Ternidens Infection

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Learning Objectives

1. To understand the importance of Ternidens infection and the need to differentiate it from Oesophagostomiasis which can present in similar manner.
2. To understand the importance of egg hatching techniques like the Harada–Mori method in definitive diagnosis.

Introduction

Ternidens deminutus, a nematode of zoonotic importance, affects both humans and non-human primates. Since the egg of the parasite resembles that of hookworm egg, *T. deminutus* has often been referred as false hookworm. The nematode is found most commonly in southern Africa, where it infects the large intestines of primates like baboons and vervet monkeys, whereas it has been documented only in monkeys in parts of Asia. A prevalence rate of up to 87% in humans has been reported in some surveyed populations in Zimbabwe. The similarity of *T. deminutus* eggs of parasite to that of hookworm poses a major challenge for both diagnosis and accurate prevalence surveys of soil-transmitted helminths (STH).

History

In 1865, these parasites were found in a vial collected during autopsy of a native of Mayotte, in the Comoro Islands of Mozambique. The autopsy was conducted by Monestier, who was a physician in the French navy. These parasites were initially identified as *Ancylostoma duodenale* and suggested as the aetiological agents of anaemia. In 1905, Railliet and Henry, while studying the collection of parasitic nematodes in the National Museum of Natural History in Paris, described this helminth as *Tropidophorus deminutus*. Subsequently, these authors established it as a new genus, *Ternidens,* in 1909. Smith, Fox and White in 1908 isolated a new worm called *Globocephalus macaci*, from a pig-tailed monkey, which died at the Philadelphia Zoo; later this worm was identified by Sandground as *T. deminutus*.

Taxonomy

The genus *Ternidens* belongs to phylum Nemathelminthes; order Strongylida; superfamily

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Strongyloidea and family Strongylidae. *T. deminutus and Ternidens simiae* are two pathogenic species that cause infections in humans and animals.

Genomics and Proteomics

The length and G + C content of the sequences of the second internal transcribed spacer (ITS-2) of rDNA of *T. deminutus* is 216 bp and ~43%, correspondingly. Studies have stated minimal (2.8%) difference in the nucleotide sequencing of parasites isolated from baboon and Mona monkey, but there was no sequence variation among *T. deminutus* parasites recovered from the baboon. These findings suggest a significant population variation or the existence of cryptic species within the *T. deminutus* species. Reports of ITS-2 sequence differences (27–48.3%) among the two taxonomic units of *T. deminutus* and hookworms (superfamily Ancylostomatoidea) formed the basis for the identification and delineation by PCR-based mutation scanning.

The Parasite Morphology

Adult Worm

T. deminutus adult males and females from humans measure 6–13 mm and 9–17 mm in length, respectively, and appear darker in colour than those adults worms isolated from baboons. Adult worms of *T. deminutus* are straight compared to the curved appearance of adult hookworms. Just below the buccal capsule lies the transverse cuticular fold. The cuticle appears opaque and has transverse striations. The sub-globose buccal capsule is large and swollen. It has three deep sets of teeth, an anteriorly facing mouth surrounded by a mouth collar and 22–24 bristles of the corona radii. The anterior end has four sub-median papillae and two lateral amphids. The oesophagus measures 525–840 mm in length. The males have a cup-shaped copulatory bursa, two spicules and a gubernaculum. The spicules measure 1116–1441 mm. Females have a protuberant vulva, located slightly anterior to the anus (Fig. 1).

Fig. 1 Adult worm of *Ternidens deminutus* (courtesy: Bradbury R. S. 2019. *Ternidens deminutus* Revisited: A Review of Human Infections with the False Hookworm. *Tropical medicine and infectious disease*, *4*(3), 106. Under Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/))

Egg

T. deminutus eggs are larger in size. They measure 70–94 μm in width and 40–60 μm in length. The greater ratio of width to length distinguishes *T. deminutus* eggs from those of hookworm eggs. Eggs have 4–32 morulae, which undergo further development within the egg and later hatch into larvae (Fig. 2).

Larva

Rhabditiform Larvae

The first-stage (L1) rhabditiform larvae of *T. deminutus* measure around 3.60 μm in length and 20 μm in width. The buccal cavity measures 10.5 × 1.5 μm in size. The oesophagus is 95 μm long. A refractile and spindle-shaped genital primordium measures 11.2 μm in length. A long flagella-like tail present in the distal end measures 70 μm in length. The second-stage (L2) larvae measure 620 μm in length and 32 μm in width, with an oesophagus of 140 μm in length.

The rhabditiform larvae *T. deminutus*, *Strongyloides* and hookworms appear to be morphologically similar to each other. Nevertheless, *T. deminutus* rhabditiform larvae can be differentiated from others on the basis of their long buccal cavity, longer tail and prominent genital primordium.

Filariform Larva

The filariform (L3) larvae measure 630–730 μm in length and 29–35 μm in width. The larva at its anterior end bears the head, followed by an indentation and a spear-shaped buccal cavity. The larva has the gut of characteristic "zigzag" appearance. The oesophagus measures 150–165 μm in length, nearly one third of the length of the intestine length, and shows a slight bulge distally. The oesophagus is separated from the intestine by two elongated sphincter cells. The intestine is palisade-shaped due to the presence of the ten pairs of large triangular cells. A genital primordium of 15 μm in length is found near the middle of the larva. The anus opening is present, 120–145 μm away from the tail end. It has a pointed tail. The filamentous end of the sheath extends a little, making it appear thread-like at the posterior end of the worm.

T. deminutus filariform larvae are readily differentiated from those of other "hookworm-like" such as *Necator* spp. and *Oesophagostomum* spp., by their greater length (702–950 μm), the "Y" form of the remnant buccal cavity, the rhabditoid oesophageal bulb, which appears wider and prominent, and the absence of sphincter cells between the oesophagus and the intestine. *Oesophagostomum* spp. filariform larvae have a round tail, and the anus opening is of much shorter distance from the tip of the tail (45–88 μm) (Fig. 3).

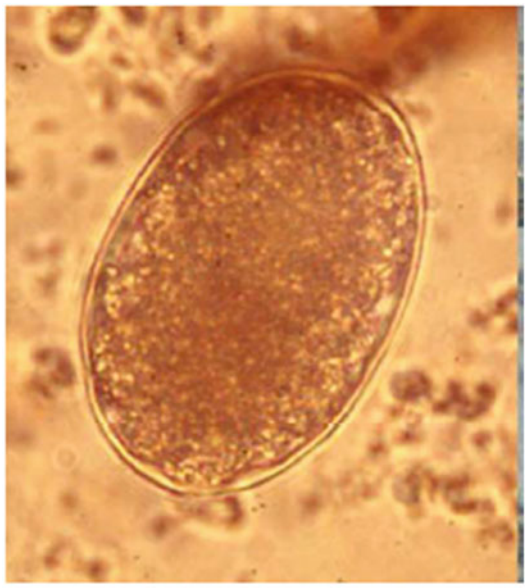

Fig. 2 Egg of *Ternidens deminutus* (courtesy: Bradbury R. S. 2019. *Ternidens deminutus* Revisited: A Review of Human Infections with the False Hookworm. *Tropical medicine and infectious disease*, *4*(3), 106. Under Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/))

Cultivation of Parasites

The Harada–Mori technique is a test tube filter paper method of stool culture. In this method, stool smeared on a moist filter paper is kept in a

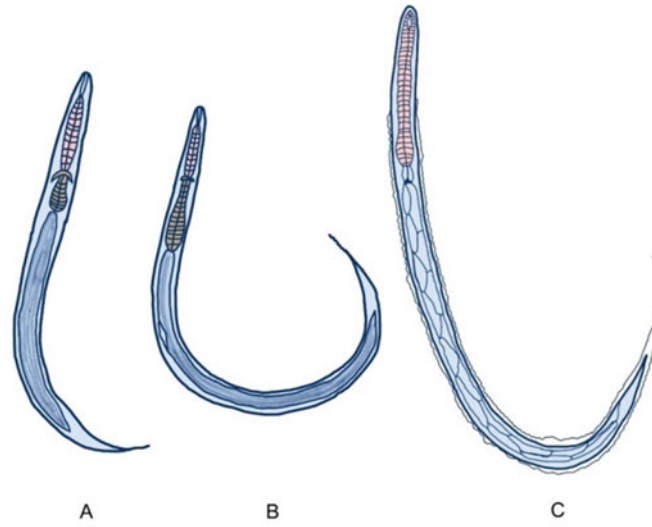

Fig. 3 Larval forms of *Ternidens deminutus:* (**a**) (L1) rhabditiform larva, (**b**) (L2) rhabditiform larva, (**c**) filariform (L3) larva

tube containing sterile water on incubation at room temperature for 8–10 days. The eggs of *T. deminutus*, if present in the stool of the host, hatch and develop into filariform larvae (L3). The method is used to differentiate the L3 larvae of *Ternidens* spp. from those of *Oesophagostomum* spp. and *Necator* spp. since eggs of all these species are morphologically similar.

Laboratory Animals

T. deminutus were identified from the autopsy of baboons, which were killed by poisoning to protect crops surrounding African settlements. In 1920 and 1930, experimental studies were carried out in human volunteers and in baboons either by ingestion of filariform larvae or cutaneous inoculation; however, this turned out to be unsuccessful.

Life Cycle of *Ternidens deminutus*

Hosts

Definite Hosts

Humans and other primates such as chimpanzees, gorillas, macaques and Cercopithecus monkeys.

Infective Stage

Filariform larvae (L3) are infective for humans and other primates.

Transmission of Infection

Humans and other primates acquire *T. deminutus* infection by ingestion of food contaminated with third-stage filariform larvae (L3). The larvae inhabit the large intestine, particularly the colon, and caecum in some individuals, unlike hookworms, which are primarily small intestine parasites. At these sites, L3 larvae attach and invade the intestinal mucosa and form nodules at the sites of attachments. The L3 larvae subsequently develop into L4 larvae. The L4 larvae are detached from the wall of the large intestine and re-enter the lumen, where they moult into adult worms. Finally, adult worms attach to the intestinal mucosa by their buccal cavity and start producing eggs that are released into lumen of the large intestine. The eggs start appearing in faeces of the infected hosts, 30–40 days after ingestion of the L3 larvae.

In the soil, the eggs become fully mature within 24–30 h of passage in the stool. The rhabditiform larvae (L1) hatch out of the eggs

after 48–72 h of presence in the soil. Further L1 larvae develop into L2 larvae after 2–3 days and finally into filariform larvae (L3), the infective stage of the parasite, after 8–10 days in the soil (Fig. 4).

Pathogenesis and Pathology

L3 larvae initiate *T. deminutus* infection by invading mucosa of the large intestine where they moult to L4 larvae and produce nodules or ulcers in the wall of the large intestine. L4 larvae detached from the wall of the large intestine moult into the adult worms in the lumen. The adult worms also produce ulcers or cystic nodules at the sites of their attachment in the intestinal wall. Heavy infections by adult worms may cause anaemia**.**

Immunology

Immune responses in chronic *T. deminutus* infection is characterized by an elevated serum IgG and IgA antibodies, specific to filariform larval antigens. However, the protective role of these serum antibodies against the nematode in infected humans is still unclear.

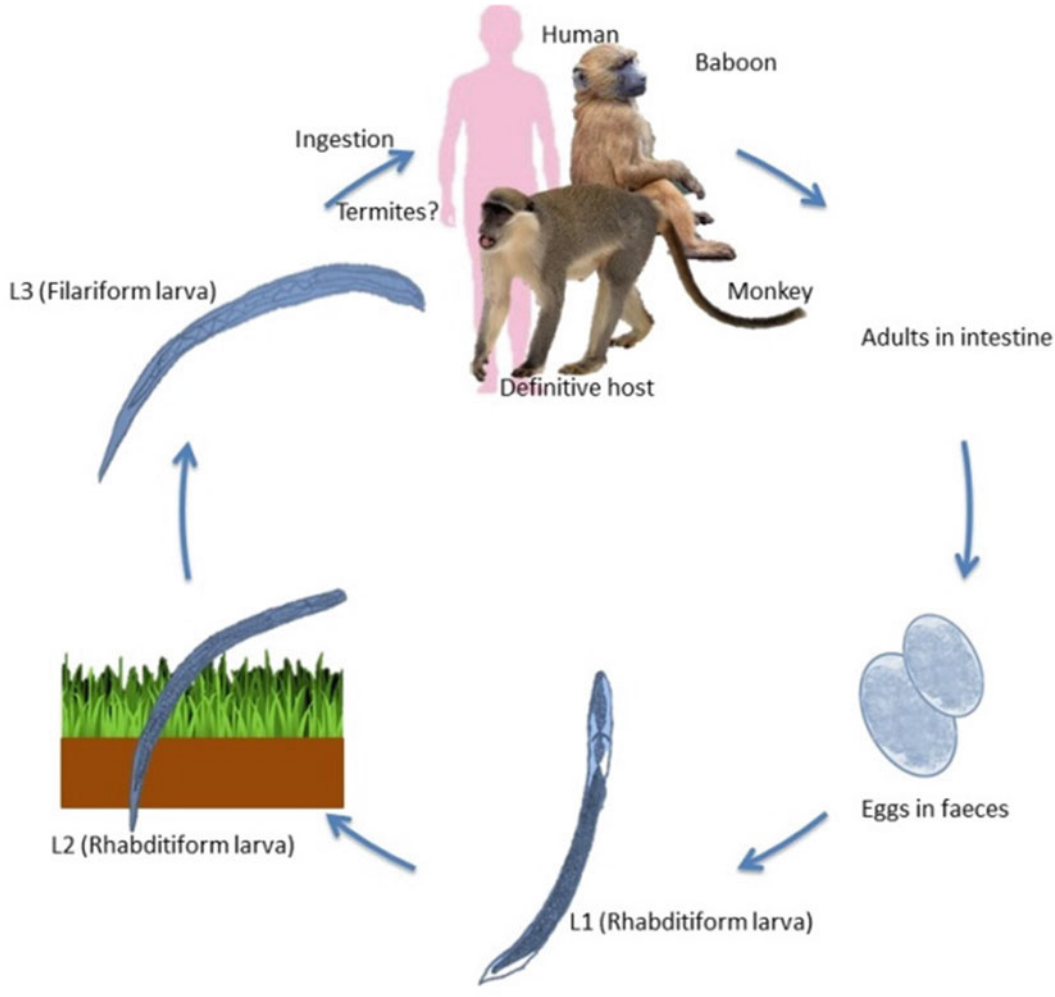

Fig. 4 Life cycle of *Ternidens deminutus*

Infections in Humans

The majority of human *T. deminutus* infections are asymptomatic.

The characteristic presentation of symptomatic chronic cases of human *T. deminutus* infection includes multiple intestinal abscesses, nodules or helminthomas of the large intestine. Adult worms may be located free in the intestinal lumen, or attached to the intestinal mucosa. Heavy infections caused by a large number of adult worms are frequently associated with malaise, obstipation and microcytic hypochromic anaemia. Co-infections of *Ternidens* with other intestinal helminthic infections have been documented in patients with poor nutritional status.

Infections in Animals

The first case of *T. deminutus* infection in primates was reported by Leiper, in a western lowland gorilla, which died at the London Zoological Gardens. Following this report, several reports of the infection in monkeys, baboons and chimpanzees were documented between 1906 and 1937, from countries in Africa and Asia. African non-human primates such as baboons and vervet monkeys are found to be more susceptible to *Ternidens* infections. The parasites are commonly found in the large intestine of primates and cause anaemia and nodules in the intestinal wall.

Epidemiology and Public Health

T. deminutus usually inhabits the large intestine of primates such as chimpanzees, gorillas, macaques and Cercopithecus monkeys in Africa, India and Indonesia. The infection has also been reported in nearly 21% of 100 Macaca mulattos from China.

Human *T. deminutus* infection has been recorded from sub-Saharan Africa (Rhodesia, Tanzania), with only one case from Thailand and two from Suriname (Table 1). No human infection has been documented from Asia, although the infection has been recorded in monkeys.

Diagnosis

The diagnosis of *Ternidens* infection is based on various laboratory methods (Table 2).

Microscopy

Stool microscopy is frequently helpful in the detection of *Ternidens* egg in the stool. These eggs, however, need to be differentiated from other hookworms based on their size and other features. Recovery of eggs in the stool is increased after concentration of stool either by the saturated salt flotation method or by the formalin-ethyl acetate sedimentation method.

Adult worms can be recovered and identified in (a) stool specimens following purgation or (b) histopathology specimen of the large intestine obtained during autopsy. It is considered to be the gold standard in diagnosis of *Ternidens* infection.

In Vitro Culture

In vitro culture of larvae to L3 stage is helpful to detect and identify *Ternidens* infection. Harada–Mori stool culture is used to detect and identify L3 stage of *Ternidens*.

Table 1 Distribution of *Ternidens* spp. of importance to humans

Species	Distribution	Definitive host
Ternidens deminutus	*Humans*—Sub-Saharan Africa, for example Rhodesia and Tanzania *Primates*—Africa, India and Indonesia	Humans, primates such as chimpanzees, gorillas, macaques and *Cercopithecus* monkeys

Table 2 Diagnostic methods for *Ternidens* infection

Diagnostic approaches	Methods	Targets	Remarks
Direct microscopy	Stool microscopy	Direct demonstration of ova and parasite	Stool concentration techniques are needed to increase the sensitivity
	Purgation or autopsy	Direct demonstration of adult worm	Gold standard method for diagnosis
Immunodiagnostics	Antibody (IFAT)	IgG and IgE antibodies	Important role in epidemiological studies *Limitation:* Cross-reaction with patient infected with related helminths
Molecular assays	PCR	ITS2	Utilized to study the prevalence and distribution of the species *Limitations:* Require skilled personnel

Serodiagnosis

Indirect immunofluorescent test (IFAT), surface precipitation test, etc., are used for the detection of specific antibodies against *T. deminutus*, in the sera for the diagnosis of *T. deminutus* infection in humans. The IFAT, which used adult worm antigen, in the test, however, showed cross-reaction with sera from a patient infected with related helminths such as *Necator americanus.* The surface precipitation test employed exsheathed larvae that were incubated with immune serum at 4 °C, following which they were sectioned and examined by electron microscopy. Serological assays also play an important role in epidemiological studies.

Molecular Diagnosis

Genetic characterization of *T. deminutus* has been performed by sequencing the second internal transcribed spacer (ITS-2) of nuclear ribosomal DNA (rDNA). This molecular characterization of *T. deminutus* was carried out in the adult worm isolated from the olive baboon and the Mona monkey. The molecular methods are extremely useful not only for identification but also for understanding the prevalence of the *Ternidens* spp. in the community (Table 2).

Treatment

Thiabendazole and pyrantel pamoate are highly effective for the treatment of *Ternidens* infections in humans, with high cure rates. Pyrantel pamoate was observed to be effective for *T. deminutus* infection with high rates of cure but with a few side effects. Albendazole, mebendazole and ivermectin have also been evaluated for the treatment of the condition with good efficacy.

Treatment of helminthic pseudo-tumours and helminthic abscess is primarily by surgical excision of the involved bowel, or removal of worms from nodules.

Prevention and Control

Prompt disposal of human and animal faeces prevents hatching and contaminating soil with the *Ternidens* eggs, which make it important for control of the parasitic infection. Routine veterinary care of pet animals and animals in zoos with regular deworming reduces environmental contamination with the zoonotic hookworm eggs and larvae. Personal hygiene and safety measures to avoid skin contact with sand or soil prevent infection with these nematodes.

Case Study

A 35-year-old man presented with fever, abdominal pain, tenderness and a right lower quadrant mass. Exploratory laparotomy showed a live worm, which was extracted from the mass found at the ileum. The worm was identified as *T. deminutus*.

1. Name the clinical condition of this patient.
2. What is the gold standard method for diagnosis of this condition?
3. How does human *Ternidens* infection occur?
4. Mention the differentiating features with other hookworms.
5. What are the various modalities of treatment of *Ternidens* infections?

Research Questions

1. How do we carry forward the research available on the knowledge about biology, transmission or the extent of its effects on primate hosts regarding *Ternidens* spp.?
2. What role is played by *Ternidens* when there is co-infection with other helminths and the contribution of *Ternidens* in causation of anaemia?

Further Readings

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