# CHAPTER TWO

# LITERATURE REVIEW

## 2.1 Intestinal Parasite

Parasitic infections, caused by intestinal helminths and protozoan parasites, are among the most prevalent infections in humans in developing countries. In developed countries, protozoan parasites more commonly cause gastrointestinal infections compared to helminths. Intestinal parasites cause a significant morbidity and mortality in endemic countries.

Helminths are worms with many cells. Nematodes (roundworms), cestodes (tapeworms), and trematodes (flatworms) are among the most common helminths that inhabit the human gut. Usually, helminths cannot multiply in the human body. Protozoan parasites that have only one cell can multiply inside the human body. There are four species of intestinal helminthic parasites, also known as geohelminths and soil-transmitted helminths: Ascaris lumbricoides (roundworm), Trichiuris trichiuria (whipworm), Ancylostoma duodenale, and Necator americanicus (hookworms). These infections are most prevalent in tropical and subtropical regions of the developing world where adequate water and sanitation facilities are lacking ([1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B1),[2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B2)). Recent estimates suggest that A. lumbricoides can infect over a billion, T. trichiura 795 million, and hookworms 740 million people ([3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B3)). Other species of intestinal helminths are not widely prevalent. Intestinal helminths rarely cause death. Instead, the burden of disease is related to less mortality than to the chronic and insidious effects on health and nutritional status of the host ([4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B4),[5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B5)). In addition to their health effects, intestinal helminth infections also impair physical and mental growth of children, thwart educational achievement, and hinder economic development ([6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B6),[7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B7)).

An intestinal parasite infection is a condition in which a [parasite](https://en.wikipedia.org/wiki/Parasite) infects the [gastro-intestinal tract](https://en.wikipedia.org/wiki/Gastro-intestinal_tract) of humans and other animals. Such parasites can live anywhere in the body, but most prefer the intestinal wall. Routes of exposure and infection include ingestion of undercooked meat, drinking infected water, [fecal-oral transmission](https://en.wikipedia.org/wiki/Fecal-oral_transmission" \o "Fecal-oral transmission) and skin absorption. Some types of [helminths](https://en.wikipedia.org/wiki/Helminths) and [protozoa](https://en.wikipedia.org/wiki/Protozoa) are classified as intestinal parasites that cause infection—those that reside in the [intestines](https://en.wikipedia.org/wiki/Intestines). These infections can damage or sicken the host (humans or other animals). If the intestinal parasite infection is caused by helminths, the infection is called [helminthiasis](https://en.wikipedia.org/wiki/Helminthiasis).

Signs and symptoms depend on the type of infection. Intestinal parasites produce a variety of symptoms in those affected, most of which manifest themselves in gastrointestinal complications and general weakness.[[1]](https://en.wikipedia.org/wiki/Intestinal_parasite_infection#cite_note-:0-1) Gastrointestinal conditions include [inflammation](https://en.wikipedia.org/wiki/Inflammation) of the [small](https://en.wikipedia.org/wiki/Enteritis) and/or [large intestine](https://en.wikipedia.org/wiki/Colitis), [diarrhea](https://en.wikipedia.org/wiki/Diarrhea" \o "Diarrhea)/[dysentery](https://en.wikipedia.org/wiki/Dysentery), [abdominal pains](https://en.wikipedia.org/wiki/Abdominal_pain), and [nausea](https://en.wikipedia.org/wiki/Nausea)/[vomiting](https://en.wikipedia.org/wiki/Vomiting). These symptoms negatively impact nutritional status, including decreased absorption of [micronutrients](https://en.wikipedia.org/wiki/Micronutrient), loss of appetite, weight loss, and intestinal blood loss that can often result in [anemia](https://en.wikipedia.org/wiki/Anemia" \o "Anemia). It may also cause physical and mental disabilities, [delayed growth](https://en.wikipedia.org/wiki/Delayed_growth) in children, and skin irritation around the anus and vulva.[[2]](https://en.wikipedia.org/wiki/Intestinal_parasite_infection#cite_note-2)

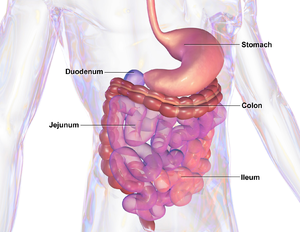


Figure 2.1: Human gastro-intestinal system

The most common intestinal protozoan parasites are: Giardia intestinalis, Entamoeba histolytica, Cyclospora cayetanenensis, and Cryptosporidium spp. The diseases caused by these intestinal protozoan parasites are known as giardiasis, amoebiasis, cyclosporiasis, and cryptosporidiosis respectively, and they are associated with diarrhoea ([8](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B8)). G. intestinalis is the most prevalent parasitic cause of diarrhoea in the developed world, and this infection is also very common in developing countries. Amoebiasis is the third leading cause of death from parasitic diseases worldwide, with its greatest impact on the people of developing countries.

In an article published in this issue of the Journal, Jacobsen et al. looked at the prevalence of intestinal parasites in young Quichua children in the highland or rural Ecuador ([13](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B13)). They have found a high prevalence of intestinal parasites, especially the intestinal protozoan parasites. They have used the traditional microscopic technique to diagnose intestinal parasitic infections. In total, 203 stool samples were examined from children aged 12-60 months and found that 85.7% of them had at least on parasite. The overall prevalence of intestinal protozoan parasites were: E. histolytica/E. dispar 57.1%, Escherichia coli 34.0%, G. intestinalis 21.1%, C. parvum 8.9%, and C. mesnili 1.7%, while the prevalence of intestinal helminthic parasites in this study were: A. lumbricoides 35.5%, T. trichiura 0.5 %, H. diminuta 1.0%, and S. stercoralis 0.7%. A recent study in Nicaragua in asymptomatic individuals found that 12.1% (58/480) were positive for E. histolytica/E. dispar by microscopy, but E. histolytica and E. disapr were positive by polymerase chain reaction (PCR) only in three and four stool samples respectively among the microscopic positive samples (Unpublished data). This study proves again that the diagnosis of E. histolytica/E. dispar is neither sensitive nor specific when it is done by microscopy. To understand the real prevalence of E. histolytica-associated infection, a molecular method must be used for its diagnosis.

Soil-transmitted helminth infections are invariably more prevalent in the poorest sections of the populations in endemic areas of developing countries. The goal is to reduce morbidity from soil-transmitted helminth infections to such levels that these infections are no longer of public-health importance. An additional goal is to improve the developmental, functional and intellectual capacity of affected children ([37](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B37)). Highly-effective, safe single-dose drugs, such as albendazole, now available, can be dispensed through healthcare services, school health programmes, and community interventions directed at vulnerable groups ([38](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B38)). As these infections are endemic in poor communities, more permanent control will only be feasible where chemotherapy is supplemented by improved water supplies and sanitation, strengthened by sanitation education. In the long term, this type of permanent transmission control will only be possible with improved living conditions through economic development. Intestinal protozoa multiply rapidly in their hosts, and as there is a lack of effective vaccines, chemotherapy has been the only practised way to treat individuals and reduce transmission. The current treatment modalities for intestinal protozoan parasites include metronidazole, iodoquinol, diloxanide furoate, paromomycin, chloroquine, and trimethoprim-sulphamethoxazole ([39](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B39)). Nitazoxanide, a broad-spectrum anti-parasitic agent, was reported to be better than placebo for the treatment of cryptosporidiosis in a double-blind study performed in Mexico ([40](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B40)). Genomes of these three important protozoan parasites have already been published ([41](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B41)–[43](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754014/#B43)), and studies are underway to understand protective immunity to these protozoan parasites to develop vaccines for them.

**2.2 Classification of Intestinal Parasite**

**2.2.1 Protozoa**

Protozoa are single-celled eukaryotic microorganisms that can infect the human gastrointestinal tract, leading to a variety of illnesses. Recent research has provided valuable insights into the classification, epidemiology, and clinical impact of protozoan intestinal parasites. Here, we will discuss protozoa in more detail, along with recent citations to support the information.

**Entamoeba histolytica:** Recent Citation: Petri, W. A., & Singh, U. (2019). Diagnosis and management of amebiasis. Clinical Infectious Diseases, 69(9), 1696-1702.

Entamoeba histolytica is a pathogenic amoeba responsible for amoebic dysentery and amoebic liver abscess. Recent research has focused on improving diagnostic methods, such as PCR-based techniques and antigen detection, to distinguish E. histolytica from non-pathogenic Entamoeba species. Furthermore, studies have explored potential drug targets for the treatment of amoebiasis.

**2. Giardia lamblia:** Recent Citation: Savioli, L., Smith, H., & Thompson, A. (2006). Giardia and Cryptosporidium join the 'Neglected Diseases Initiative.' Trends in Parasitology, 22(5), 203-208.

Giardia lamblia, the causative agent of giardiasis, remains a common waterborne parasite with global significance. Recent research has highlighted the importance of molecular epidemiology in tracking the sources of Giardia infections, particularly in outbreaks. Additionally, studies have focused on drug resistance and the development of new treatment strategies for giardiasis.

**3. Cryptosporidium spp.:** Recent Citation: Checkley, W., White Jr, A. C., Jaganath, D., Arrowood, M. J., Chalmers, R. M., Chen, X. M., ... & Guerrant, R. L. (2015). A review of the global burden, novel diagnostics, therapeutics, and vaccine targets for cryptosporidium. The Lancet Infectious Diseases, 15(1), 85-94.

Cryptosporidium spp. are protozoan parasites responsible for cryptosporidiosis, a diarrheal disease with a significant impact on public health, especially in immunocompromised individuals. Recent research has focused on improving diagnostics, such as the development of molecular methods and antigen-based tests. The search for effective treatments and vaccine candidates against Cryptosporidium has also been an area of active investigation.

Recent research has expanded our knowledge of other protozoan intestinal parasites, including Entamoeba coli, Dientamoeba fragilis, and Balantidium coli. While these parasites are generally considered non-pathogenic, some studies have indicated potential associations with gastrointestinal symptoms, prompting further investigation into their clinical significance.

**2.2.2 Helminths (Worms)**

Helminth is a general term meaning worm. The helminths are invertebrates characterized by elongated, flat or round bodies. In medically oriented schemes the flatworms or platyhelminths (platy from the Greek root meaning “flat”) include flukes and tapeworms. Roundworms are nematodes (nemato from the Greek root meaning “thread”). These groups are subdivided for convenience according to the host organ in which they reside, e.g., lung flukes, extraintestinal tapeworms, and intestinal roundworms. This chapter deals with the structure and development of the three major groups of helminths.

Helminths develop through egg, larval (juvenile), and adult stages. Knowledge of the different stages in relation to their growth and development is the basis for understanding the epidemiology and pathogenesis of helminth diseases, as well as for the diagnosis and treatment of patients harboring these parasites.

Platyhelminths and nematodes that infect humans have similar anatomic features that reflect common physiologic requirements and functions. The outer covering of helminths is the cuticle or tegument. Prominent external structures of flukes and cestodes are acetabula (suckers) or bothria (false suckers). Male nematodes of several species possess accessory sex organs that are external modifications of the cuticle. Internally, the alimentary, excretory, and reproductive systems can be identified by an experienced observer. Tapeworms are unique in lacking an alimentary canal. This lack means that nutrients must be absorbed through the tegument. The blood flukes and nematodes are bisexual. All other flukes and tapeworm species that infect humans are hermaphroditic.

With few exceptions, adult flukes, cestodes, and nematodes produce eggs that are passed in excretions or secretions of the host. The various stages and their unique characteristics will be reviewed in more detail as each major group of helminths is considered.

## 2.2.3 Flukes (Trematodes)

The structure of flukes is summarized in figure 2.2 below. A dorsoventrally flattened body, bilateral symmetry, and a definite anterior end are features of platyhelminths in general and of trematodes specifically. Flukes are leaf-shaped, ranging in length from a few millimeters to 7 to 8 cm. The tegument is morphologically and physiologically complex. Flukes possess an oral sucker around the mouth and a ventral sucker or acetabulum that can be used to adhere to host tissues. A body cavity is lacking. Organs are embedded in specialized connective tissue or parenchyma. Layers of somatic muscle permeate the parenchyma and attach to the tegument.

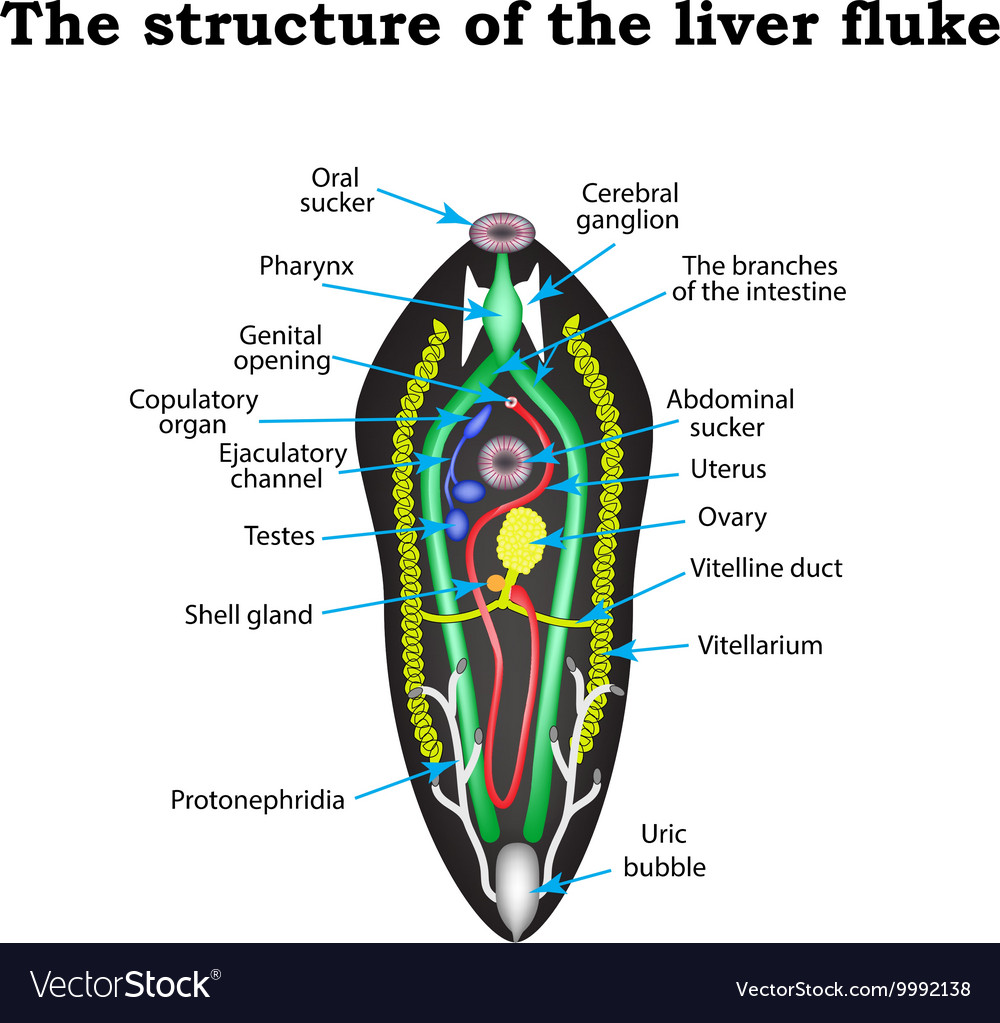


Figure 2.2: Structure of fluke

Flukes have a well-developed alimentary canal with a muscular pharynx and esophagus. The intestine is usually a branched tube (secondary and tertiary branches may be present) consisting of a single layer of epithelial cells. The main branches may end blindly or open into an excretory vesicle. The excretory vesicle also accepts the two main lateral collecting ducts of the excretory system, which is of a protonephridial type with flame cells. A flame cell is a hollow, terminal excretory cell that contains a beating (flamelike) group of cilia. These cells, anchored in the parenchyma, direct tissue filtrate through canals into the two main collecting ducts.

Except for the blood flukes, trematodes are hermaphroditic, having both male and female reproductive organs in the same individual. The male organ consists usually of two testes with accessory glands and ducts leading to a cirrus, or penis equivalent, that extends into the common genital atrium. The female gonad consists of a single ovary with a seminal receptacle and vitellaria, or yolk glands, that connect with the oviduct as it expands into an ootype. The tubular uterus extends from the ootype and opens into the genital atrium. Both self- and cross-fertilization occur. The components of the egg are assembled in the ootype. Eggs pass through the uterus into the genital atrium and exit ventrally through the genital pore. Fluke eggs, except for those of schistosomes, are operculated (have a lid).

The blood flukes or schistosomes are the only bisexual flukes that infect humans ([Fig. 86-1](https://www.ncbi.nlm.nih.gov/books/NBK8282/figure/A4545/?report=objectonly)). Although the sexes are separate, the general body structure is the same as that of hermaphroditic flukes. Within the definitive host, the male and female worms inhabit the lumen of blood vessels and are found in close physical association. The female lies within a tegumental fold, the gynecophoral canal, on the ventral surface of the male. The medically important flukes belong to the taxonomic category Digenea. This group of flukes has a developmental cycle requiring at least two hosts, one being a snail intermediate host. Depending on the species, other intermediate hosts may be involved to perpetuate the larval form that infects the definitive human host.

Flukes go through several larval stages, each with a specific name, before reaching adulthood. Taking into account variations among species, a generalized life cycle of digenetic flukes runs the following course. Eggs are passed in the feces, urine, or sputum of humans and reach an aquatic environment. The eggs hatch, releasing ciliated larvae, or miracidia, which either penetrate or are eaten by a snail intermediate host. In rare instances land snails may serve as intermediate hosts. A saclike sporocyst or redia stage develops from a miracidium within the tissues of the snail.

The sporocyst gives rise either to rediae or to a daughter sporocyst stage. In turn, from the redia or daughter sporocyst, cercariae develop asexually and migrate out of the snail tissues to the external environment, which is usually aquatic.

The cercariae, which may possess a tail for swimming, develop further in one of three ways. They either penetrate the definitive host and transform directly into adults, or penetrate a second intermediate host and develop as encysted metacercariae, or they encyst on a substrate, such as vegetation, and develop there as metacercariae. When a metacercarial cyst is ingested, digestion of the cyst liberates an immature fluke that migrates to a specific organ site and develops into an adult worm.

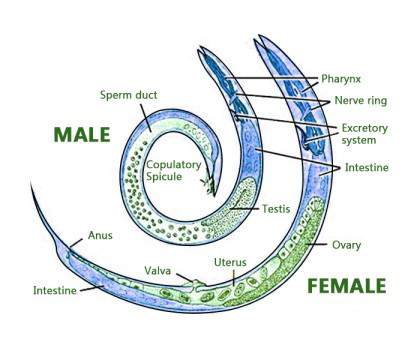
## 2.2.4 Tapeworms (Cestodes)

As members of the platyhelminths, the cestodes, or tapeworms, possess many basic structural characteristics of flukes, but also show striking differences.  Anatomically, cestodes are divided into a scolex, or head, which bears the organs of attachment, a neck that is the region of segment proliferation, and a chain of proglottids called the strobila. The strobila elongates as new proglottids form in the neck region. The segments nearest the neck are immature (sex organs not fully developed) and those more posterior are mature. The terminal segments are gravid, with the egg-filled uterus as the most prominent feature.

The scolex contains the cephalic ganglion, or “brain,” of the tapeworm nervous system. Externally, the scolex is characterized by holdfast organs. Depending on the species, these organs consist of a rostellum, bothria, or acetabula. A rostellum is a retractable, conelike structure that is located on the anterior end of the scolex, and in some species is armed with hooks. Bothria are long, narrow, weakly muscular grooves that are characteristic of the pseudophyllidean tapeworms. Acetabula (suckers like those of digenetic trematodes) are characteristic of cyclophyllidean tapeworms.

## 2.2.5 Roundworms (Nematodes)

In contrast to platyhelminths, nematodes are cylindrical rather than flattened; hence the common name roundworm. The body wall is composed of an outer cuticle that has a noncellular, chemically complex structure, a thin hypodermis, and musculature. The cuticle in some species has longitudinal ridges called alae. The bursa, a flaplike extension of the cuticle on the posterior end of some species of male nematodes, is used to grasp the female during copulation.



*Figure 2.3: Structure of nematodes.*

The cellular hypodermis bulges into the body cavity or pseudocoelom to form four longitudinal cords—a dorsal, a ventral, and two lateral cords—which may be seen on the surface as lateral lines. Nuclei of the hypodermis are located in the region of the cords. The somatic musculature lying beneath the hypodermis is a single layer of smooth muscle cells. When viewed in cross-section, this layer can be seen to be separated into four zones by the hypodermal cords. The musculature is innervated by extensions of muscle cells to nerve trunks running anteriorly and posteriorly from ganglion cells that ring the midportion of the esophagus.

The space between the muscle layer and viscera is the pseudocoelom, which lacks a mesothelium lining. This cavity contains fluid and two to six fixed cells (celomocytes) which are usually associated with the longitudinal cords. The function of these cells is unknown.

The alimentary canal of roundworms is complete, with both mouth and anus. The mouth is surrounded by lips bearing sensory papillae (bristles). The esophagus, a conspicuous feature of nematodes, is a muscular structure that pumps food into the intestine; it differs in shape in different species. The intestine is a tubular structure composed of a single layer of columnar cells possessing prominent microvilli on their luminal surface.

The excretory system of some nematodes consists of an excretory gland and a pore located ventrally in the mid-esophageal region. In other nematodes this structure is drawn into extensions that give rise to the more complex tubular excretory system, which is usually H-shaped, with two anterior limbs and two posterior limbs located in the lateral cords. The gland cells and tubes are thought to serve as absorptive bodies, collecting wastes from the pseudocoelom, and to function in osmoregulation.

Nematodes are usually bisexual. Males are usually smaller than females, have a curved posterior end, and possess (in some species) copulatory structures, such as spicules (usually two), a bursa, or both. The males have one or (in a few cases) two testes, which lie at the free end of a convoluted or recurved tube leading into a seminal vesicle and eventually into the cloaca.

The female system is tubular also, and usually is made up of reflexed ovaries. Each ovary is continuous, with an oviduct and tubular uterus. The uteri join to form the vagina, which in turn opens to the exterior through the vulva.

Copulation between a female and a male nematode is necessary for fertilization except in the genus *Strongyloides,* in which parthenogenetic development occurs (i.e., the development of an unfertilized egg into a new individual). Some evidence indicates that sex attractants (pheromones) play a role in heterosexual mating. During copulation, sperm is transferred into the vulva of the female. The sperm enters the ovum and a fertilization membrane is secreted by the zygote. This membrane gradually thickens to form the chitinous shell. A second membrane, below the shell, makes the egg impervious to essentially all substances except carbon dioxide and oxygen. In some species, a third proteinaceous membrane is secreted as the egg passes down the uterus by the uterine wall and is deposited outside the shell. Most nematodes that are parasitic in humans lay eggs that, when voided, contain either an uncleaved zygote, a group of blastomeres, or a completely formed larva. Some nematodes, such as the filariae and *Trichinella spiralis*, produce larvae that are deposited in host tissues.

The developmental process in nematodes involves egg, larval, and adult stages. Each of four larval stages is followed by a molt in which the cuticle is shed. The larvae are called second-stage larvae after the first molt, and so on. The nematode formed at the fifth stage is the adult.

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