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Digenea, Plagiorchiida

Echinostomata La Rue, 1926 (Suborder)

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Phylum Platyhelminthes

Class Trematoda

Subclass Digenea

Order Plagiorchiida

Suborder Echinostomata

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Chapter 38

Echinostomata La Rue, 1926 (Suborder)

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Introduction

Echinostomata is a suborder, belonging to the order Plagiorchiida, which includes numerous species of trematodes that are parasites of humans and are of great health significance. Moreover, other species of the suborder are of importance in the veterinary sciences. According to Olson and colleagues (2003), this is a monophyletic taxon including only the Superfamily Echinostomatoidea.

Superfamily Echinostomatoidea

Classification

Echinostomatoidea is a large and cosmopolitan group of hermaphroditic digeneans that parasitize, as adult forms, all classes of vertebrates, but exhibit particularly high diversity in birds (Kostadinova and Jones, 2005). Trematodes that are members of this superfamily are characterized by having a morphologically complex structure, high species diversity with substantial species richness (Tkach et al., 2016).

The taxon was first defined by Faust (1929); however, it was first recognized as a natural group (at the subordinal rank, Echinostomata) by Szidat (1939). Subsequently, La Rue (1957) established the order Echinostomida, including the suborders Echinostomata (comprising the superfamily Echinostomatoidea) and Paramphistomata (including Notocotyloidea and Paramphistomoidea). Cribb and colleagues (2001), after a phylogenetic analysis, supported the validity of the Echinostomatoidea as a superfamily, including 4 families, including: Echinostomatidae, Philophtalmidae, Fasciolidae, and Cyclocoelidae. The most recent classifications of Echinostomatoidea have shown that the superfamily is characterized by a broad diversity comprising 80 species representing 8 families and 40 genera (Kostadinova and Jones, 2005; Tkach et al., 2016). Tkach and colleagues (2016), using 28S rDNA gene sequences, performed a detailed analysis of the phylogeny of the superfamily Echinostomatoidea. Herein will follow the systematic summary (classification) of the Echinostomatoidea proposed by Tkach and colleagues (2016) and we will review species in the 8 families that he recognized in addition to a brief review of species of the 2 families that were not represented in their work including species of the families Rhytidodidae and Calycodidae, both comprising parasites of marine turtles. Species representing these 2 families were not represented in the analysis of Tkach and colleagues (2016).

Identification

Members of Echinostomatoidea are elongate, oval, or foliate and usually the tegument is armed (has spines). The oral sucker is commonly subterminal and the ventral sucker is larger and pre-equatorial. A pharynx is commonly present. They possess 2 testes in the hindbody. The ovary is pretesticular and adults of Echinostomatoidea include a Mehlis' gland and a uterine seminal receptacle. The male and female ducts open separately into a genital atrium. The eggs are operculated, except in Philophtalmidae (Kostadinova and Jones, 2005).

Life Cycles

The life cycles of the Echinostomatoidea have a rich and diverse ecological milieu. Miracidia typically hatch from eggs that are passed from the definitive host into an aquatic environment and actively search and penetrate the first intermediate host (which are gastropods). Miracidia respond with positive chemotaxis to glycoproteins emitted by the gastropod for the host finding (Haberl et al., 2000). Cercariae are simple-tailed and produced by rediae in the first intermediate host and may encyst on vegetation to form infective (to the definitive host) metacercariae in the environment (that is, Fasciolidae) or within a second intermediate host (that is, Echinostomatidae), commonly molluscs, frog tadpoles, crabs, or fishes, among others. To find the second intermediate host, the free-swimming cercariae use different cues than the miracidia used in order to locate the second intermediate host.

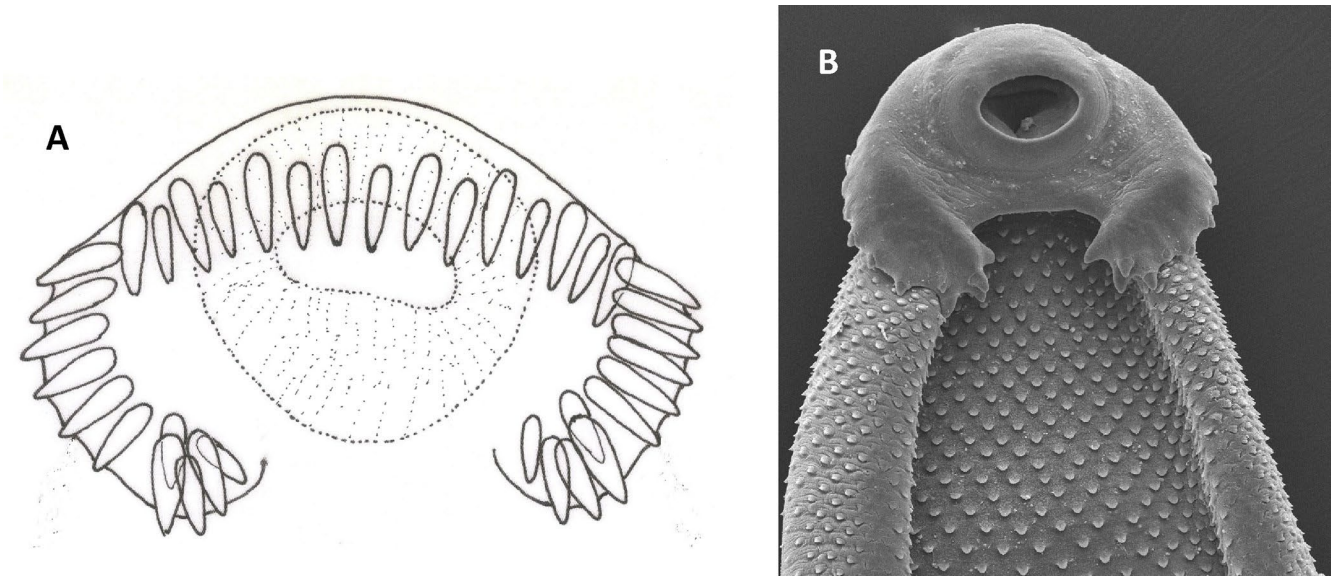

Figure 1. A) Cephalic collar of spines of *Echinostoma* sp. (Echinostomatidae) arranged in a double row (original); B) SEM microphotography of the forebody of *Echinostoma* sp. (Echinostomatidae) showing the cephalic collar of spines. Source: R. Toledo, B. Fried, and L. Acosta Soto. License: CC BY-NC-SA 4.0.

Cercariae swimming in the water commonly respond to low molecular weight molecules such as organic acids (Haberl et al., 2000). A vertebrate definitive host becomes infected after ingestion of the metacercariae.

Family Echinostomatidae Looss, 1899

The family Echinostomatidae is a heterogeneous group that predominately parasitize as adult forms a great spectrum of vertebrate hosts, such as birds, mammals and, occasionally, reptiles and fishes (Toledo et al., 2009). They are also able to parasitize humans, when people eat uncooked vegetables or crabs or crayfish, causing the foodborne infection echinostomiasis.

This family exhibits substantial taxonomic diversity and the morphological criteria adopted by different authors has resulted in a huge number of subfamilies. Kostadinova (2005a) accepted 11 subfamilies and 44 genera within Echinostomatidae as a result of a comparative morphological study, based on the examination of type materials and an evaluation of the previously published data, *Echinostoma* being the type genus.

Identification

Species of the family Echinostomatidae are mainly characterized by the presence of a prominent cephalic collar of spines (Figure 1). The spines of the cephalic collar may be arranged in 1 or 2 circles and the number of spines is usually constant within the individuals of a species. The tegument contains scale-like spines on both dorsal and ventral surfaces, though the number and size of the spines is reduced in the posterior half of the body. The oral and ventral suckers are close to each other. The 2 testes, usually situated in the body in tandem, are located posterior to the ovary. The uterus is intercecal and normally pre-ovarian. The vitellarium is follicular, in 2 lateral fields, usually in the hindbody but may extend into the forebody (Figure 2). Considerable variation exists in the size of echinostomes depending upon species and range from 5 mm to longer than 10 mm.

At the generic level, the main characters for identification are the morphology and the degree of development of the collar, the morphology of the male terminal genitalia, the position of the ovary and testes, the location and structure of the internal seminal vesicle, and the structure of the tegumental armament (Kostadinova, 2005a). Specific diagnosis within this family is difficult due to the morphological similarity of several species and, sometimes, molecular analysis is required.

Life cycles

Echinostomatid adults are hermaphroditic digeneans that live in the intestine and bile ducts of numerous vertebrates. To be viable, eggs released with feces must reach freshwater such as ponds, streams, or lakes. The fertilized eggs are undeveloped when laid and take about 2–3 weeks to reach the fully developed miracidial stage. Miracidia hatch from eggs and actively locate the first intermediate snail host in response to host signals and emitted products. Several species

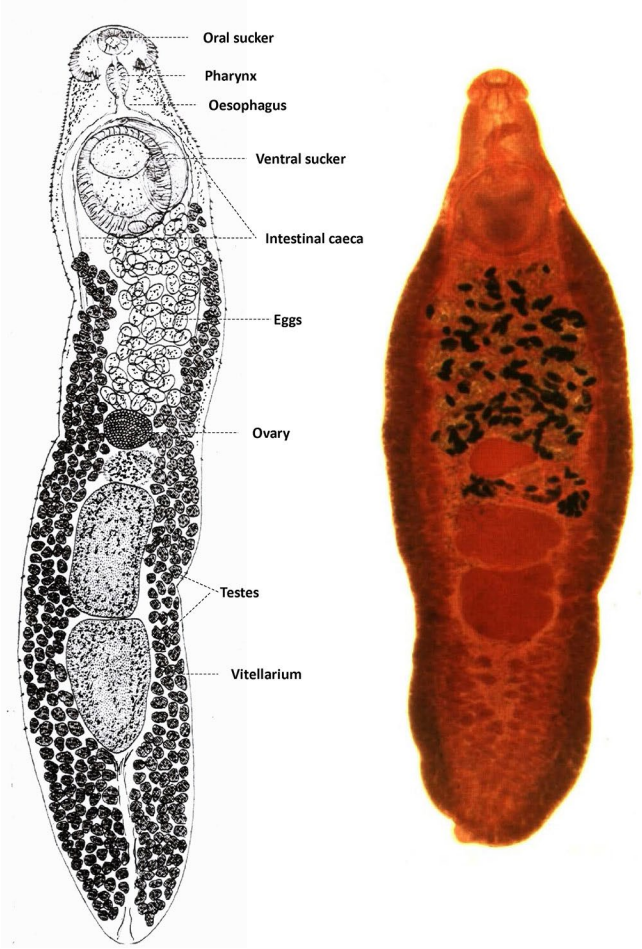

Figure 2. A) Adult *Echinostoma* sp. (Echinostomatidae); B) Adult specimen of *E. caproni* (Echinostomatidae) stained with Grenacher's borax carmin. Source: R. Toledo, B. Fried, and L. Acosta Soto. License: CC BY-NC-SA 4.0.

of planorbids, lymnaeids, and bulinids have been recorded as the first intermediate hosts. After penetration of the snail, miracidia transform into sporocysts in the heart and develop mother rediae. Mother rediae reproduce asexually and produce daughter rediae which develop in the digestive gland-ovotesis complex. Cercariae begin to emerge from infected snails from 4 to 6 weeks post-infection. *Echinostoma* cercariae show a low degree of host range and several species of snails, frogs, tapdoles, and fishes may serve as second intermediate hosts. Cercariae encyst within the second intermediate host. Definitive hosts become infected after ingestion of the second intermediate host harboring encysted metacercariae. Following infection of the definitive host, the metacercariae excyst in the duodenum and the juvenile parasites migrate to the small intestine where they attach to the mucosa by the ventral sucker (Figure 3).

Human echinostomiasis

In general, the specificity of echinostomatids toward the vertebrate is low and humans can become infected when they eat raw or inadequately cooked food, especially fish, snakes, amphibians, clams, and snails containing encysted echinostome metacercariae (Figure 3). Distribution of human echinostomiasis is strongly determined by dietary habits. Infections are most prevalent in areas where traditional cultural practices encourage ingestion of raw or undercooked wild animals. Moreover, it has been shown that drinking untreated water containing echinostome cercariae can be a source of human infection (Toledo et al., 2014; Toledo and Esteban, 2016). Most human infections are reported from foci in East Asia and Southeast Asia. Echinostomiasis is relatively rare, yet the foci of transmission remain endemic owing to local dietary preferences as noted above. Most of these endemic foci are localized in China, India, Indonesia, Korea, Malaysia, Philippines, Russia, Taiwan, and Thailand. Moreover, occasional cases have also been reported in other countries. Current incidence of human echinostomiasis is difficult to determine with any accuracy because of the lack of availability of epidemiological surveys. A total of 24 species of echinostomatids have been recorded infecting humans (Toledo and Esteban, 2016).

Major clinical symptoms due to echinostome infection may include abdominal pain, diarrhea, easy fatigue, and loss of body weight. Although the clinical signs in echinostomiasis in humans are poorly known, morbidity is due to the prolonged latent phase, symptomatic presentations, and similarity of symptoms with other intestinal helminth infections. The severity of the symptoms depends on the parasite load. Heavy infections are associated with local eosinophilia, abdominal pain, watery diarrhea, anemia, edema, and anorexia, and pathological features include catharral inflammation, erosion, and even ulceration (Toledo et al., 2006). Chai and colleagues (1994), in an endoscopic analysis of a human infection with an echinostomatid, showed that adult worms were attached to an ulcerated mucosal layer in the distal part of the stomach. The lesion was accompanied by stage IIc or stage III early gastric cancer and multiple ulcerations and bleeding in the stomach and duodenum. Ulceration and bleeding appeared to be caused by the worms. Other factors observed by endoscopy are mucosal erosions, ulcerative lesions, and signs of chronic gastritis.

Family Caballerotrematidae Tkach et al., 2016

This family was established by Tkach and colleagues in 2016. These authors analyzed the phylogenetic relationships of several Echinostomatoidea, including *Caballerotrema* spp. They concluded that *Caballerotrema* represents a unique group, comprising 3 valid species (*C. brasiliense, C. aruanense*, and *C. piscicola*) parasitic in the intestine of

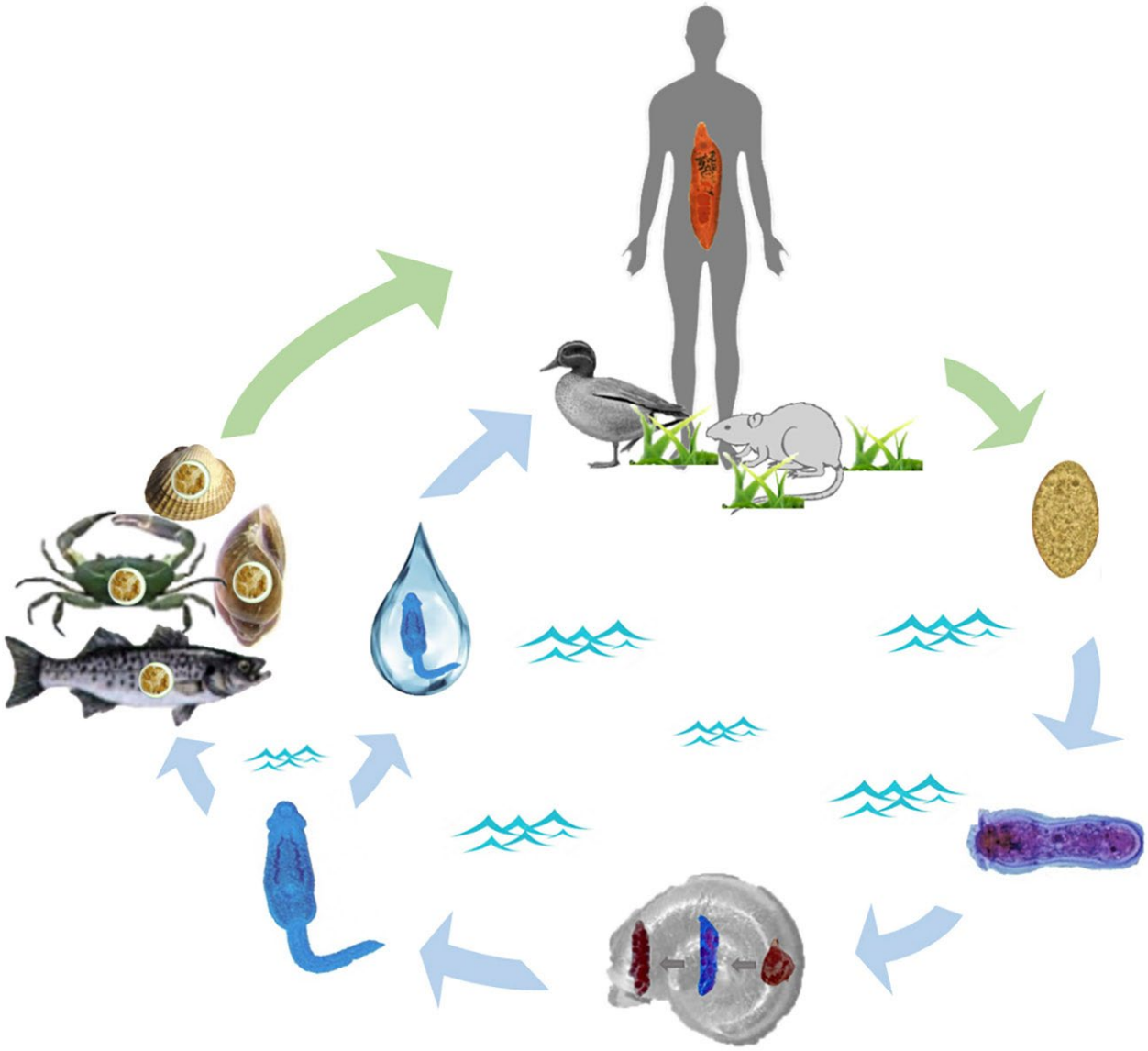

Figure 3. Generalized life cycle of echinostomes: Adult worms inhabiting the small intestine of several vertebrate hosts, including humans; eggs are voided with host feces; miracidia hatch in freshwater and actively infect the snail first intermediate host; intramolluscan stages, that is, sporocysts, mother rediae, and daughter rediae, develop within the snail; cercariae are released by the first intermediate host and swim to locate the second intermediate host (snails, amphibians, bivalves, fishes) which they penetrate; cercariae become metacercariae after encystation within the second intermediate host; and metacercariae are ingested by the definitive host and excyst to become adults. It has also been suggested that drinking water containing cercariae is a source of human infection. Source: R. Toledo, B. Fried, and L. Acosta Soto. License: CC BY-NC-SA 4.0.

freshwater fishes of South America. The genus *Caballerotrema* appeared as a separate branch closest to the Echinostomatidae. This fact together with several morphological characteristics and the use of cold-blooded vertebrates as definitive hosts led to Tkach and colleagues (2016) to distinguish *Caballerotrema* at the family level. Members of Caballerotrematidae are characterized by presenting its maximum width at the level of the collar.

Family Cyclocoelidae Stossich, 1902

Trematodes of the family Cyclocoelidae parasitize, as adult worms, the nasal cavity, hypothalamus, orbit, esophagus, trachea, air sacs, intestine, liver, kidneys, and abdominal cavity of birds feeding on molluscs. Cyclocoelidae has been an unsettled group and its taxonomic status is controversial. Kanev and colleagues (2002) placed Cyclocoelidae within the superfamily Cyclocoeloidea (Plagiorchiida) following La

Rue (1957). However, recent molecular studies have recovered this family within the Echinostomatoidea (Olson et al., 2003; Tkach et al., 2016). Thus, the superfamily Cyclocoeloidea was synonymized with Echinostomatoidea (Tkach et al., 2016).

The number of valid subfamilies, genera, and species within Cyclocoelidae is uncertain due to the continuous revisions of this group. Over 50 genera, tribes, families, and subfamilies have been included in the taxonomic organization of this group (Kanev et al., 2002). Yamaguti (1971) recognized 3 subfamilies (Cyclocoelinae, Promptenovinae, and Typhlocoelinae) and a total of 22 genera. Kanev and colleagues (2002) clarified the taxonomic situation of Cyclocoelidae by recognizing 3 subfamilies (Cyclocoelinae, Ophtalmophaginae, and Haematotrephinae) based on the relative position of the ovary respect the testes (Figure 4). Studies by Dronen (2007) and Dronen and Blend (2015) recognized a total of 6 subfamilies:

- **Cyclocoelinae** in which the ovary is intertesticular forming a triangle with the testes;
- **Haematotrephinae** in which the position of the ovary ranges from being pretesticular to opposite to the anterior testis forming a triangle with the testes;
- **Szidatitreminae** Dronen, 2007 in which the position of the ovary ranges from being posttesticular to opposite to the posterior testis forming a triangle with the testes;
- **Ophthalmophaginae** in which the ovary is posttesticular forming a straight, or nearly straight line with the tandem testes;
- **Hyptiasminae** in which the ovary is intertesticular and the testes are tandem to nearly tandem; and
- **Skrjabinocoelinae** in which the ovary is intertesticular and nearly in a straight line with the side-by-side testes.

Moreover, 22 genera and 128 species were recognized. Genera were assigned to these subfamilies based primarily on the position of the genital pore relative to the pharynx, the distribution of the vitelline fields posteriorly, and the orientation of the testes and ovary (Dronen, 2007; Dronen and Blend 2015). *Cyclocoelum* is the type genus (Figure 4).

The Cyclocoelidae are cosmopolitan and are characterized by an abbreviated life cycle in which the tail-less cercaria encysts within the first intermediate host (which are freshwater or terrestrial snails), which is eaten directly by the definitive host (Cribb et al., 2003).

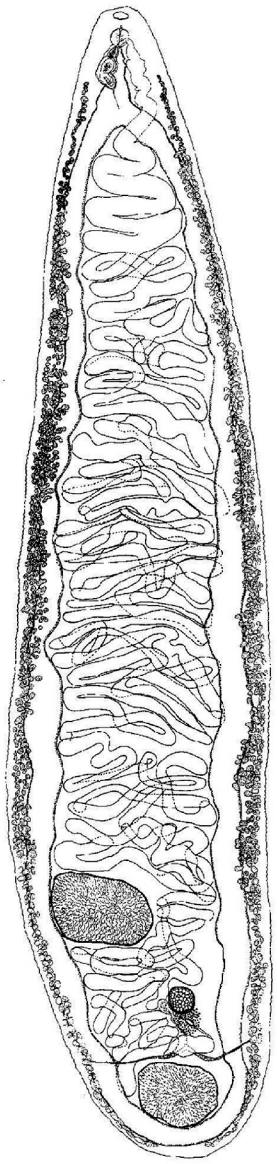

Figure 4. Adult specimen of *Cyclocoelum obscurum* (Cyclocoelidae). Source: Lamothe-Argumedo and Orozco-Flores, 2000. License: CC BY.

Family Echinochasmidae Odhner, 1910

This group was defined by Odhner (1910) as a subfamily (Echinochasminae). Posteriorly, Odening (1963) elevated the subfamily to full family rank. However, this was not followed by several authors (Skrjabin and Bashkirova, 1956; Yamaguti, 1971; Kostadinova, 2005b). Recently, molecular analyses based on concatenated amino acid sequences of 12 protein genes and 28S RNA gene sequences have strongly supported the elevation of the subfamily Echinochasminae to family status, as suggested on the basis of morphological studies by Odening in 1963 (see Le et al., 2016; Tkach et al., 2016).

This family includes cosmopolitan digenean parasites of birds, reptiles, and mammals. Echinochasmidae are characterized by the absence of a ventral connecting ridge on the collar of spines in a dorsally interrupted row (Kostadinova, 2005a). Moreover, echinochasmids have also been differentiated from other Echinostomatoidea by the even number of spines in the collar and the short pre-testicular uterus (Figure 5A) (Odening, 1963).

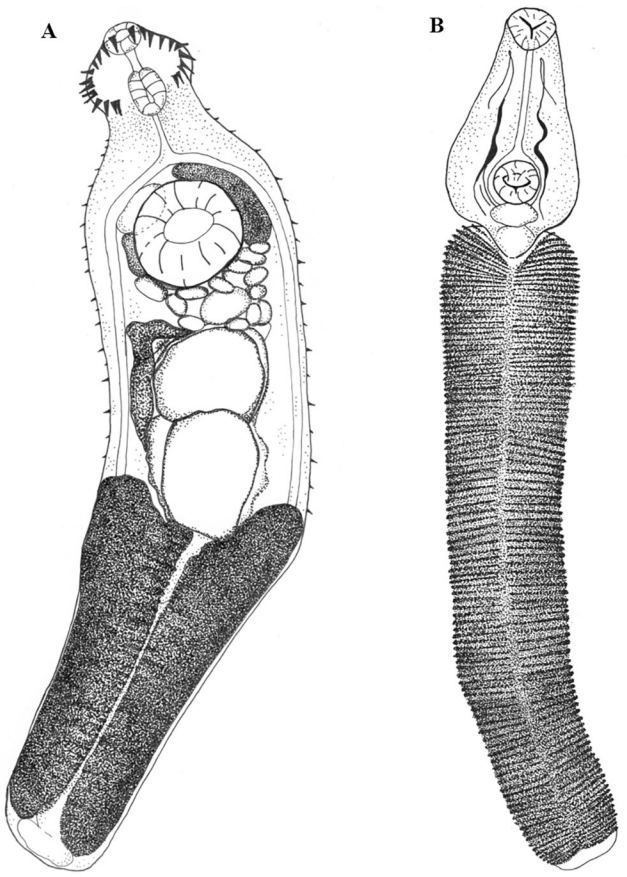

Figure 5. A) Adult specimen of *Stephanoprora* sp. (Echinochasmidae); and (B) cercariae magnacauda of *Stephanoprora* sp. (Echinochasmidae). Source: R. Toledo, B. Fried, and L. Acosta Soto. License: CC BY-NC-SA 4.0.

The life cycle of these species is triheteroxenous and involves brackish and freshwater snails (first intermediate hosts), molluscs, amphibians, and fishes (second intermediate hosts), and reptiles, piscivorous birds, and mammals as definitive hosts. Some members of Echinochasmidae infecting warm-blooded animals can cause diseases in humans, for example ,*Echinochasmus japonicus, E. perfoliatus, E. liliputanus*, and *E. fujianensis*, causing gastrointestinal disorders mainly in Asia (Toledo and Esteban, 2016). Another features of interest of the Echinochasmidae are the first intermediate host used and the morphology of the cercariae. Most other Echinostomatoidea for which life cycles are known use pulmonate snails as first intermediate hosts, whereas echinochasmids and other related families (Philophthalmidae, Psilostomidae) use prosobranch molluscs. Moreover, some species of this group have cercariae of the magnacauda type (Figure 5B).

According to Tkach and colleagues (2016) Echinochasmidae comprises a total of 6 genera (*Dissurus, Stephanoprora, Mehrastomum, Pulchrosomoides, Saakotrema*, and *Echinochasmu*s, the type genus) and more than 120 nominal species. Genera are mainly differentiated by the extension of the vitelline fields, number of spines in the collar, and the position of the ovary and testes.

Family Fasciolidae Railliet, 1895: The Liver Flukes

Fasciolidae is a family of trematodes that includes several parasites of importance in veterinary and medical sciences. In fact, it constitutes one of the most relevant families of digeneans in terms of veterinary and public health. The members of Fasciolidae are collectively referred to as the **liver flukes**.

Fasciolids are really large worms (some species getting as large as 50 mm in length) that parasitize wild and domesticated herbivorous vertebrates but some species can parasitize omnivores, including humans. Most species inhabit the bile ducts and liver, though there some species of the genera, *Fasciolopsis* and *Protofasciola*, that inhabit the intestine of the vertebrate hosts. Geographical distribution varies with the species. Some species are cosmopolitan while others show a more restricted distribution (Jones, 2005). The life cycles are diheteroxenous including a metacercarial stage that encysts on vegetation.

As currently structured, the family comprises 3 subfamilies, differentiated by the morphology of the cecae and the testes, and contains 6 genera: Fasciolinae (*Fascioloides, Fasciola*, and *Tenuifasciola*), Fasciolopsinae (*Fasciolopsis* and *Parafasciolopsis*), and Protofasiolinae (*Parafasciola*) (Jones, 2005). The subfamilies Fasciolinae and Fasciolopsinae includes several species that are of great importance in veterinary and human health.

The subfamily Fasciolinae include the digeneans (*Fasciola hepatica* and *F. gigantica*) that are of great importance in human health. These species infect the liver mammal hosts and are transmitted by snails of the family Lymnaeidae (which serves as the intermediate host). Adults of both species have a leaf-shaped body, with a broadly pointed posterior end. The 2 suckers are relatively small and located close to one another in a cone-like anterior extension of the body. The intestinal ceca are long, reaching the posterior end of the body and presenting lateral branches. The testes are branched and located in tandem, within the second- and third-fourth of the body. The branched ovary is pretesticular and dextral. The vitellaria extend bilaterally up to the hindbody. The short uterus is located between the ovary and the cecal bifurcation (Figure 6). Both species can be differentiated by their respective size. The adult stage of *F. hepatica* has a maximum length of 29.0 mm and a maximum width of 14.1 mm, whereas *F. gigantica* shows a maximum size reaching 52.3 mm and 11.8 mm, respectively. The eggs are operculated, ovoid, yellow, and non-embryonated when laid (Mas-Coma et al., 2014a).

Figure 6. A) Adult *Fasciola hepatica* (Fasciolidae); B) live adult specimen of *Fasciola hepatica* (Fasciolidae). Source: R. Toledo, B. Fried, and L. Acosta Soto. License: CC BY-NC-SA 4.0.

Human fascioliasis

Fascioliasis is a neglected tropical disease caused by infection with the trematodes, *Fasciola hepatica* and *F. gigantica* (Mas-Coma et al., 2009). This is a worldwide water- and foodborne zoonotic infection that occurs on all continents except Antarctica (Hillyer and Apt, 1997; Fuentes et al., 1999; Hotez et al., 2014). *Fasciola hepatica* occurs worldwide, whereas *F. gigantica* is found in tropical areas of Asia and Africa (Cwiklinski et al., 2016; Roberts and Suhardono, 1996). The adult stages of both species inhabit the large biliary ducts and the gallbladder of herbivorous mammals, mainly sheep and cattle. Humans are incidental hosts and become infected by ingesting contaminated watercress or water (Croese et al., 1982; Ashrafi et al., 2006; Berger et al., 2010). It is estimated that 2 to 17 million humans are currently infected in 75 countries, and about 180 million people are at risk of infection (Hotez et al., 2014; Ashafi et al., 2014).

Life cycle

The life cycle of both fasciolids follows a similar pattern and takes around 14–23 weeks (Figure 7). Adult worms produce eggs that are passed with feces that eventually reach freshwater bodies. The miracidium hatches and swims to locate and penetrate the intermediate host, freshwater snails of the family Lymnaeidae (Bargues et al., 2001; Mas-Coma et al., 2009). The development within the intermediate snail host includes sporocyst and redial generations, to finally produce cercariae that are released to reach a solid support (water plants), where they encyst (Rondelaud et al., 2009). The definitive host becomes infected by ingestion of the encysted cercaria (metacercariae) in watercress or by drinking water containing cercariae (Hodasi, 1972). Metacercariae excyst in the small intestine, penetrating the host's intestine wall, and juveniles migrate to the liver across the abdominal cavity. They become sexually mature in the bile ducts. Eventually, infection also can be acquired by eating undercooked sheep or goat livers that contain immature forms of the parasite (Mas-Coma et al., 2014b).

Symptoms and phases of the illness

Several clinical periods may be distinguished in human fascioliasis. The incubation period that lasts from few days to 3 months (from the ingestion of metacercariae to the appearance of the first symptoms) is characterized by fever, abdominal pain, and gastrointestinal and respiratory symptoms. The invasive or acute period involves flukes migrating to the bile ducts. This phase is characterized by mechanical destruction of the hepatic tissue and the peritoneum by migrating juvenile flukes. The major symptoms of this phase are: Fever, abdominal pain, gastrointestinal disturbances, respiratory symptoms, hepato-splenomegaly, ascites, anemia, and jaundice. The latent period is initiated after the establishment of the adult worms in the bile ducts and may last from months to years from the infection. Symptoms during this phase can include eosinophilia, gastrointestinal complaints, inflammation, hyperplasia of the epithelium, and thickening and dilatation of the bile duct and gallbladder walls. The infection may cause obstruction of the bile ducts (Gulsen et al., 2006; Mas-Coma et al., 2014b).

Diagnosis, treatment, and prevention

Fascioliasis can be diagnosed by both direct parasitological techniques or indirect immunological tests. Coprological examination is still the fastest method and the so called "gold standard method" for the diagnosis of fascioliasis, but several serological, intradermal, antigen-detection and PCR methods have been developed (Mas-Coma et al., 2014a).

Triclabendazole is the recommended treatment against fascioliasis and may therefore be employed during the acute and chronic phases (WHO, 2007).

The prevention of human infection may be achieved by strict control of the human infection sources as well as education, especially in endemic zones. Additionally, preventive chemotherapy, mass drug administration, treatment of

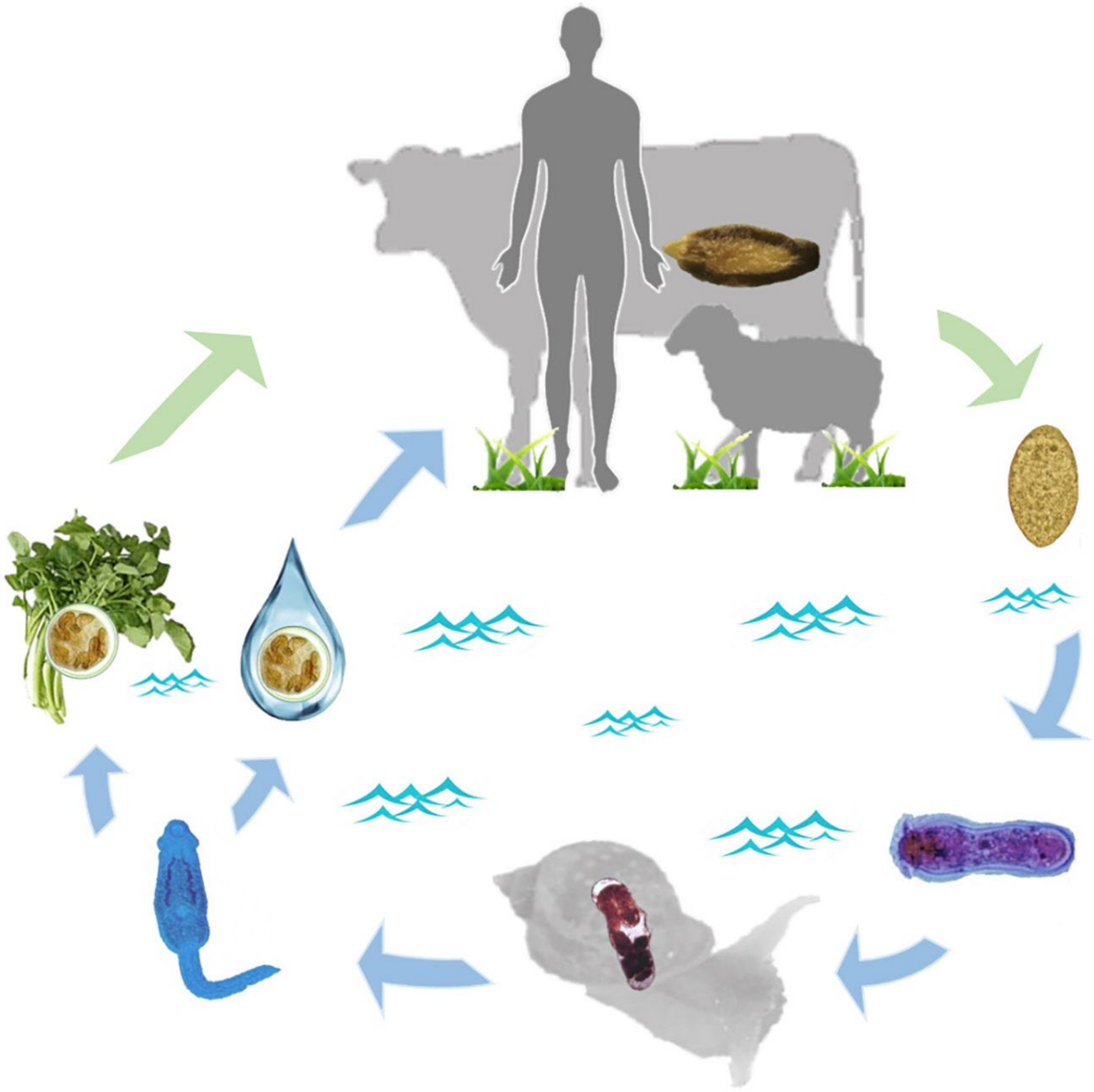

Figure 7. Generalized life cycle of *Fasciola* spp. (Fasciolidae): adult worms inhabiting the biliary ducts of several vertebrate hosts, including humans; eggs are voided with host feces; miracidia hatch in freshwater and actively infect the snail first intermediate host (Lymnaeidae); intramolluscan stages, that is, sporocysts and rediae, develop within the snail; cercariae are released by the first intermediate host and swim to locate freshwater plants, especially watercress, where cercariae encyst; and metacercariae are ingested by the definitive host and excyst to migrate through the intestinal wall, the peritoneal cavity, and the liver parenchyma into the biliary ducts, where they develop into adults. It has also been suggested that drinking water containing cercariae is a source of human infection. Source: R. Toledo, B. Fried, and L. Acosta Soto. License: CC BY-NC-SA 4.0.

infected people, accurate diagnoses to prevent new cases, and development of advanced morbidity can be adopted (WHO, 1995; Mas-Coma et al., 2018).

Human fasciolopsiasis.

Fasciolopsis buski is a species belonging to the subfamily Fasciolopsinae that causes intestinal infections in humans, referred to as human fasciolopsiasis. This is the largest trematode parasitizing humans (8–10 × 1–3 cm) and a common intestinal parasite of humans and pigs in Asia. Human infections are mainly found in East Asia and Southeast Asia (Toledo et al., 2012; 2014).

The life cycle of *Fasciolopsis buski* is similar to that of the above described for *Fasciola* spp., with several species

of the genera *Segmentina* and *Hippeutis* serving as intermediate hosts. Humans commonly become infected by eating raw or undercooked aquatic plants, but infection can be also contracted by the drinking or use of contaminated water or processing of the water-derived plants.

Clinical symptoms in *Fasciolopsis buski* infections in humans are related to parasite load and can be fatal in heavy infections. In light infections, symptomatology may include anemia, eosinophilia, dizziness, and gastrointestinal symptoms. In moderate and heavy infections there may be severe epigastric and abdominal pain, diarrhea or bowel obstruction, nausea, acute ileus, anasarca, and eosinophilia and leucocytosis. Moreover, the parasite can induce duodenal erosions, ulceration, hemorrhage, abscesses, and catarrhal inflammation. Eventually, it may cause intestinal perforation (Toledo et al., 2012; 2014).

Family Himasthlidae Odhner, 1910

Members of the family Himasthlidae are common parasites in birds and mammals worldwide, with some reported cases of human infections. This taxon was created as a subfamily, Himasthlinae, by Odhner (1910) on the basis of the length of the cirrus sac which extends beyond of the posterior border of the ventral sucker, the armed cirrus and the presence of a pars prostatica. However, Tkach and colleagues (2016), in their phylogenetic analysis based on the 28S rRNA gene sequences of several members of the group, concluded that Himasthlinae should be elevated to the family rank, accepting the boundaries proposed by Odening (1963) and Kostadinova (2005a), with the exceptions of the genera *Caballerotrema* (elevated to family rank) and *Artyfechinostomum* (allocated to Echinostomatidae). According to Tkach and colleagues (2016), Himasthlidae comprises 5 genera (*Acanthoparyphium, Aporchis, Cloeophora, Curtuteria*, and the type genus is *Himasthla*). These genera are differentiated on the basis of the extension of the vitelline fields, the morphology of the body and testes, and the structure of the spined collar.

Representatives of the family Himasthlidae have several interesting morphological and biological characteristic features. At the level of adult worms, they are characterized by exhibiting a very wide and dorsoventrally flattened body with finger-like processes on each ventrolateral edge, an intestinal bifurcation that is dorsal to a ventral sucker, and an extensive pars prostatica. Cercarial morphology is characterized by possessing collecting ducts forming numerous lateral branches in the forebody filled with excretory concretions. Moreover, Himasthlidae (with the exception of *Artyfechinostomum*) are among the few members of Echinostomatoidea with a marine life cycle. Interestingly, Himasthlidae, together with Psilostomidae and Philophthalmidae, are the only ones within the Echinostomatoidea using prosobranchs, such as littorinids, as the first intermediate host. They follow a 3-host life cycle with bivalves and clams as the second intermediate host and birds and mammals as the definitive hosts.

Only 2 species of Himasthlidae have been reported to infect humans, including *Acanthoparyphium tyosenense* which is known to have infected people who ate improperly cooked marine bivalves in South Korea and Japan. *Himasthla muehlensi* was reported in a German patient who had eaten raw clams (Toledo et al., 2014).

Family Philophthalmidae Looss, 1899

Digeneans of the family Philophthalmidae are parasites of the eyes, intestine, and bursa Fabricii of birds and, rarely, reptiles, and may accidentally infect humans. This group was established by Looss (1899) as a subfamily on the basis of the interrupted vitelline fields, a long cirrus sac, and embryonated eggs containing a fully developed miracidium. Adult worms may or may not present a cephalic collar of spines. Travassos (1918) elevated the group to full family rank. The status of rank at the family level was supported recently by Tkach and colleagues (2016) by molecular methods. These latest authors accepted 3 subfamilies (Philophthalminae, Parorchiinae, and Cloacitrematinae) in contrast to Kanev et al. (2005) who had recognized 5 subfamilies (Philophthalminae, Ommatobrephinae, Echinostephilinae, Cloacitrematinae, and Parorchiinae). Subfamilies are mainly differentiated on the basis of the site of the infection, the vertebrate host, and the morphology of the testes and esophagus. Kanev and colleagues (2005) accepted a total of 10 genera within Philophthalmidae, with *Philophthalmus* as the type genus.

Philophthalmids have a 2-host life cycle. Fully-embryonated eggs are shed into the water from the definitive host's eyes and miracidia hatch almost immediately in the water and penetrate the snail intermediate host, which commonly are prosobranch snails. Within the snail host, the miracidia undergo a series of stages and become cercariae. Cercariae are released from the snail and encyst on aquatic vegetation or other solid objects in the water. The definitive host, which is usually an aquatic bird, becomes infected upon ingestion of the metacercariae. Metacercariae excyst in the mouth and migrate to the eye where the adults reside. Humans rarely serve as incidental hosts but may do so when they ingest metacercariae on aquatic vegetation. Known human cases are from the United States, Central Europe, the Middle East, Southeast Asia, and Japan, and are caused by a species of the genus *Philophthalmus.*

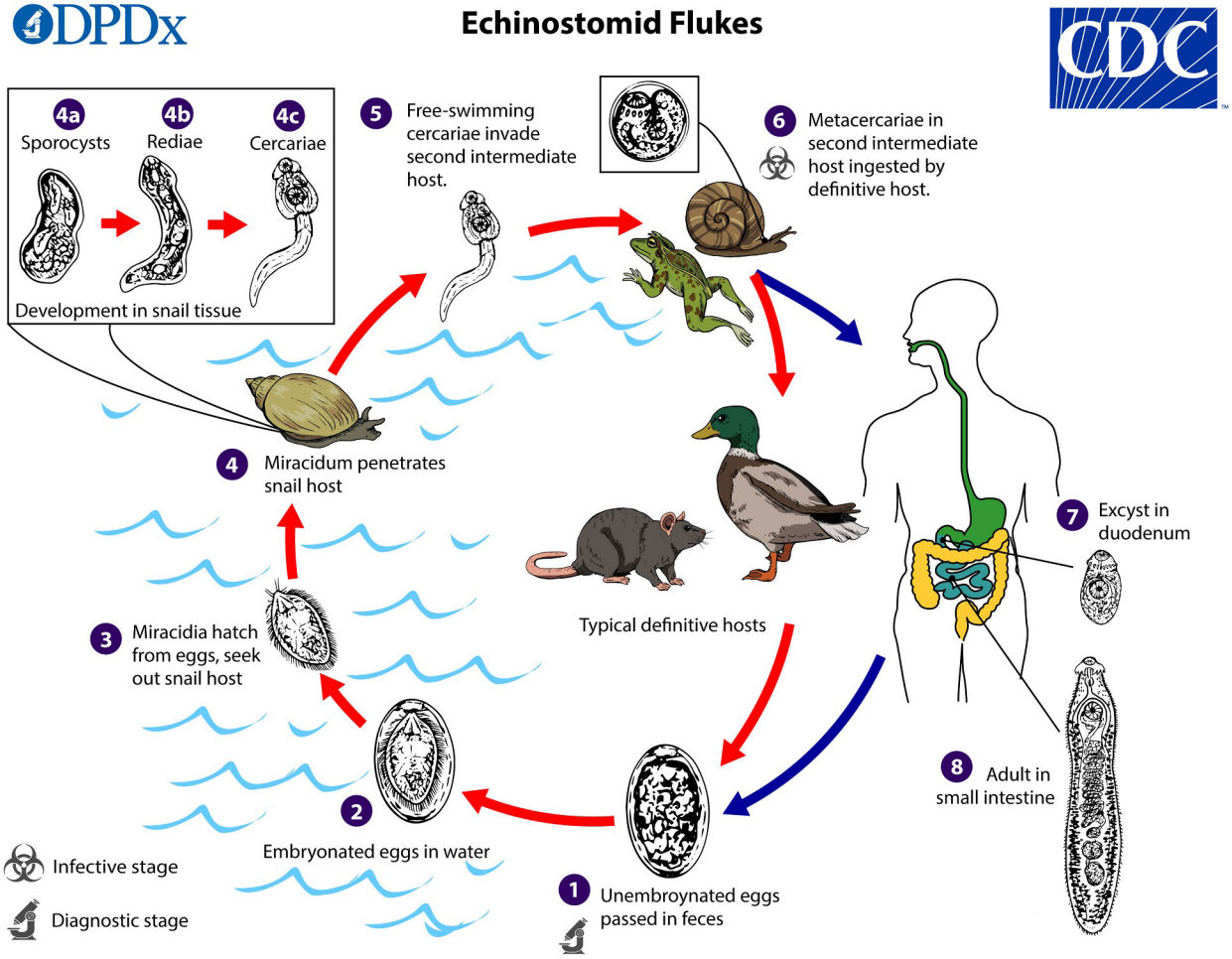

Figure 8. Life cycle of echinostomatid trematodes (flukes). Like many trematodes, echinostomid flukes undergo a multi-host (indirect) life cycle. Unembryonated eggs are passed in feces of infected definitive hosts (1) and develop in water (2). Miracidia usually take about 3 weeks to mature before hatching (3), after which they swim freely and penetrate the first intermediate host, a snail (4). The intramolluscan stages include a sporocyst stage (4a), 1 or 2 generations of rediae (4b), and cercariae (4c), which are released from the snail. The cercariae may encyst as metacercariae within the same first intermediate host or leave the host and penetrate a new second intermediate host (5). The definitive host becomes infected after eating metacercariae in infected second intermediate hosts (6). Metacercariae excyst in the duodenum (7) and adults reside in the small intestine (for some species, occasionally in the bile ducts or large intestine) (8). Source: United States Centers for Disease Control and Prevention, Division of Parasitic Diseases and Malaria (DPDx), 2019. Public domain.

Family Psilostomidae Looss, 1900

The family Psilostomidae constitutes a small group of digeneans within the Echinsotomatoidea including gastrointestinal parasites of birds and mammals worldwide (Kostadinova, 2005b). The traditional systematics of this family has been based on the morphology of the sexually mature adult worms. Since its establishment by Looss (1900), the taxonomic structure of Psilostomidae has been the subject of several revisions (Odhner, 1910; Kostadinova, 2005b; Tkach et al., 2016; Kudlai et al., 2017). According to the revision by Kostadinova (2005b), the family contains 6 subfamilies and 13 genera: *Mehlisia, Psilochasmus, Psilorchis, Psilostomum*, and *Psilotrema* (Psilostominae); *Apopharynx* and *Psilotornus* (Apopharynginae); *Grysoma* (Grysominae); *Ribeiroia* and *Trifolium* (Ribeiroiinae); *Astacatrematula* and *Sphaeridiotrema* (Sphaeridiotrematinae); and *Stephanoproraoides* (Stephanoproraoidinae).

Tkach and colleagues (2016) assessed the phylogenetic position of Psilostomidae within Echinostomatoidea and proposed the allocation of *Ribeiroia* and *Trifolium* within Echinostomatidae, synonymizing the subfamily Ribeiroiinae. Thereafter, 3 new genera have been added to the Psilostomidae (*Neopsilotrema, Bydtrema*, and *Macracetabulum*) (Kudlai et al., 2016; 2017).

Morphologically, members of the Psilostomidae closely resemble those of the Echinostomatidae, except for the absence of a circumoral head-collar. The main features used for the differentiation at the subfamilial and generic levels are: The shape and size of the body, the position of the ventral sucker, the development of the pharynx, the structure of the male terminal genitalia and the vitellarium, the length of the post-testicular area, and the egg size (Kostadinova, 2005b).

The life cycle of the members of Psilostomidae is a 3-host life cycle similar to that of echinostomatids, using prosobranch gastropods as the first intermediate host. The second intermediate host commonly are amphibians or bivalves. The definitive host becomes infected as a result of ingestion of the second intermediate host harboring metacercariae.

Family Calycodidae Dollfus, 1929

Members of the family Calycodidae can be distinguished from other echinostomatoids by their prominent ventral and dorsal ridges at the level of the pharynx and an esophagus diverticulum (Bray, 2005). This family only comprises a single genus (*Calycodes*) and 2 species (*C. anthos* and *C. caborojoensis*) that are parasites of marine turtles (Bray, 2005).

Family Rhytidodidae Odhner, 1926

Members of Rhytidodidae are parasites of the intestine and gallbladder of marine turtles in tropical and subtropical seas. They are characterized by possessing a small lateral projection on each side of the oral sucker. They can be differentiated from Calycodidae by the absence of the ventral ridge at the anterior extremity and the lack of esophageal diverticulum (Blair, 2005). The family comprises 2 genera: *Rhytidodides* and *Rhytidodes*, which is the type genus. Both genera are differentiated on the basis on the location of the testes, ventral sucker, and vitelline follicles (Blair, 2005).

Life Cycle Diagram of Echinostomatid Trematodes

A life cycle diagram from the Division of Parasitic Diseases and Malaria of the United States Centers for Disease Control and Prevention (DPDx, 2019) is shown in Figure 8 and demonstrates how humans may become infected by echinostomatid trematodes (here referred to as flukes).

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