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Hymenolepiasis

AUTHORS DETAIL

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INTRODUCTION

Two cestodes species are known for producing hymenolepiasis in human beings, namely, *Hymenolepis diminuta* and *H. nana*. Out of these, *H. nana* is the main culprit that affects humans worldwide in most cases. It especially affects the children living in areas with lower hygiene standards. *H. nana* infections are frequent in countries with mild and tropical weather. They are usually asymptomatic, whereas heavy infections can present many gastrointestinal symptoms and allergic responses. *H. nana* carries out a monoxenic life cycle with a single final host, which can be a man, mice, or rats. Also, this cestode can be carried out in a heteroxenic cycle in which an arthropod is involved (Kim et al. 2014; Cabeza et al. 2015; Panty et al. 2017).

H. diminuta, on the other hand, mainly affects rodents mostly, though it may also infest humans by chance. It is one of the non-invasive parasites as it lacks the tapeworm scolex hooks that injuriously invade the host body. Despite this non-invasive behavior, it is still a threat to the host as its metabolic secretions hinder the normal functioning of the host's alimentary tract. *H. diminuta* carries out only an heteroxenic cycle. This is a zoonotic cestode parasitizing the small intestine of rodents (definitive hosts). Humans can become unintentionally intermingled in cestodes life cycle upon ingestion of insects infested with infective parasites (Kapczuk et al. 2018; Panty et al. 2020).

Etiological Agents

Almost all cestodes, or tapeworms (class Cestoda in the phylum Platyhelminthes), are parasitic as adults in the intestinal tract of vertebrates. They are bilaterally symmetric, usually flattened dorsoventrally, and lack a body cavity (Smyth 1994). The cestodes are broadly classified as pseudophyllidean and cyclophyllidean cestodes. *Hymenolepis* species (spp.) fall into the cyclophyllidean group, which is characterized by the presence of four cup-like structures in the scolex/head called suckers. The suckers are either armed (presence of hook-like structures) or unarmed (no hooks). *Hymenolepis* spp. is armed with the presence of a single round of hooks around the suckers (Kandi et al. 2019).

The disease known as Hymenolepiasis in humans is produced by the infection with either of two parasitic cestode species: *H. nana* or *H. diminuta*. *H. nana* adult size 15 to 40 mm in length. The second one is also known as the rat tapeworm and the adults measure 20 to 60 cm in length (Fig. 1,2) (Al-Olayan et al. 2020).

The scolex of *H. nana* bears a retractable rostellum, armed with a single circle of 20 to 30 hooks (Fig. 2). The neck is long and slender, and the proglottids are wider than they are long. Genital pores are unilateral; each mature segment contains three testes. Gravid segments break off from the strobila and disintegrate, releasing eggs 30 to 47 µm in diameter. The oncosphere is covered with a thin hyaline outer membrane and an inner thick membrane, with polar thickenings that bear several hair-like filaments embedded in the inner membrane (Schantz, 1996).

The body of *H. diminuta* has three sections of it is body: a scolex also called the head, neck, and a strobilus. It has four suckers and at scolex, it has an apical organ, but it does not have rostellar hooks. In both male and female sexual organs, the strobilus is detached into a proglottid (Arai 1980; Deines et al. 1999; Pappas, 2000).

Life Cycle *of Hymenolepis* spp.

The *Hymenolepis* spp. has two types of life cycles, direct and indirect life cycle (Fig. 3). In the case of humans, the source of infection is the ingestion of food contaminated with embryonated eggs of parasites and water which is contaminated with feces. Inside the human, which is a definitive host, the parasite followed the direct life cycle for its propagation (Ito and Budke 2021). Upon arrival in the stomach, the eggs which are in the infective phase hatch due to the action of gastric and biliary juices which soften the walls of the egg and result in the release of oncospheres.

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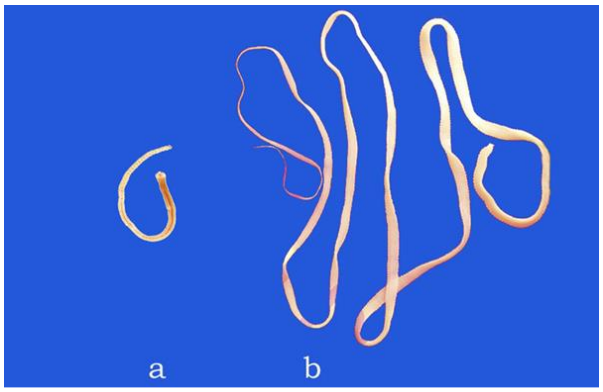

Fig. 1: Comparative size between *Hymenolepis nana* (a) and *H. diminuta* (b) (Composition by Carlos R. Bautista-Garfias).

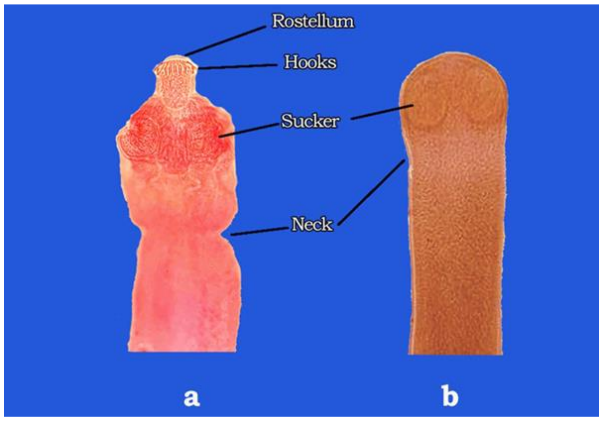

Fig. 2: Adults: (a) *Hymenolepis nana*, and (b) *H. diminuta* (Composition by Carlos R. Bautista-Garfias).

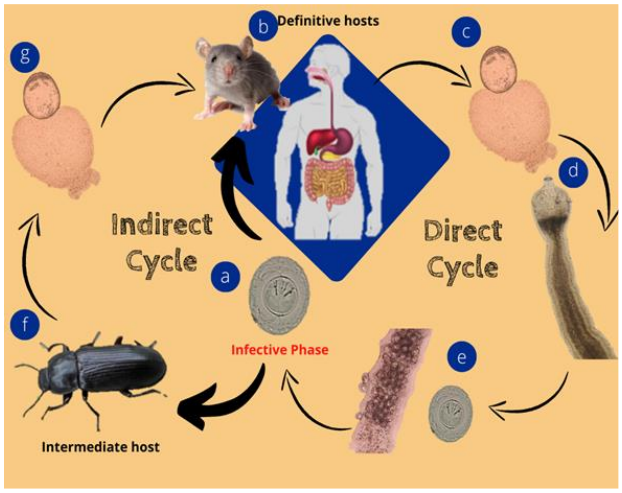

Fig. 3: *Hymenolepis* spp. life cycle. (a) Embryonated egg in the external environment (b) Definitive hosts: human and rodents. (c) Cysticercoid larvae develop in small intestine microvilli. (d) The adult phase develops in the ileum. (e)Eggs released from gravid proglottids (f) Arthropod intermediate host: *Tenebrio*. (g) Cysticercoid larvae develop in insects (Composition by Belén Mendoza-Galves).

The oncospheres once released start penetrating microvilli of the small intestine (doubtful). On the fifth day of the life cycle, the oncosphere is now a cysticercoid larva that is able to move through the jejunum and ileum and transformed into the adult phase. The gravid proglottids are now detached and release eggs that infect other or the same host through feces (Gutierrez and Ruiz 2014).

The indirect cycle requires two hosts to complete the cycle (the definitive host and the intermediate host). This occurs mainly in rodents and occasionally in humans by accidental ingestion of coprophagous arthropods (Galán-Puchades 2015), more commonly flour beetles, belonging to the genera *Tenebrio* and *Tribolium*, as well as flea larvae such as *Xenopsylla cheopis*, *Ctenocephallides canis*, and *Pulex irritans* which are intermediate hosts, these, in turn, have been infected by feeding on fecal matter containing the eggs of *Hymenolepis* spp., harboring the cysticercoid larvae stage, which settles in the hemocoel of the insect until it is ingested by its host definitive, where the cysticercoid larvae are released, migrates to the ileum and settles to complete its adult stage (Al-Mekhlafi 2020).

The host can get the infection through autoinfection, in which the eggs are not passed through the feces and grow into the adult phase inside the same host intestine. Only those people who get infected through this mechanism have slow intestinal movements which give parasites a long period to stay in the body (Galan-Puchades 2015).

Diagnosis

The diagnosis of hymenolepiasis may be: clinical, parasitological, or molecular, although the first after it has been carried out by an experienced medical practitioner, requires a confirmative laboratory test. It has to bear in mind that the majority of infections are asymptomatic.

Clinical

It is based on clinical signs such as crampy abdominal pain, diarrhea, anorexia, and anal pruritus. The affected person may also exhibit dizziness, irritability, sleep disturbance, and seizures (Kandi et al. 2019).

Parasitological

Eggs in fecal samples can be identified by performing a microscopic examination of the sample (Galos et al. 2022). A simple test tube floatation technique (FLOTAC) is a reliable qualitative test reliable method for copro-diagnostic purposes and can be effectively performed to detect the presence of nematode and cestode eggs of *H. diminuta* and *H. nana*. *H. nana* infection can be differentially diagnosed by measuring 30 × 47 µm in diameter parasite eggs. These eggs when observed in stool slide appear to have double membranes. On the other hand, *H. diminuta* eggs are measured to be 70 × 80 µm in diameter (Fig. 4) (Steinmann et al. 2012).

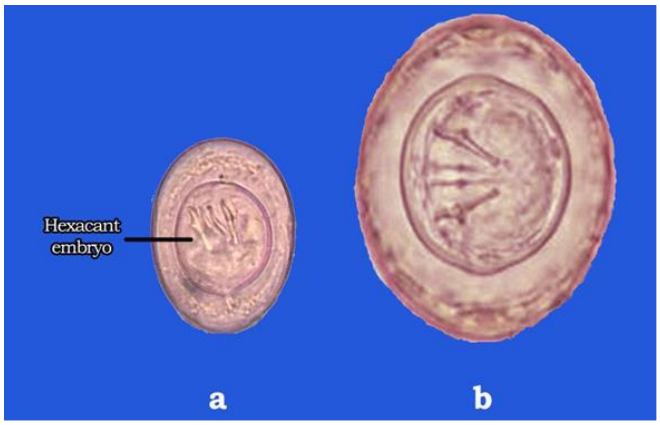

Fig. 4: Eggs: (a) *Hymenolepis nana* and (b) *H. diminuta*. (Composition by Carlos R. Bautista-Garfias).

Molecular

Sharma et al. (2016) carried out Restriction Fragment Length Polymorphism (RFLP) and Polymerase Chain Reaction (PCR) studies of the nuclear ribosomal internal transcribed spacer 2 (rDNA-ITS2) gene markers. The researchers found that both *H. nana* and *H. diminuta* displayed distinct restriction patterns when digested with one of the enzymes namely RsaI, HaeIII, or HhaI. The annotated rDNA-ITS2 sequences from the two species turned out to be different in the length; a clear demarcation was also seen between the secondary folded structures of the two species along with length difference in helices. The pyrimidine-pyrimidine mismatches and sites of motifs occurrence were also found to be varying. Yang et al. (2017) got the molecular diagnosis of *H. nana* and *H. diminuta*, evaluated in rats by amplification of the internal transcribed spacer 2 (ITS2) region of the nuclear ribosomal RNA gene and the mitochondrial cytochrome C oxidase subunit 1 (COX1) gene, through PCR.

Epidemiology

With an estimated 50-75 million human carriers worldwide *H. nana* and *H. diminuta* probably are the most common cestode parasites of humans. Afghanistan, Argentine, Africa, Asia, Australia, Central and South America, India, Italy, Spain, Mexico, North America, and southern and eastern Europe are the endemic areas for these cestodes with prevalence rates going from as low as 1% to as high as 30%. The institutionalized populations are most prone to infections with prevalence rates reaching up to 8% in patients suffering from immunity or nutritional issues. In children, *H. nana* can have a prevalence of 5–25%. In contrast to this *H. diminuta* is distributed multi-ethnically and its prevalence in some parts of India is found to be up to 1%. Children that are exposed to rodents and stored cereals or grains have the highest chances of getting infected (Besedina 1970; Buscher and Haley 1972; Ghadirian, 1972; Cabeza et al. 2005; Guerrant et al. 2011; Burton et al. 2013; Mega et al. 2013; Abrar et al. 2015; Cabada et al. 2016; Cabada et al. 2017; Bennet et al. 2020). Throughout the Northern Territory of Australia, *H. nana* remains endemic, predominantly infecting Indigenous children less than 5 years of age (Hamid et al. 2015).

Panti-May et al. (2020) to get a more accurate estimate of human cases that got infected with *H. diminuta*, a literature review of published records was conducted. This review was from the literature about human infection with *H. diminuta*. An overview explaining human infections with this parasite. From an exhaustive list of 80 countries, one thousand five hundred and sixty-one published records of infection with *H. diminuta* were identified. The review displays an estimated number of *H. diminuta* infection cases in humans with an overview of the current prevalence rate, symptoms, geographic distribution, diagnosis of the disease, mechanism of exposure to infective stages, and approaches for the treatment of this underestimated tapeworm with zoonotic potential (Nasir et al. 2004).

Panti-May et al. (2020) with the aim to describe the role of rodents as a potential zoonotic source of infection, conducted a morphological and molecular survey on cestodes in rural "Paraiso" and "Xkalakdzonot" villages from Yucatan, Mexico. *H. nana* infected to 7.8% of children from Paraíso, *H. microstoma* was isolated in 4.4% of *Mus musculus* from Paraíso, and *H. diminuta* in 15.3% of *Rattus rattus* from Xkalakdzonot villages (Goudarzi et al. 2021).

Parasitic infection is a major health issue that affects humans in developing countries. (Kheirandish et al. 2014) in a study people working as staff in fast food shops, roast meat outlets, and restaurants of Khorramabad and southeast of Kerman provinces (Western Iran), people were selected and then checked for the infestation of parasites. The percentage of intestinal parasites found in this study is as follows: *Giardia lamblia* 2.9%, *Entamoeba coli* 4.3%, *Blastocystis* sp. 1.4%, and *H. nana* 0.5%-2.5% (Willcocks et al. 2002; Kheirandish et al. 2014; Panti-May et al. 2020a; Panti-May et al. 2020b). *H. nana* (2.4%) a helminthic parasite is found as the most common parasite of the intestine in a study of the southeast of Kerman province southeastern Iran. Many authors logistic regression proved that *Hymenolepis* is associated with parasitic intestinal infections which spread through drinking water and residential status (rural/urban) (Daryani et al. 2015; Sadeghi et al. 2019; Khojasteh et al. 2021). Near the southeastern coast of continental North America, wild animals have been found for specimens of *Peromyscus polionotus* and species *hymenolepidid* have been found in the old field mouse and these cestodes are attributed to *Hymenolepis*. *H. folkertsi* n. sp. It belongs to a diverse genera *Peromyscus* which has 56 unique species in the Nearctic. Recent research and evidence show that the diversity of tapeworms is due to the huge variety of hosts including small rodents of the family Cricetidae, murid, and geomyid in sympatry (Abbaszadeh et al. 2020). The distribution of Hymenolepiasis around the world is shown in Fig. 5.

Fig. 5: The worldwide *Hymenolepiasis* distribution. (Composition by Germán R. Colmenares Viladomat).
Regions with Hymenolepiasis Regions free

Factors Involved in the Transmission of *Hymenolepis* spp.

With no requirement for an intermediate host in its life cycle makes *H. nana* one of its kind and unique cestode. Both man and rodents can act as final and intermediate hosts simultaneously for this parasite. Some arthropods can also serve intermediate hosts including fleas and grain beetles. The eggs present in the contaminated hands, fomites, soil, water, and food can serve as a source of infection in humans if ingested. This is the reason for the high prevalence of these parasites in populations with low hygiene standards and a high number of rodents. Sometimes the accidental ingestion of insects containing this parasite can also lead to the transmission of infection to humans. The factors like the seasons of the year or the socio-economic conditions may favor the transmission of *H. nana*. Lack of hygiene plays a vital role in spreading infection. The precarious housing conditions and the presence of animal feces in public parks. Most children are affected due to the lack of good hygiene habits. Consuming unwashed and dirty vegetables or fruits is also a factor that supports the spread of infection. It is a well-known fact that vegetables are irrigated with sewage making them a suspect of harboring parasitic agents (Loján-Neira et al. 2017; Chitsaz et al. 2018; Murillo-Zavala et al. 2018).
H. diminuta causes disease in humans less frequently than it does in animals. Various larvae and adult insects are susceptible to infection with this parasite. The ingestion of this parasite's eggs by insects (e.g. flour beetles or larvae of fleas) leads to the formation of the cysticercoid larva inside their body cavity. Humans may have a chance of infection if they orally consume these larvae along with raw or undercooked insects that were already infested. Oral ingestion is the only route of transmission. The prevalence of this parasite mainly occurs in individuals living in areas with lower hygiene standards, the presence of rodents in living premises, and a history of careless behavior with animals. It is especially important in areas where insects are commonly consumed as food (Martínez-Barbabosa et al. 2012; Melhorn 2016).

Control

The use of oral praziquantel (single dose of 20-25 mg/kg for children as well as adults) is the most common way of treatment. After using the drug, a copro-parasitoscopic follow-up is done after 3 weeks. Besides this nitazoxanide is used as an alternative treatment if the parasitosis is 82% (Apt 2013).
The drug praziquantel works by increasing the permeability of the tegument of the helminth resulting in the rupture of the tegument and death of the helminth occurred (Cruz and Camargo 2001). While the mechanism of action of nitazoxanide is the inhibition of tubulin, which causes destabilization in the tubulin-microtubule balance, thus causing the parasite to lose cell homeostasis and thus detachment and death (Scarcella et al. 2007).
The side effects that praziquantel generates in greater proportion are headache, abdominal pain, nausea, dizziness, drowsiness, and rarely fever, hives, and seizures, for which research has been carried out in the search for an alternative treatment for the elimination of the parasite reducing the adverse effects or that they do not alter the daily life of the patient (Pabón 2014).

Alternatives for Controlling Hymenolepiasis

The use of medicinal plants like spice and culinary herb "cinnamon" is an alternative method to control hymenolepiasis. Different studies reveal that the bark of cinnamon has organic extracts, proanthocyanidin tannins, and trans-cinnamaldehyde. Since this knowledge is not enough and further studies are required on the antiparasitic properties of *Cinnamonum* spp. and some action of this plant is shown in some infections of cestodes (Castañeda-Ramírez et al. 2020).
On the other hand, the use of extracts from edible mushrooms for medicinal purposes has become more evident today and they have been shown to help reduce or eliminate the number of parasites in certain infections. A study by Velazco-Cruz (2017), evaluated the hydroalcoholic extract of the edible mushroom *Pleurotus ostreatus* in rodents infected with *H. diminuta*. The (ECS-1123) strain of the edible mushroom *P. ostreatus* was obtained from the mycological strain collection of the Tropical Fungi Laboratory (Colegio de la Frontera Sur located in Tapachula, Chiapas, Mexico) under the prior authorization of Dr José E. Sánchez. The hydroalcoholic extract was obtained by the maceration method, it was administered orally to a batch of rats and its activity was evaluated at the egg and adult levels. Obtaining a reduction at the egg level of 29.8% and 67.56% at the adult level at a concentration of 8 mg/mL.

Conclusion

H. nana is the main culprit that causes hymenolepiasis in humans across the world. It especially affects the children living in areas with lower hygiene standards. It is important

to emphasize having a three-party vision of a global one-health triad that lets humans, animals, and the environment join forces to understand their interrelationship in maintaining the ecosystem. The concept of "One Health" presented an idea that was already known to man for more than a century, human and animal well-being are interdependent and connected to the health of the ecosystems in which they co-exist. We accepted and applied this approach as a collaborative goal of the global effort to understand the risks faced by human and animal health as well as the well-being of the ecosystem as a whole unit.

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