NON-PATHOGENIC HUMAN PARASITES

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ABSTRACT

This paper presents the most important non-pathogenic parasitic organisms that can occur in the human body. They generally do not cause any symptoms of disease in humans. Symptoms of their presence are observed in cases of intense infection, in the absence or weakening of immunity, or in association with other diseases. In this paper, we will focus on the most important species, presenting their characteristics and possible disease symptoms.

Keywords: Nonpathogenic intestinal protozoa, mites, worms. Entamoeba, Trichomonas, Demodex, and others.

INTRODUCTION

Parasitism is a type of coexistence between two organisms, one of which benefits from the relationship, while the other is harmed. However, not all parasites cause harm within the host organism – for some, the relationship with the other organism can be described as commensalism, a type of coexistence in which one species benefits, while the other is unaffected by the relationship, and therefore is neutral to it.

Parasites present in the human body are usually associated with the diseases they cause. However, we must not forget the existence of parasites that are common within the human body, a permanent fixture, and yet do not cause any disease. At the same time, some of these organisms can even have a beneficial effect on the host organism. Typically, only coexisting diseases or massive infections can cause symptoms, usually mild and self-limiting. This paper focuses on non-pathogenic human parasites.

These organisms can be divided into two groups: ectoparasites, which live on the surface of the human body, and endoparasites, which live inside the host organism, which includes the rest of the parasites described in this paper.

ENTAMOEBA GENUS

Entamoeba is a genus of eukaryotic unicellular protists belonging to the group Amoebozoa. Members of this genus are internal parasites or commensals of various animal species, including humans (Lösch, 1875). Of the nine species known to inhabit humans, virtually the only pathogenic species is *E. histolytica*, which causes a disease called amoebiasis or amoebiasis. The remaining eight species are commensals of the gastrointestinal tract (Hooshyar et al., 2015), capable only of causing opportunistic infections (Riccardi et al., 2019). This article discusses the nonpathogenic species in humans below.

Entamoeba coli

E. coli is a cosmopolitan, mono- and homoxenous species that inhabits the human large intestine and cecum. Its developmental cycle includes a metabolically active, feeding trophozoite and a spore-forming cyst (Haidar and De Jesus, 2023; Hooshyar et al., 2015).

The trophozoite is 20-25 μm in diameter, mononuclear, with visible digestive vacuoles and cytoplasm divided into endoplasm and ectoplasm. It develops short, rounded pseudopodia, which it uses primarily for phagocytosis of other intestinal microorganisms, such as members of the Enterobacteriaceae, but also other intestinal protists, such as Giardia intestinalis. Its movement is very limited. It can reproduce by fission, resulting in two daughter organisms from a single parent organism.

The cyst is spherical, 10-35 μm in diameter, and is characterized by the presence of 8 or even 16 nuclei, distinguishing it from other representatives. It is excreted in the feces and constitutes the invasive form of this organism. Excystization occurs within the small intestine of the host (human), and the resulting trophozoites settle in their final habitat (Haidar and De Jesus, 2023). Physiologically, E. coli infection is asymptomatic, but in immunocompromised conditions, it can manifest as loose stools, colic, and flatulence. If the population grows significantly and colonizes the upper gastrointestinal tract, gastritis, dyspepsia, and hyperacidity may also occur (Haidar and De Jesus, 2023).

Entamoeba dispar

E. dispar is a cosmopolitan, polyxenous, and homoxenous species that also inhabits the large and small intestines. It can colonize these parts of the digestive tract in humans, but also in monkeys such as chimpanzees, macaques, and baboons. Similar to E. coli, its life cycle includes a metabolically active, feeding trophozoite form and a spore-forming cyst (Hooshyar

et al., 2015). Both forms are morphologically identical to those of pathogenic E. histolytica (CDC, 2024).

The trophozoite is 15-20 μm in diameter, mononuclear, with visible digestive vacuoles and cytoplasm divided into endoplasm and ectoplasm. Like E. coli, it develops rounded pseudopodia, which it uses primarily for phagocytosis of other intestinal microorganisms. However, these also enable progressive movement, distinguishing it from the E. coli trophozoite. Despite its morphological similarity to E. histolytica, digestive vacuoles may be a distinguishing feature. E. histolytica vacuoles typically contain phagocytosed erythrocytes, reflecting its ability to infect tissues. E. dispar, as a nonpathogenic species, has no access to the bloodstream and will not contain erythrocytes in its vacuoles. Mitotic division also occurs (CDC, 2024; Hooshyar et al., 2015).

Interestingly, E. dispar has been found to possess the same virulence factor as E. histolytica (cysteine protease), but its expression is approximately 10-1000 times lower than in E. histolytica (Oliveira et al., 2015).

The cyst is spherical, 12-15 μm in diameter, and typically has four nuclei. This makes it indistinguishable from E. histolytica cysts or cysts of other, less common species, such as E. moshkovskii and E. hartmanni. It is excreted in the feces and constitutes the invasive form of this organism. Excystation occurs within the host's (human) small intestine, and the resulting trophozoites settle in their final habitat (CDC, 2024; Hooshyar et al., 2015).

Physiologically, E. dispar infection is asymptomatic, but in immunocompromised conditions it can manifest as non-dysentery or dysenteric colitis, and when it invades the upper gastrointestinal tract, it can also cause liver abscesses (Oliveira et al., 2015).

Entamoeba moshkovskii

E. moshkovskii differs in its habitat and geographic range from previously described species. It is not a cosmopolitan species, and its distribution is limited to North America, Italy, South Africa, and Bangladesh. Unlike most members of the genus, it is capable of leading a free-living lifestyle. Its natural habitats include sediments at the bottom of rivers and coastal lakes, as well as sewage. Infection can occur through the ingestion of contaminated water, and the trophozoites are capable of surviving in the host's gastrointestinal tract, making it a facultative commensal. It is a mono- and homoxenic organism – its only potential host is humans. The developmental cycle includes a metabolically active, feeding trophozoite and a spore-forming cyst (Heredia et al., 2012; Hooshyar et al., 2015).

The trophozoite is 11-13 μm in diameter, mononuclear, with visible digestive vacuoles and cytoplasm divided into endoplasm and ectoplasm. It develops rounded pseudopodia, which it uses primarily for phagocytosis of other intestinal microorganisms and, like E. dispar, enables progressive movement. Despite its morphological similarity to E. histolytica, E. moshkovskii digestive vacuoles do not contain erythrocytes. Like other members of the genus, mitotic division occurs (Heredia et al., 2012). The trophozoite exhibits greater tolerance to environmental conditions – it is osmotolerant, can survive in the trophozoite form at room temperature, and is resistant to emetine, to which E. histolytica and E. dispar are sensitive (Ali et al., 2003).

The cyst is spherical, 10-12 μm in diameter, and is usually characterized by the presence of four nuclei, making it difficult to distinguish from E. histolytica cysts and other species that produce four-nucleated cysts. Both the trophozoite and the cyst are invasive (Heredia et al., 2012; Ali et al., 2003).

Physiologically, E. moshkovskii infection is asymptomatic, but in immunocompromised conditions, it can manifest as diarrhea, abdominal pain, and sometimes dysentery (Heredia et al., 2012).

Entamoeba gingivalis

E. gingivalis is a cosmopolitan, homoxenous species distinguished by its habitat. While most Entamoeba species inhabit the large intestine of animals, *E. gingivalis* inhabits the oral cavity. It primarily occupies the periodontal pockets, teeth, and interdental spaces in humans, as well as in dogs, cats, horses, pigs, and monkeys. It has a unique developmental cycle, consisting exclusively of the trophozoite - no cyst stage (Hooshyar et al., 2015; Błaszczak et al., 2018).

The trophozoite is 10-20 μm in diameter, mononuclear, with visible digestive vacuoles and cytoplasm divided into endoplasm and ectoplasm. It develops rounded pseudopodia, which it uses primarily for phagocytosis of oral microorganisms, but also macrophages and neutrophils. As with *E. dispar* and *E. moshkovskii*, these enable progressive movement. These pseudopodia contain unique proteins AGC kinase-1, that allow *E. gingivalis* to perform a process called "trogocytosis," which involves the detachment and phagocytosis of small fragments of host cells (Bonner, 2018). Morphologically, it is indistinguishable from members of Entamoeba, but its unique habitat allows for relatively easy species identification. Mitotic division occurs as in other members of the genus. As the only life form, it is also the invasive

form of this species. The main routes of infection are kissing, respiratory droplets, and sharing cutlery (Błaszczak et al., 2018).

Physiologically, *E. gingivalis* infection is asymptomatic, but in immunocompromised conditions it can manifest as gingivitis and periodontitis (Sumaiah and Abbas, 2012).

Entamoeba hartmannii

E. hartmannii, like other species of the genus Entamoeba, is an intestinal amoeba whose primary habitat is the large intestine. Morphologically, it differs slightly from *E. histolytica*, reaching smaller sizes in both developmental stages. The life cycle consists of a mononuclear trophozoite, approximately 5-12 μm in diameter, exhibiting non-progressive motile behavior, and an octanucleate cyst, approximately 6-8 μm in diameter (Deryło, 2011). Individuals residing in the large intestine are incapable of causing disease. However, they are diagnostically significant because cysts and trophozoites are transmitted only in feces. The presence of this pathogen in a patient's stool samples may suggest direct contact with infected stool or indirect contact, for example, through the consumption of contaminated food. Identification of *E. hartmannii* may indicate possible infection with other potentially pathogenic organisms present in stool. This suggests the need for additional testing for other pathogens in the gastrointestinal tract and allows for early treatment to prevent disease progression.

OTHER INTESTINAL AMOEMOTE SPECIES

Iodamoeba butschii

I. butschlii has a worldwide distribution. Its identification is based on recognizing its trophozoite and cyst stages. The species received its name due to the characteristic mass of glycogen present in its cyst form. It is considered a nonparasitic amoeba, a commensal of the human large intestine, as well as other primates and pigs. It can serve as an indicator of water and food contamination via the oral-fecal route (Iglesias-Osores and Failoc-Rojac, 2018).

Trophozoites present in the intestines feed on other microorganisms, such as bacteria and yeasts. They possess low motility due to hyaline pseudopodia. They can be observed using ferric hematoxylin and trichrome staining. Trophozoites range in size from 6 to 25 μm. The cytoplasm contains a single nucleus as well as inclusions that give it a granular appearance (Iglesias-Osores and Failoc-Rojac, 2018).

A significant diagnostic feature for this species is the presence of a large, compact mass (vacuole) of glycogen in the cyst stage. Although this mass may be visible in wet slides without staining, it appears darker, reddish-brown in iodine-stained slides. The glycogen vacuole does not stain with trichrome but appears as a well-defined mass (Garcia, 2007).

Dientamoeba fragilis

The unicellular flagellate protozoan, D. fragilis, is one of the most frequently diagnosed parasites in the human gastrointestinal tract, with a global distribution. However, important aspects of its biology remain incompletely understood or controversial, particularly its life cycle, host range, transmission routes, and disease-causing capacity. Molecular epidemiological studies are rarely performed and are limited by the lack of informative genotyping tools (Cacciò, 2017).

The trophozoite, a vegetative form that develops in the intestine, was for a long time the only known form; later, a cyst stage was also described. Two main routes of transmission have been considered: the first suggests the involvement of a vector – an intestinal helminth (Enterobius or Ascaris), while the second suggests a typical fecal-oral route (Cacciò, 2017).

The introduction of polymerase chain reaction (PCR) has become a versatile and sensitive diagnostic method for detecting intestinal parasites, and in some Western countries, PCR has virtually completely replaced microscopic diagnosis. However, PCR has led to an increase in the number of patients with positive D. fragilis results. The questionable pathogenic nature of this intestinal parasite and the apparent increase in patients with positive PCR results have renewed discussions between physicians and microbiologists regarding management of infected patients (van Gestel et al., 2019).

D. fragilis is treated with iodoquinol, paromomcin, or combination therapy. Observable symptoms include diarrhea lasting more than two weeks and abdominal pain (Stark et al., 2010).

Endolimax nana

This protozoan from the genus Archamoebae inhabits the human large intestine. It occurs in approximately 13.9% of the human population. Trophozoites move via pseudopodia and feed on bacteria and can survive in stool for one day at room temperature, while cysts can survive in stool for up to two weeks at room temperature and up to two months at lower temperatures (Veraldi et al., 2020). Transmission of parasites from this group occurs through the consumption of raw vegetables and fruits contaminated with cysts and unboiled water, as well as through contact with infected animals (Poulsen and Stensvold, 2016).

E. nana is considered a nonpathogenic species and does not cause any symptoms, but this issue is still under investigation. Some scientists claim that this parasite can cause irritation within the crypts of the intestinal mucosa, and there are also frequent reports linking the presence of E. nana protozoa with chronic diarrhea, urticaria, and polyarthritis, although the evidence for this is considered insufficient (Poulsen and Stensvold, 2016).

FLAGLADES OF THE GENUS TRICHOMONAS

The genus Trichomonas belongs to the protozoan group of flagellates. They are single-celled organisms with a spindle- or pear-shaped shape, possessing flagella or flagellate-less forms, but possessing a motor apparatus.

Protozoa of the genus Trichomonas are usually pathogenic parasites, although nonpathogenic species also occur. Many species of the genus Trichomonas are host-specific, meaning they occur only in a single host species. Some *Trichomonas* species are transmitted directly from host to host in the form of a trophozoite, as they do not have a cystic form.

Trichomonas tenax

T. tenax is a protozoan that primarily inhabits the human oral cavity. It is an anaerobic parasite – it does not possess mitochondria. T. tenax trophozoites, which are the invasive form, typically manifest as oval forms, although other morphologies, such as round or ellipsoidal ones, are occasionally encountered. However, these are not part of the developmental cycle, as previously believed, but rather an adaptation to the conditions prevailing in the host site (Matthew et al., 2023). It can be transmitted through kissing or by sharing cutlery with an infected person. The invasive form is the trophozoite.

Debates continue as to whether this protozoan is pathogenic (Kellerova and Tachezy, 2017). It has been linked to periodontal disease because it secretes an enzyme, cysteine protease, whose activity may potentially contribute to the development of symptoms (El Sibaei et al., 2012). Further research is recommended to better understand its role in these disorders (Taghipour et al., 2022). T. tenax has been observed more frequently in individuals with poor oral hygiene, and is also more prevalent in smokers, the elderly, and those with chronic diseases such as diabetes or cardiovascular disease (Mohammed and Alwaaly, 2019).

Pentatrichomonas hominis

P. hominis belongs to the trichomonad group and is a parasite without mitochondria. It is characterized by the presence of three to five anterior flagella and a single posterior flagellum. The invasive form is trophozoites (Gookin et al., 2007). It colonizes the gastrointestinal tract, most commonly the large intestine, and the reproductive tract of humans and other animals (Bastos et al., 2018). Transmission occurs via the fecal-oral route. A link between the presence of the parasite and the development of colon cancer has been suggested (Zhang et al., 2019). The parasite affects the composition of the microbiome, leading to a reduced diversity of species within it (Hongbo et al., 2022).

Molecular methods and electron microscopy observations are used to identify the exact Trichomonas species, as identification under a light microscope is virtually impossible (Weizhi et al., 2014)

OTHER SPECIES OF NON-PATHOGENOUS INTESTINAL PROTOZOAS

Blastocystis hominis

B. hominis is a single-celled organism that is one of the most common fecal pathogens. Most infected patients are asymptomatic carriers. Diagnosis of infection is based on the presence of more than five identified organisms per high-magnification field of view. The parasite, comparable in size to a macrophage (approximately 5-40 μm), resides in the large intestine and is transmitted via the fecal-oral route (Janarthanan et al., 2011).

Initially, various morphological forms were identified, such as vesicular, granular, and amoeboid; later studies revealed several additional forms - avesicular, multivesicular, and cystic. The biochemistry of the organism and the functions and structure of its organelles have not yet been sufficiently studied, and none of the proposed life cycles have been experimentally confirmed. The form in which it is transmitted has also not been defined.

Infections with this organism occur worldwide and affect both immunocompetent and immunocompromised individuals. Symptoms attributed to B. hominis infection are rare and usually nonspecific. Diarrhea, abdominal pain, nausea, and occasionally, in more severe cases, fever and sometimes even gastrointestinal bleeding are observed. Infection is diagnosed by microscopic examination of stained smears or wet mounts of fecal material. Most laboratories identify B. hominis by observing the vesicular form, although morphological studies indicate

that other forms, such as cysts and the multivesicular form, should also be sought for diagnosis (Stenzel and Boreham, 1996).

The need for treatment for blastocytosis is debated. However, there are known cases in which the parasite was unsuccessfully eradicated. To prevent blastocytosis, the so-called "dirty hands disease," it is recommended to avoid consuming food and water that could be contaminated with cysts. Great caution should be exercised when traveling to countries with poor sanitary and hygiene standards. Personal hygiene is also crucial – thoroughly washing hands with soap after using the toilet, changing diapers, contact with animals, and before preparing meals (Wiercińska, 2022). Gamma-irradiation plays a significant role in the inactivation of *B.* spp., and can be a preventative tool for sterilizing water against *B.* spp. (Mohammad et al., 2022).

Balantidium coli

B. coli is an endoparasite that inhabits the large intestine. The parasite, in its trophozoite form, has cilia, is oval, and grows to a large size. It can cause ulceration of the large intestinal wall because the trophozoites secrete proteolytic enzymes capable of digesting the mucosa. The primary hosts are pigs, and the cysts contained in their feces are the invasive form. Humans become infected by swallowing the cysts through contaminated food or water, so people who have direct contact with pigs are most susceptible to the disease (de Oliveira et al., 2022). It can cause balantidiasis, usually manifested by diarrhea.

DEMODEX MITES

Demodex mites are parasites belonging to the family Demodicidae. This article discusses two species within this genus: D. folliculorum and D. brevis, which live on the surface of human skin and in hair follicles. They can be found on all parts of the body, but are most common on the face. Under physiological conditions, they occur at a density of up to 5 individuals per cubic centimeter (however, with increasing host age, this number increases – in people over 70 years of age, colonies of this parasite can number from 1,000 to 2,000 individuals (Hom et al., 2013). These organisms are essentially non-pathogenic, but with intense infestation, they can cause disease.

A disease that can be caused by this parasite is demodicosis, which is diagnosed when the parasite density exceeds 5 individuals per cubic centimeter or when they penetrate the dermis (Karabay and Çerman, 2020). The cause of demodicosis in humans is most likely a

weakened immune system. Secondary symptoms caused by Demodex include inflammation of the eyelid margins -blepharitis (Czepita et al., 2007).

These are the only parasites which inhabit human eyelashes, and humans are their sole hosts. Their adaptation to the hair and sebaceous glands is their four pairs of appendages, which stabilize them within the structures mentioned above. It is estimated that the parasite takes two weeks to develop from egg to larval stage, while its total lifespan is approximately three weeks. Demodex is an integral part of the eyelash flora and is the most common human parasite, which can manifest itself through certain symptoms (e.g., chronic blepharitis) (Fromstein et al., 2018).

Demodex folliculorum

They are found primarily at the base of hair follicles and in epithelial cells. The sebaceous glands of the face. The parasites lay their eggs in these areas, which can result in eyelash pathology and dermatitis (Fromstein et al., 2018).

Demodex brevis

It occurs in the sebaceous glands, which results in rapid transmission of the parasite from the mother to the child. Demodex *brevis* can be present in the nipple, and therefore can be transmitted during breastfeeding. Its numbers then increase with growth due to the increased variety of food intake and increased secretion from the sebaceous glands during puberty (Elston and Elston, 2014).

NONPATHOGENOUS HUMAN NEMATOD

Enterobius gregorii

E. gregorii is a helminth that can cause an infection in its host, called enterobiasis. Symptoms of enterobiasis may include perianal itching, abdominal pain, insomnia, and skin irritation in the area. The parasites may also be present in fecal material, which may increase the risk of infecting others.

E. gregorii is a nematode found primarily in humans. It can be found worldwide, but is most common in countries with a temperate climate. This parasite is found primarily in the large intestine, and its eggs are primarily excreted in the feces. E. gregorii was initially considered a developmental form of E. vermicularis, but observations of varying spine lengths in males of this species (Hasegawa et al., 1983) led to the separation of a new species. The

spines of E. gregorii are shorter, ranging from 70 to 80 µm, than those of E. vermicularis, ranging from 100 to 120 µm (Totkova, 2003). Females are morphologically indistinguishable (Chittenden and Ashford, 1986).

The long-term presence of E. gregorii in the body can lead to complications such as appendicitis, enteritis or urinary tract infections.

Summary

Some organisms previously considered parasites are now considered commensals. These organisms coexist with the host without significantly affecting its health. A parasite that is generally nonpathogenic does not cause disease symptoms, but this is possible with large numbers of parasites, with comorbidities, and in immunocompromised individuals. In individuals with severely weakened immune systems, even normally nonpathogenic organisms can cause disorders and increase the risk of secondary infections. This applies to transplant patients, individuals undergoing chemotherapy, and individuals with advanced HIV.

Most nonpathogenic parasites do not require treatment if the individual is asymptomatic, does not belong to a risk group, and test results do not indicate a coexisting pathogenic parasite. However, treatment may be indicated when diagnostic uncertainty exists due to the lack of available molecular testing.

Furthermore, it is important to remember that nonpathogenic human parasites can play several important roles, both neutral and potentially beneficial. Some of them compete with pathogenic parasites for space and nutrients, may inhibit their excessive growth and be an indicator of the overall condition of the microbiome.

Conflicts of Interest - None

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