an infection of the hematopoetic system by Plasmodium vivax, Plasmodium malariae, Plasmodium ovale, or Plasmodium falciparum. The occurrence of the disease is predicated upon the distribution of the Anopheles mosquito, of which at least 50 species support the life cycle of the Plasmodia.

The serious nature of the disease has historically been most appreciated by those involved in military operations in endemic areas. During World War I, almost 80% of European troop hospitalizations were due to malaria. During the Korean conflict there were five times the number of man-days lost due to malaria as compared to battle injuries. Aggressive control, prophylaxis and therapy reduced this to a 2:1 ratio by the
time of the Vietnam War. Today malaria is once again becoming a major international problem with rising counts being reported in many areas which were nearly free of disease twenty years ago. The disease is endemic in nearly all of Latin America. The primary cause for the renewed widespread incidence, which the World Health Organization estimates has increased 25% in the past two years, is an apparent combination of mosquito resistance to insecticides and protozoal resistance to antimalarial drugs. In 1977 there were three times as many cases of malaria reported among U. S. civilians as in 1972, and 12% of these were contracted in Latin America. In addition, at least eleven cases occurred among U. S. military personnel in 1977.

The protean nature of malaria has been well recognized by its ability to produce a variety of clinical manifestations. Semiology may include severe gastrointestinal symptoms, renal dysfunction, coronary congestion, pulmonary edema, and cerebral involvement. However, the most prominent sign which clinically characterizes an acute attack is pyrexia of a specific periodicity. The clinical features are the result of a combination of effects which occur in the circulatory system, both in response to the high fevers and to the stasis caused by variations in size of the infected erythrocytes.

The high fevers which characterize this disease are worthy of brief discussion. These generally begin with an initial stage of severe chills with rigors, followed by a hot stage during which the temperature reaches 105°F or higher. The fever may last two hours or more, followed by flushing of the skin and profuse sweating, with return to normal or subnormal temperature.
P. vivax and P. ovale produce tertian malaria characterized by fevers which recur at 48 hour intervals. The fever of subtertian malaria, caused by P. falciparum recurs at 36 hour intervals, and that of quartan malaria (P. malariae) recurs every 72 hours. The periodicity of the fevers corresponds with the periodic hemolysis due to parasite sporulation.

Of the four species, P. falciparum is the most virulent and the only one that is generally fatal. Untreated infections caused by the other species often undergo spontaneous cure following a clinical course of six weeks to three months.

Oral manifestations have been described as being of three types. Vesiculoulcerative lesions characteristic of herpes labialis have been reported occurring during the acute attack or, more often, during a two to three-day prodromal period. Herpes labialis has been associated with nearly one-third of all cases of malaria. Other oral manifestations indicative of the hemolytic anemia may be expected: pallor of oral mucosa, icterus, and delayed healing of procedures requiring surgery or other tissue manipulation. The most serious of reported oral complications is a gangrenous stomatitis producing large necrotic areas involving the cheeks, gingiva, lips, and nose. This occurs primarily in untreated cases of subtertian malaria and is attributed to formation of thromboemboli created by phagocytic cells, infected erythrocytes, and the rapidly multiplying parasites. These lesions heal following local treatment and antimalaria therapy.
Diagnosis of malaria is confirmed primarily by demonstrating parasites either in peripheral blood smears or in bone marrow.

3. Mastigophora

The class Mastigophora are divided into (a) those infecting the alimentary and urogenital tissues, and (b) those infecting the blood and other body tissues. The first group is composed primarily of the trichomonads: *Trichomonas tenax*, *Trichomonas vaginalis*, *Trichomonas hominis*, and *Giardia lamblia*. Only *T. tenax* is associated with the oral cavity, where it is considered a nonpathogenic commensal, most often occurring in soft calculus, caries, and periodontal pockets. It is rarely found in the normal healthy oral cavity. The most important organisms of the second group include the Leishmania and Trypanosoma.

**Leishmaniasis.** The *Leishmania* which are infectious for man include *Leishmania donovani*, *Leishmania braziliensis*, *Leishmania mexicana*, and *Leishmania tropica*. Morphologically they are identical, however, their clinical and serological manifestations are distinguishable. Leishmaniasis is a disease of the reticuloendothelial system, the primary infection being transmitted by the bite of the sandfly. The life cycle of each type of *Leishmania* is dependent on a particular sandfly species and its geographic distribution. Clinical forms of the disease include mucocutaneous leishmaniasis caused by *L. braziliensis*, and visceral leishmaniasis (kala-azar) caused by *L. donovani*, which have their highest incidence in South America.

The initial lesions of mucocutaneous leishmaniasis present after a variable incubation period as inflamed papules, plaques, or verrucoid lesions of skin which resemble those of tuberculosis, sarcoid, or leprosy. These lesions ulcerate within four weeks and have a raised
border with a granulating base. Mucosal involvement occurs by metastasis or secondary extension and may not become evident until one to six months after initial onset. Salgado and Loureiro found that almost 80% of mucosal lesions involved nasal mucosa and 90% were ulcerative lesions.

Oral and nasal lesions are characterized as extensively destructive granulomatous lesions which persist for months to years after the primary cutaneous lesions heal. These may be so extensive as to destroy the nasal septum, ala, palate, and tongue.

Untreated mucocutaneous leishmaniasis may be further complicated by a latent involvement of oral, nasal, and upper respiratory mucosa. This may not become evident for 10 to 25 years following a primary or occult infection with L. brasilensis. Mucosal lesions of this latent form, called espundia, are extensive mutilating granulomata affecting nasal membranes, palate, and upper lip. Mucocutaneous leishmaniasis must be differentiated from South American blastomycosis, which may have a very similar clinical presentation.

In Latin America the visceral form has particularly high incidence in children. In this form of the disease the parasites spread through the body's reticuloendothelial system, multiplying in macrophages, and producing granulomatous lesions in bone marrow, spleen, liver, kidneys, and lymph nodes. South American kala-azar produces greatest damage to bone marrow.

The oral manifestations most commonly observed include cheilitis and a red tongue devoid of normal papilla. Petechiae, mucosal purpura
and spongy, hemorrhagic gingiva may be indicative of decreased plasma prothrombin level. In advanced disease, patients may suffer from periodontitis and exfoliation of the teeth.¹⁶

Prior to the development of antimonial chemotherapeutic drugs, this disease was 90% fatal. This is now the cure rate.

Cutaneous leishmaniasis is generally of a much less severe nature than the other forms. The organisms invade the reticuloendothelial cells of the skin causing granulomatous ulcers similar to the mucocutaneous form. However, these are usually not accompanied by systemic involvement or mucosal extension, and a lasting immunity develops. A species labeled *L. mexicana* has been recognized in the western hemisphere, being particularly prevalent in Central and South America. This form most commonly produces a single self-healing lesion.²¹

The diagnosis of leishmaniasis may be verified from aspirations, smears, or biopsy through (a) identification of Leishman-Donovan bodies, a nonflagellated form in tissue macrophages, (b) a positive Montenegro skin test, and (c) indirect fluorescent antibody technique. Treatment is most effective with pentavalent antimonial compounds.

Trypanosomiasis. Infection due to species of the *Trypanosoma* are associated with clinically different diseases and specific geographic prevalence.

In the western hemisphere, the species *Trypanosoma cruzi* is most common, with highest prevalence in South America. The life cycle of this species is dependent upon the blood-sucking, cone-nose bug of the family Reduviid. Parasites within the insect's excrement contaminate
cutaneous wounds and mucous membranes causing an infection of the reticuloendothelial system called Chagas' disease (South American trypanosomiasis). The insect vector prefers to take its blood meal from the mucocutaneous junctions, particularly about the eyes and lips.\textsuperscript{11}

Earliest signs of parasitemia begin two weeks after infection with a diffuse painless urticaria. This may be associated with or subsequently followed by fever, vomiting, anorexia, and obstinate cough. Within one to two weeks, the rash fades. The most notable primary lesion (the chagoma) occurs within one to two weeks after infection and consists of a nodular proliferation of trypanosomes in the subcutaneous tissue. This is often associated with a nonpurulent unilateral palpebral edema and conjunctivitis with ipsilateral regional lymphadenopathy (Romana's sign).\textsuperscript{3}

A particular oral manifestation described as being pathognomonic of \textit{T. cruzi} infection in young children has been termed lipochagomata genii.\textsuperscript{11} These lesions are described clinically as nodular, purple colored patches occurring bilaterally over the buccal fat pad within the cheeks. The lesions are painful, ovoid, rubbery formations which histologically consist of intense inflammatory infiltrates associated with large numbers of \textit{T. cruzi} and necrosis of subdermal buccal fat. The occurrence of lipochagomata genii frequently may be the only significant clinical indication of infection other than the nonspecific fever, anorexia, and irritability common to so many other tropical infections.
Diagnosis of Chagas' disease is determined from clinical manifestations, immunological assays (in particular, complement fixation and immunofluorescent antibody tests), by demonstration of the parasites in biopsied tissue, and by xenodiagnosis.

The disease is treated with such antitrypanosomial drugs as nitrofurans, 8-aminoquinolines, or metronidazole.

HELMINTHIC INFECTIONS

Helminthic infections in man may be grouped into those caused by round worms (Nematodes) and infestations by flat worms (Platyhelminthes). There are few among these that are significant within the context of this study. However, those to be discussed do present an interesting variety of clinical manifestations.

Hookworm. The hookworm infection is caused by the closely related nematodes *Ancylostoma duodenale* and *Necator americanus*. The disease is so widespread, particularly in tropical areas, that an estimated 25% of the world's population is infected with these parasites. Areas of poor sanitation and inadequate nutrition are most heavily affected. Hookworms are intestinal parasites. Female worms may deposit 10,000 to 20,000 eggs into the feces daily. The eggs hatch in the feces and the larvae develop in fecally enriched soil. Infection occurs when the larvae penetrate the skin, most commonly of the feet, and enter the bloodstream. Larvae are carried to the lungs where they migrate through alveolar spaces, along bronchiolar passages, up the trachea, and down the esophagus to the small intestine, where they mature to adult worms. The worms attach themselves to the intestinal mucosa and exsanguinate the host. A single
worm may ingest .05 ml of blood per day,\textsuperscript{9} and a heavily infected individual may lose 200 ml a day with a daily iron loss in excess of 30 mg.\textsuperscript{6}

Clinical symptoms begin with a pruritic, erythematous, papular eruption at the site of entry and lasting two weeks. A transient bronchitis, with occasional bloody sputum coincides with movement of the larvae through the lungs. Mild epigastric discomfort, with occasional diarrhea or constipation may occur with intestinal infestation. The most significant constitutional complaints are usually indicative of the chronic iron-deficiency anemia which results. The degree of iron deficiency is variable depending on the severity of depletion of the body's iron stores. Thus, symptoms may be innocuous in mild cases, to fatal in heavily infected children.

Oral manifestations are primarily indicative of the iron-deficiency anemia; i.e., extreme pallor of the oral mucosa, lips and gingiva, glossodynia and atrophy of papillae on the dorsum of the tongue, and angular cheilosis.\textsuperscript{16}

Diagnosis of hookworm is confirmed by identification of worms and ova in stool examinations. Treatment involves administration of appropriate antihelminthic agents such as tetrachloroethylene and thiabendazole, and iron supplements.

Filariasis. Filariasis is caused by the filarial worm \textit{Wucheria bancrofti}. The disease occurs predominantly in Africa and southeast Asia although there is significant distribution along the northeastern coastal areas of Central and South America. Larval forms are transmitted by mosquito to man. The adult worms invade and mature within lymph nodes.
and lymphatic vessels. The primary manifestation of the infestation is lymphatic blockage with characteristic elephantoid changes of the extremities.

Oral manifestations, although very rare, have been reported to present as similar vasculolymphatic engorgement of the lips and tongue. Diagnosis of filariasis is confirmed by demonstrating microfilaria in peripheral blood. Infections are treated by administration of antimicrofilarial agents, specifically, diethylcarbamazine.

**Trichinosis.** Trichinosis, also called trichiniasis or trichenellosis, is a parasitic infection caused by the nematode *Trichinella spiralis*. This worm also infests a variety of carnivorous animals including rats, bears, and pigs. Parasitization most commonly is associated with ingestion of raw or incompletely cooked pork which contains the parasitic larvae in cystic capsules within striated muscle. Gastric enzymes digest the capsule, freeing the larvae which mature into adult worms in the small intestine of man. Following copulation the female worm releases many immature larvae which migrate through the blood to skeletal muscle. There, the larvae become encysted and may remain viable as such for many years.

Clinical features may vary from a mild subclinical form, the only manifestation being eosinophilia, to a severe disseminated infection with involvement of kidneys, lungs, and central nervous system.

Clinical oral semiology includes pain in affected muscles, difficulty with mastication, deglutition, and speech. This is due to formation of larval cysts which occasionally occur within the tongue, masseter muscle, and laryngeal muscles.
Diagnosis of trichinosis is usually confirmed by demonstration of larval cysts in muscle biopsy. Complement fixation has also been used with good reliability to verify the diagnosis.

Treatment of trichinosis has been primarily through the use of corticosteroids to reduce the hypersensitivity reactions which frequently accompany many parasitic infections. The drug thiabendazole has been the most effective against *T. spiralis*, however, its many adverse side-effects complicate its use.7

**Tapeworms.** Among the platyhelminthic family the two species which most commonly affect man are *Taenia saginata* and *Taenia solium*. The diseases associated with these parasites are of two types: infestation by the adult tapeworm, called Taeniasis, and infestation by the less mature form, called Cysticercosis.

The taenia are ribbon-like adult worms which may grow to a size of 20 mm wide and 12 meters long.1 Taeniasis is an intestinal parasitosis which occurs following the ingestion of the immature cysticerci by eating incompletely cooked beef or pork. The cysticerci mature into the adult taeniae within the small intestine of man. Manifestations may consist of a variety of vague disturbances including anorexia, diffuse abdominal pains, neuropsychic disturbances varying from hyperirritability to apathy, and various cutaneous, cardiovascular, and respiratory disturbances.

Oral manifestations of taeniasis may include a variable ulcerative, hemorrhagic or hypertrophic gingivitis, stomatitis, and stomadynia.22
These features may occur as either a response to a toxemia created by the parasite or as a hypersensitivity reaction to the parasite.

_Cysticercus cellulosae_ and _Cysticercus bovis_ are the immature cystic forms of _T. saginata_ and _T. solium_, respectively. Cysticercosis, the parasitosis caused by these cysticerci, occurs following the ingestion of ova of the _T. saginata_ or _T. solium_. This may occur by eating contaminated fruit or vegetables as well as by poor self-hygiene practices. The eggs pass into the intestine, become disseminated by the general circulation and ultimately settle in various tissues of the body where the cysticerci mature and form nodular lesions, each containing a single organism, and varying in size up to 1.0 cm. Nodular cystic lesions occur most commonly in ocular and cerebral areas as well as in hepatic, pulmonary, cardiac, muscular, and subcutaneous tissues. Multiple lesions have been reported within masseter muscle, the lips, chin, and tongue where they are generally well tolerated. Treatment consists of surgical extirpation.

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REFERENCES


