



Symptoms of selected parasitic diseases in the oral cavity

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Abstract

Introduction. Parasitic diseases are caused by many species of protozoa, helminths, and arthropods. Parasitosis can be divided into gastrointestinal, tissue and skin diseases and can appear in many different parts of the body. The most common route of transmission is via ingestion. The oral cavity may be a place of colonization for pathogens, resulting in lesion formation.

Objective. The aim of the study is to characterise and describe the most important symptoms of parasitic diseases that can be diagnosed during dental examination.

Abbreviated description of the state of knowledge. In this study there are discussed diseases caused by the most common protozoa and the nematodes in the oral cavity. Leishmaniasis is caused by *Leishmania* spp. protozoa, and its most common symptom observed in the oral cavity are painful ulcerations. Toxoplasmosis usually manifests itself through enlargement of the lymph nodes, and the appearance of antibodies in saliva. *Entamoeba gingivalis* and *Trichomonas tenax* cause periodontitis chronica and inflammation of the soft tissue. The first of the nematodes, *Gongylonema pulchrum*, is the reason for, among others, the itchy sensation of a moving foreign body under the mucosa. The most common symptoms of *Ancylostoma* infection are erythematous papules. Filariæ causes an infection that manifests through swelling, abscesses, and painless nodules inside the mouth.

Conclusions. New pathogens are emerging worldwide and pose a threat to health. They can manifest their symptoms in the oral cavity, but the diagnosis of the disease by the dentist is not easy and requires interdisciplinary knowledge and consultation.

Key words

parasitic diseases, protozoan infections, nematode infections, oral cavity, periodontics

INTRODUCTION

Parasitic diseases are human and/or animal parasitic-induced illness caused by protozoa, helminths, and arthropods. There may be about 300 species of parasites in the human body. Parasites are plant or animal organisms that live in a host tissue and cause parasitosis. Parasitic infection is not always accompanied by symptoms, which may appear only during immunosuppression, for example AIDS. The study distinguishes between internal and external parasites. Due to their place of existence, parasitosis can be divided into gastrointestinal, tissue and skin diseases [1]. A human can be both an intermediate host and definitive host, in which a parasite reaches the adult stage and reproduces sexually. They can occur in different parts of the human body, manifesting themselves through symptoms in the digestive, muscle, nervous, immune system and external symptoms, including emotional ones. The most common route of transmission is via ingestion. Consumption of raw meat, dirty vegetables and fruits or contaminated water, and not following the rules of personal hygiene favour parasite infection. The oral cavity

is a natural reservoir of many species of bacteria, fungi, and protozoa, and often becomes a mirror of the body's health. Disturbance of the biological balance in the oral cavity results in lesion formation. Furthermore, a large number of systemic diseases manifest themselves in the oral cavity; therefore, a dental examination, especially of the oral mucosa, may be essential for their early diagnosis [2].

OBJECTIVE

The aim of the study is a short description and characteristics of the most important symptoms of parasitic diseases that may appear within the masticatory system, and can be diagnosed during a dental examination in a dentist's surgery. Diseases caused by protozoa (*Leishmania*, *Toxoplasma gondii*, *Entamoeba gingivalis*, *Trichomonas tenax*) and the nematodes (*Gongylonema pulchrum*, *Ancylostoma*, filariæ) are discussed.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Leishmania. Leishmaniasis is defined as a group of diseases caused by more than 20 species of protozoa of the genus

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Leishmania. Vectors of the protozoa are dipteran flies of the genus *Lutzomyia* and *Phlebotomus*, which have the colloquial name of sand fly. According to the World Health Organisation (WHO), leishmaniasis is endemic in 88 countries. It is a tropical disease that affects more than 12 million people. Three main clinical forms of leishmaniasis can be distinguished: cutaneous, visceral (also called kala-azar) and mucocutaneous. Cutaneous leishmaniasis is the most common form of leishmaniasis, which results in skin lesions, mainly ulcers on exposed parts of the body. These alterations often leave scars for a lifetime. Its transmission is induced by *Leishmania tropica*, *Leishmania major*, *Leishmania mexicana* or *Leishmania aethiopica*, the cutaneous form of which most frequently occurs in the Middle East, Central and East Asia, Africa and Central America. Visceral leishmaniasis is the most severe form of leishmaniasis, which often causes death. The main vectors are flies of the *Leishmania donovani*, *Leishmania infantum* and *Leishmania chagasi* species. The endemic areas are African countries, Central and Eastern Asia, as well as Central America. Damage to the parenchymatous organ and bone marrow, accompanied by a complex of symptoms, including fever, weight loss, splenic and liver enlargement, anaemia, oedema and diarrhoea, occurring in the course of visceral leishmaniasis. Mucocutaneous leishmaniasis is caused by *L. major*, *L. tropica*, *L. aethiopica*, *L. mexicana*, *L. brasiliensis* (Central America, less often East Africa) [3]. It develops from 1 – 5 years after cutaneous leishmaniasis has healed, although in some cases mucosal and skin lesions may overlap. Scars and skin discoloration were observed in approximately 90% of patients. In this clinical form, symptoms also appear in the oral cavity. The damage of tissues of the nose, mouth and larynx leads to disfigurement ('white leprosy'). Mucocutaneous leishmaniasis is transmitted through the bite of an infected female of *Phlebotomus* or *Lutzomyia* fly. After the bite, the fly injects saliva into the human blood, which contains ingredients that inhibit blood clotting, dilate the blood vessel, as well as enzymes with anti-inflammatory and anaesthetic properties. There are also protozoan promastigotes in the saliva, which are then phagocytosed by macrophages and monocytes of the subcutaneous tissue. In these cells, it causes the transformation of the form of promastigote into spheromastigote, and then into amastigote, which is multiplied by simple division. As a result of amastigote division, the cell ruptures, further phagocytic cells are infected and the disease spreads. However, this is not the only route of infection. It is also possible to become

infected by crushing the insect and rubbing it into the wound. Wild animals are also reservoirs, for example, monkeys; however, infected dogs that live in the immediate vicinity may be a significant threat to humans. Exclusive involvement of the oral mucosa is very rare. Most often, the disease begins with a skin lesion – primary an outbreak at the site of the bite by an infected fly. Similar lesions occur in cutaneous leishmaniasis. Involvement of the mucous membranes of the mouth, nose, larynx, pharynx or trachea is possible due to the transmission of amastigote through the circulatory system. It starts as erythema and ulceration, leading to perforation of the nasal septum. Inflammatory lesions can also involve oral tissues [4]. Documented clinical cases are presented Table 1 [4, 5, 6, 7].

On the basis of the presented cases, it can be noted that the most common symptom observed in the oral cavity as a result of infection, is ulceration, usually painful with irregular edges, hard with granular structure. Pathological changes may include the mucosa of the soft tissues of the oral cavity, such as: lips, frenulum, gums, cheeks, tongue, hard and soft palate, as well as the oral part of the throat. The aim of the prevention is to reduce the parasite's transmission. This goal can be achieved, among others, by controlling the population of vector flies, by spraying residual insecticides in homes, and by using insecticide-impregnated bed nets [8]. Individual protection measures include protecting the body from contact with flies by wearing clothes with long sleeves and legs, and using insect repellent. Moreover, health education and prophylaxis are an important aspect which increases the awareness of people at risk. In addition, blood donors should be tested for *Leishmania* antibodies to minimize the risk of infection by blood transfusions.

***Toxoplasma gondii*.** *Toxoplasma gondii* is a worldwide widespread intracellular parasite in mammals and birds. Toxoplasmosis is much less of a problem in regions with a cold climate, such as Scandinavia, and in places with a predominantly dry and cold climate. The most common infection occurs through ingestion. *Toxoplasma* parasitizes a wide range of warm-blooded animals, including humans and rodents, as intermediate hosts, with cats as the definitive host. After the protozoan enters the host's organism, sporozoites are released from oocysts. They transform into tachyzoites which have the ability to move in the small intestine, and penetrate the interior of enterocytes and cells of the reticuloendothelial system where they rapidly multiply. After being released from the cell, tachyzoites spread throughout the body via the

Table 1. Symptoms of leishmaniasis in the oral cavity

Patient	Type of lesion	Location	References
70-year-old man	painful ulceration, 2cm in diameter, hard, with irregular edges	floor of the oral cavity, close to the opening of the Wharton duct	[4]
41-year-old man, infected with HIV	painful ulceration, 2cm in diameter	mucosa of the right cheek	[4]
50-year old man, infected with HIV	painful with granular surface	region of alveolar process from 17 - 22, on the vestibular and palatal surfaces, maximum 5 cm in diameter	[4]
31-year-old woman	submandibular lymphadenopathy and ulceration	frenulum of lower lip, gingiva, nasal septum	[5]
71-year-old man	ulceration, size of lesion 5 cm x 4 cm, with granular structure and elastic texture	hard and soft palate	[6]
51-year-old man	hard, scattered, nodular ulceration (smaller than 1 cm), cobblestone appearance of upper gingiva, with erythema and inflammatory hyperplastic granulation	hard and soft palate, maxillary gingiva	[7]

haematological and lymphogenic routes, inhabiting distant tissues and organs. The parasite can potentially develop in any tissue and organ, but it has the highest affinity for nerve and muscle tissue, including the heart muscle. In these locations, tachyzoites develop into tissue cyst bradyzoites. There are three predominant sources of infection in humans, namely: ingestion of undercooked meat containing cysts, oocysts in cat stool and transplacental transfer from mother to foetus. Toxoplasmosis can manifest by classic flu-like symptoms, such as low-grade fever or fever not exceeding 38.5°, myalgia, general weakness, decreased exercise tolerance, headache, less often sore throat and pharyngitis [9]. Toxoplasmosis sometimes do not have any symptoms because of the human immune system. In immunocompromised patients, *T. gondii* may cause weakness, headache, dizziness, higher temperature, muscle, and joint pain, but the most important manifestation are swollen lymph nodes. Submandibular lymph nodes are one of the areas where protozoans may accumulate which leads to swelling and pain. Before any visible signs appear, fever occurs. During palpation, a swollen node may measure approximately 4x2 cm, and normal, inflammable nodes no bigger than 1 cm [10]. This illness does not have direct symptoms in the oral cavity, but during a dental visit, palpating submandibular lymph nodes should not be overlooked and, in this way, the dentist is able to detect toxoplasmosis. Another symptom is the appearance of antibodies IgA and IgG in human saliva. According to research, *Toxoplasma*-specific IgG and *Toxoplasma*-specific IgA antibodies have been found in 20% of samples of oral fluid [11]. This fact may be exploited as the one of the options to detect that disease.

Summarizing, toxoplasmosis causes enlargement of the lymph nodes, most often the cervical along the posterior edge of the sternocleidomastoid, nuchal and occipital muscles (less commonly, generalized lymphadenopathy), with the clinical picture resembling mononucleosis. According to the guidelines of the Centres for Disease Control and Prevention, the risk of infection may be reduced by cooking meat at the temperature of at least 63–74° C. The temperature ought to be measured by a food thermometer in the thickest part of meat. It may also be reduced by freezing the meat for several days at a temperature below -17° C prior to preparing, peeling and thoroughly washing vegetables and fruits before eating, avoiding drinking untreated water, daily changing the cat litter box. During pregnancy and immunosuppression, cleaning the cat litter box and keep cats indoors should be avoided.

Entamoeba gingivalis. *Entamoeba gingivalis* is a commensal that can be found in the human oral cavity. Poor oral hygiene, gingivitis, periodontitis and coexisting systemic diseases, such as diabetes and haematological diseases, can lead to the population growth of this protozoan in the oral cavity [12]. The presence of *E. gingivalis* in inflamed tissues of the periodontium has been documented in many scientific reports, whereas the protozoan's role in the etiology of this disease is not fully understood. The most common location of the protozoan in the oral cavity are the periodontal pockets, in which the anaerobic conditions favour their colonization. By colonizing the soft tissues in the oral cavity, *E. gingivalis* can also induce changes leading to the creation of a favourable anaerobic environment [13]. The mucosa of gingivae, palatine tonsils and soft palate can also be a habitat of *E. gingivalis*.

In 2018, a subtype of *E. gingivalis* ST2 was identified – the kamaktli variant, which is 89% identical to *E. gingivalis* ST1 [12]. Their occurrence depends on the condition of the oral cavity, namely, in people with healthy periodontium, *E. gingivalis* ST1 occurred in 48.6%, and *E. gingivalis* ST2-kamaktli in 29.5%. In people with periodontal disease, the presence of *E. gingivalis*-ST1 was reported in 57.8%, and *E. gingivalis* ST2-kamaktli in 50.0%. According to scientific research, 47.5% of patients undergoing orthodontic treatment carried *E. gingivalis* ST1, while 73.8% had *E. gingivalis* ST2-kamaktli. The presented results suggest that the subtypes differ in terms of genetics and pathogenicity [14]. *E. gingivalis* attacks the inflamed and damaged oral mucosa; in the microscopic image, it occurs in almost all layers of epithelial tissue and is surrounded by a large number of neutrophils. It inhibits cell proliferation, whereby the damaged tissue cannot regenerate. It also activates the secretion of interleukin 8 by endothelial cells and fibroblasts, causing an increase in the migration of neutrophils, monocytes and T lymphocytes, and induces the release of histamine from basophiles, which intensifies inflammation [15]. The destruction of tissues favours the further development of protozoa in the oral cavity. The macroscopic image shows periodontitis leading to irreversible damage to the epithelial attachment and loss of bone tissue of the alveolar process, resulting in tooth loss or total toothlessness. Periodontitis is accompanied by severe pain and bad breath. Clinical examination shows bleeding, swollen gingivae and increased tooth mobility [16]. According to the Centres for Disease Control and Prevention, trophozoites, or active stage capable of division and movement which are present in the oral cavity, are transmitted through the oral route; in other words, by kissing and using shared utensils and cutlery. Unfortunately, an improved and complete development cycle of *Entamoeba* is still lacking, which is a significant problem in establishing sufficient and effective protection against infection. Prevention includes avoiding portals of entry: not using the same utensils and cutlery at the same time without washing it first, having own cleaning products, such as toothbrushes, and avoiding kissing if there is a risk that the person may be a carrier [13].

Trichomonas tenax. *Trichomonas tenax* (oral trichomonas) belongs to the group of cosmopolitan, anaerobic protista – flagellates causing oral trichomoniasis. It occurs in the form of a trophozoite with a variable shape, most often oval or round. *T. tenax* usually does not cause symptoms in patients with a properly functioning immune system [17, 18]. It is a protozoa often found in the human oral microbiota and colonizes on the edges of the gums, in the interdental spaces, pathological periodontal pockets, cavities, as well as on the diseased oral mucosa. The presence of *T. tenax* in the oral cavity of people with periodontitis has been the subject of few clinical trials to-date.

Periodontal diseases (gingivitis, periodontitis) result from disturbed homeostasis of the microbiome in the mouth of the host. However, the role that *T. tenax* may play in the etiopathogenesis of periodontal diseases is still unclear [19]. In the published results of studies on oral protists *Trichomonas* sp. (by culture and PCR), 53 protist strains were obtained from periodontal samples. 37/106 (34.90%) *T. tenax* from patients with periodontitis and 16/85 (18.80%) *T. tenax* from control patients were detected by culture. 60 from 191 samples were tested positive for *T. tenax* by qPCR – 24/85 (28%) controls

and 36/106 (34%) patients with periodontitis ($p = 0.089$). Combining both results, 45/106 (42.5%) patients were positive by culture and/or PCR, as compared to 24/85 (28.2%) controls ($p = 0.042$) [20]. Research shows that, similar to *E. gingivalis*, *T. tenax* accompanies periodontal diseases, while its impact on pathophysiology of periodontium remains a subject of discussion. The connection between *T. tenax* and the severity of periodontitis was also confirmed. The protozoan was most often detected in the initial phase of periodontitis. Patients diagnosed with *T. tenax* most often report dry mouth, burning mouth syndrome, spontaneous pain, and pain during swallowing. Pathological pockets, glossitis inflammatory foci within the oral mucosa can be noticed in the intraoral examination [17]. Dutko and Kurnatowska indicate that in patients infected with trichomoniasis, pathological pockets with a depth of more than 5.5 mm were more common, and chronic periodontitis was diagnosed in all patients. However, no statistically significant differences were found between gender, age and smoking in individual groups of patients with confirmed *T. tenax* infection [21].

For the prevention of infection, it is important to reduce the population of protozoa in the oral cavity. Most authors state that the increased incidence of protozoa in oral cavity (*T. tenax* and *E. gingivalis*) is usually accompanied by poor oral hygiene, and age > 40 years is a significant factor affecting the immune system and therefore the appearance of protozoa in the mouth [22, 23]. Another important factor affecting the contagion is the duration brushing the teeth. Spending less than 1 minute on these activities, as well as too infrequent brushing, negatively affects the condition of the oral cavity and promotes the occurrence of protozoa [24]. On the other hand, the improper use of additional mechanical oral hygiene devices, such as dental floss or toothpicks, also has a negative effect. Protists are more likely to occur in people using mechanical means. This is probably due to the mishandling of these devices, which can damage the gum tissue and therefore cause inflammation.

Nematodes. Nematodes (roundworms) are macroscopic, multicellular parasitic helminths that have rounded, elongated and not-segmented body shape [25, 26]. They have a simple digestive tract starting with the oral cavity at the front and ending with the anus at the back. Some of them need several hosts to fulfil their life cycle. Nematode infections have high prevalence in tropical and subtropical climate. Oral manifestations of nematode infections are rather rare. *Gongylonema pulchrum* is a helminth that infects wild and domesticated mammals, mostly ruminants [26, 27]. Gongylonaemiasis is spread worldwide, although human infections with this nematode are exceedingly rare. The final host discharges eggs in its faeces. Subsequently, eggs are swallowed by coprophagous insects (intermediate hosts) in which they transform to the infective larvae. The definitive host becomes infected by consumption of the infective third-stage (L3) larvae [28, 29]. The human, as its accidental definitive host, can become infected by ingesting tap water and unwashed fruits and vegetables. Good personal hygiene is the only way of prevention. Clinical manifestations include an intermittent, itchy sensation of a moving foreign body under the oral and the esophageal mucosa. Occasionally, a small spiral shape can be observed on the mucous membrane. Often these are the only occurring symptoms [27, 28, 30, 31]. Other symptoms include irritation,

minor pain, hypersalivation, nausea and vomiting, cough and pruritus [32]. The parasite can be manually removed by the use of fingers or forceps. Thereafter, the symptoms disappear without further treatment, although the administration of an anti-helminthic drug is often advised. *G. pulchrum* infection is a minor epidemiological problem. Only several dozen cases have been reported since 1850 [28, 29]. Five cases of gongylonemiasis have been described in the last 5 years (Slovenia, USA, and China) [27, 28, 29, 32, 33]. *Ancylostoma sp.*, also known as a hookworm, is a parasite of wild cats and dogs. Infections with this nematode occur mostly in tropical and subtropical climates due to the warm and humid conditions [26, 34, 35]. The species that affect the oral mucosa are *Ancylostoma brasiliensis* and *Ancylostoma caninum*. The disease is caused by a hookworm-related cutaneous larva migrans (HrCLM) or 'creeping eruption'. Wild cats and dogs dispose their eggs in their faeces. The eggs need approximately one day in warm soil to hatch, and one week to develop to infectious filariform larvae. Humans become infected when larvae penetrate the skin pores, hair follicles or damaged skin, mainly on hands, arms, feet, genitalia and buttocks [25, 26]. The infection of the oral mucosa is rare, but possible, and occurs when mucosa comes into contact with objects contaminated with larvae, such as a blade of grass or a fishing hook [21]. Humans are an accidental host in which larvae cannot continue their life cycle, and unable to mature, eventually die after 4–8 weeks. Common symptoms of HrCLM are painful, pruritic, erythematous papules and lesions, dark serpiginous elevated tracks on the palate, retromolar region and cheeks, and a sensation of a 'crawling bug' inside the mouth. Parasites reaching the throat may even cause dyspnea [25, 26, 34, 35]. Although HrCLM is a self-limiting disease, an anti-helminthic drug, such as thiabendazole, may be applied in the healing process.

Prevention of this disease is through proper personal hygiene, especially after contact with cats and dogs, and washing fruits and vegetables before eating [34]. Ten papers about *Ancylostoma sp.* infection have been published since 2015.

Filarial infection is a serious health problem in tropical and subtropical regions of Asia, Africa, Central and South America. Filariasis is caused by various nematode species belonging to genera such as e.g., *Dirofilaria*, *Wuchereria*, *Onchocerca*, *Brugia*, *Dipetalonema*, *Mansonella*. Filarial disease associated with the oral cavity is called Perioral lymphatic filariasis (LF). The adult forms live in vertebrate hosts (mainly equines, bovines and canines) and their larvae can be transmitted only by proper arthropod vectors, such as *Anopheles*, *Aedes*, *Mansonia*, *Culex*, *Culicoides*, *Simulium*, *Chrysops*. Once the larvae penetrate the human skin, they migrate and settle in various internal organs (heart, lungs, skin, subcutaneous tissue, connective tissue, body cavities, eyes, blood and lymphatic vessels, CNS, etc.). The larvae, known as microfilariae, can be found in blood. Perioral manifestations of lymphatic filariasis (LF) include swelling of intra-oral tissues, the external mandibular area or submandibular abscesses, that do not respond to appropriate treatment. The emergence of painless nodules has also been reported. The most representative systemic symptom of filariasis is elephantiasis which is a significant enlargement and hardening of an extremity due to obstruction of the lymphatic vessels. The drug administered in the case of LF is

Table 2. Characteristics of pathogens and related symptoms in oral cavity

Pathogen	Signs and symptoms in the region of the oral cavity	Location	References
<i>Leishmania</i>	ulceration, usually painful, with irregular edges, hardened with a granulomatous structure.	mucosa of the soft tissues of the oral cavity such as: lips, frenulum, gums, cheeks, tongue, hard and soft palate, and the oral part of the throat	[4, 5, 6, 7, 8]
<i>Toxoplasma gondii</i>	swollen lymph nodes, weakness, headache, dizziness, higher temperature, muscle and joint pain (resemble mononucleosis)	submandibular lymph nodes	[10]
<i>Entamoeba gingivalis</i>	periodontitis chronica, inflammation of soft tissue in the oral cavity	mucosa of soft tissues in the oral cavity	[13, 16]
<i>Trichomonas tenax</i>	periodontitis chronica, inflammation of soft tissue in the oral cavity	mucosa of the soft tissues in the oral cavity	[17, 19]
<i>Gongylonema pulchrum</i>	itchy sensation of a moving foreign body under the oral and oesophageal mucosa. Irritation, minor pain, hypersalivation, nausea and vomiting, cough and pruritus	mucosa of soft tissues in the oral cavity	[27, 28, 30, 31, 32]
<i>Ancylostoma</i>	painful, pruritic, erythematous papules, dark serpiginous elevated tracks on palate, retromolar region and cheeks, and a sensation of a 'crawling bug' inside the mouth	mucosa of soft tissues in the oral cavity	[25, 26, 34, 35]
Filariæ	swelling of intra-oral tissues, external mandibular area or submandibular abscesses, painless nodules	mucosa of soft tissues in the oral cavity	[25, 26, 35]

diethyl carbamazine, often in combination with ivermectin or albendazole. The prevention of LF is mainly by limiting contact with insects which carry the disease [25, 26, 35]. Thirty-four papers found in the PubMed database about filarial infection have been published in recent years. The symptoms of all discussed parasitoses are presented in Table 2.

CONCLUSIONS

Parasitic diseases are widespread all over the world, and are a huge risk to health. The progress of civilization and appearance of new pathogens and their resistance to drugs increase the spread of parasitic diseases in our environment. Some pathogens may also manifest their symptoms in the oral cavity, as evidenced by numerous reports in medical publications. The diagnosis of parasitic diseases based on the symptoms in the oral cavity is difficult and is a challenge for the dentist. The absence of characteristic symptoms requires differentiation from other diseases, and interdisciplinary cooperation. Nevertheless, regular and proper oral hygiene is crucial as an important factor in prevention.

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