

University of Salahaddin

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Biology Department



**Snails as Intermediate Hosts in Parasitic Infections: Host-Parasite Relationships and Intervention Methods**

**A Review Article in**

**(Diagnostic parasite)**

**In Partial Fulfillment of the Requirements for The Degree of (PhD)**

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## Abstract

A comprehensive understanding of the life cycles, host specificity, and geographical distribution of medically and veterinary significant parasites transmitted by intermediate host snails is essential in combating these parasites. Given the global efforts of scientists to gather specimens from natural environments and generate enormous quantities of sequencing data, there exists significant potential to enhance our understanding of host-parasite interactions without the need for fieldwork by conducting research from a desk. Taking into consideration these underlying motives, a bioinformatics tool was devised that has demonstrated efficacy in terms of both time efficiency and accuracy, specifically for the expeditious detection of concealed parasites within datasets that are publicly accessible. The advancement of molecular and genetic techniques has led to enhanced comprehension and accelerated advancements in the field. Consequently, novel opportunities are emerging for managing and eliminating diseases induced by vector-borne parasites. In order to investigate essential interactions between parasites and snails and disrupt the infection process, it is advantageous to manipulate the genetic makeup of the host organism.

**Keyword:** Snail, Gastropod diseases, parasitic infection, control methods

## Introduction

The term "parasitism" originates from the Latin derivation of the Greek term "parasitos," which signifies "one who consumes food at the expense of another" (Van Beest and Born-Torrijos., 2019). If one were to adopt a comprehensive interpretation of parasitism, encompassing the obligatory consumption of a living organism without causing the death of the host, it could be observed that nearly 50% of identified animal species can be categorized as parasites (Vorburger and Perlman., 2018). Utilizing more stringent criteria, wherein an organism is deemed parasitic only if it exhibits total dependence on the host for a substantial duration of its existence, would result in more conservative estimations. Because every metazoan species living freely is host to at least one species of obligatory parasite, it becomes evident that the diversity and interactions among parasite species are pervasive. However, their full extent still needs to be fully recognized (Preisser, 2019).

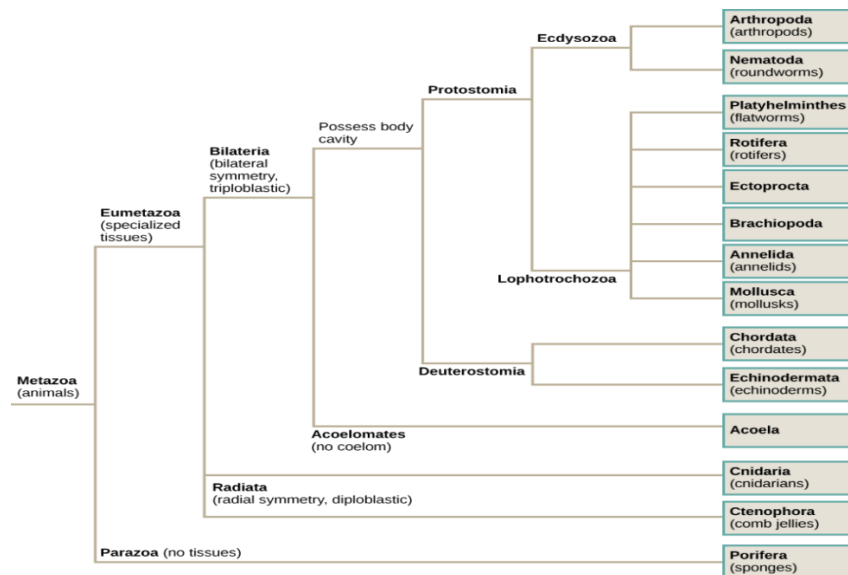
Transitioning from a free-living existence to adopting parasitic traits is believed to be one of the most prevalent types of significant evolutionary conversions in life on Earth (Nguyen & van Baalen., 2020). Although the investigation of helminths, a synthetic category encompassing worm-like parasites from diverse and sometimes distantly related groups, currently holds a prominent position in parasite research, it is noteworthy that only 20% of metazoan parasite taxa that have evolved independently belong to these groups. Additionally, numerous transitions are observed in other taxa, such as Mollusca, Rotifera, Annelida, and Cnidaria.

Notably, parasitism is largely uncommon among deuterostomes, with only a few parasitic species in this group. These include Petromyzonidae (lampreys), certain fishes of the Carapidae family (such as *Fierasfer*) and Trichomycteridae family (such as *Vandalia*), as well as (the vampire bat), all of which belong to the Vertebrata phylum. The significant disparity in the distribution of representatives of this particular lifestyle throughout the evolutionary tree implies that while worm-like physical characteristics and associations with hosts are prevalent among various animal

species, the evolutionary progression toward parasitism is likely hindered by the simultaneous need for both symbiotic and trophic interactions. This constraint may prevent the transition from more ancient consumer strategies, such as those observed in generalist herbivores, omnivores, carnivore predators, and filter feeders (Weinstein & Kuris., 2016) (Figuer1).

Numerous morphological and physiological adaptations are closely linked to the parasitic lifestyle. Throughout evolutionary history, numerous distinct lineages of parasites have undergone independent transitions from a free-living lifestyle to a parasitic mode of existence. As a result, these lineages have converged and developed shared characteristics, allowing them to exploit their hosts in comparable manners. To date, genome mining has not succeeded in identifying a singular gene or a specific group of genes that may universally be linked to parasitism, as indicated by the findings of (Sun et al, 2021). The utilization of sequencing technology and comparative genomics has revealed a growing consensus that the evolution of parasitism cannot be attributed to a singular gene or a defined set of genes. According to (Prabh et al., 2018), when examining parasite genomes, it is observed that they exhibit certain similarities, such as a decrease in genome size, amplification of specific genes, and increased expression of certain genes at the transcriptional level, in comparison to non-parasitic species.

However, these shared characteristics are more likely to result from selective pressures associated with parasitism rather than a common genetic background. The pressures encompass metabolic processes, geographical limitations associated with the lifestyle, and strategic chemicals utilized in invasion and other interactions between hosts and parasites (Cavalier and Smith., 2018). The phenomenon of nuclear genome decreases in parasites, compared to their free-living counterparts, has been documented throughout various branches of the evolutionary tree. This behavior is observed in various organisms, such as amoebozoans (Kjellin et al., 2021), mites (Mounsey et al., 2012), worms (Prabh et al., 2018), and parasitoid hymenopterans (Moura et al., 2019).



**Figure 1.** The classification of parasites that are categorized inside the artificial group are known as helminths.

## Snails serve as intermediary hosts for helminth parasites.

Snails, belonging to the phylum Mollusca, serve as intermediate hosts for helminth infections. With over 65,000 species, Gastropoda is the biggest group within the phylum and exhibits a wide distribution across many ecosystems on Earth (Onyishi et al., 2018). The members of this taxonomic group can be observed in many terrestrial habitats such as gardens, woodlands, deserts, and mountains. Similarly, aquatic representatives of this group can be found in a wide range of habitats, including tiny ditches, rivers, lakes, estuaries, mudflats, the rocky intertidal zone, the sandy subtidal zone, and even the deep ocean. The remarkable ability of gastropods to thrive in various habitats has established them as highly suitable hosts for a wide range of parasites, many of which possess significant medicinal or veterinary implications.

In addition to acting as the sole intermediate hosts for all documented species within the Trematoda group, which encompasses more than 18,000 parasites that infect vertebrates, individuals from this group also function as hosts for numerous species of metastrongylid nematodes (Bray et al., 2020). Helminths are an artificially created group of invertebrate parasites characterized by elongated, flat, or round bodies (worm-like shape) but are not necessarily related evolutionarily (Rodrigo et al., 2018). There is no real consensus on the helminth's taxonomy (or groupings), particularly within the nematodes. However, for practical considerations, the term helminth is currently used to describe members of four phyla with superficial similarities: Platyhelminthes, Annelida, and Syndermata from the superphylum Lophotrochozoa and Nematoda belonging to Ecdysozoa (Figure.2)

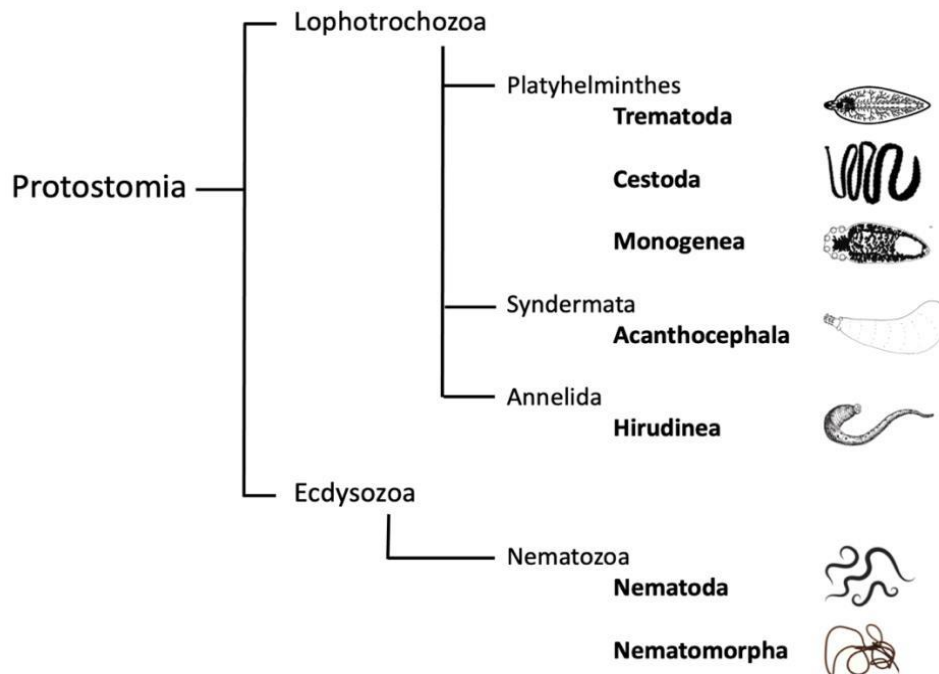


Figure 2. Classification of parasites belonging to the artificial group helminths.

## **The roles of snails in the life cycles of helminths**

there are six distinct parasite developmental cycles in which snails assume the role of an intermediate host, based on the specific functions performed by the snails and the developmental phases of the parasites they harbor (Marti, 2019). The initial developmental stage is characterized by the presence of first-stage larvae (L1). *Cantonensis* is capable of traversing the gastrointestinal tract of rats and is subsequently excreted through the fecal matter. Terrestrial or freshwater snails can acquire infection through the ingestion of feces that are contaminated, or from the penetration of their body wall or respiratory pores by these larvae. The first larval stage (L1) undergoes two moulting events to transform into a third-stage larvae (L3). This L3 stage is then consumed by either a wide range of paratenic hosts or the definitive rat host, as described by (Rollins et al., 2021).

The second type of parasite cycle involving snails is exemplified by schistosomes. In this cycle, the snail becomes infected when miracidia, which are newly hatched from eggs released into freshwater through the excrement of definitive hosts, penetrate its body (Konecny, 2022). Gastropods serve as hosts for parasites that undergo asexual replication, progressing through two generations of sporocysts. Ultimately, a large number of cercariae are released into the water column (Moazeni et al., 2018). These cercariae actively invade animals, including humans, upon contact with water that has been contaminated by the parasites (Konecny, 2022). The third category encompasses a situation wherein two intermediate hosts are involved, with snails assuming the role of the initial intermediate hosts through the ingestion of parasite eggs. In this particular scenario, the cercariae, which are discharged from the snail, proceed to infiltrate the second intermediate hosts, namely freshwater fish. Within these hosts, the cercariae enter a state of dormancy referred to as metacercariae until they are ingested by the definitive hosts, which are mammals that devour fish (Konecny, 2022). *Clonorchis sinensis* serves as a prototypical illustration of this particular life cycle (when mammals ingest parasites, the parasites undergo maturation and mating in the lungs. Subsequently, the eggs are expelled through sputum or feces upon ingestion (Wang et al., 2018), (Brewer and Greve., 2019).

## **Gastropod-borne diseases (GBDs)**

The global incidence, mitigation, and management approaches of several parasites, for which gastropods serve as intermediate hosts, have been associated with severe afflictions in both human and animal populations (Konecny, 2022). At present, it is estimated that gastropod-borne helminths (GBHs) are responsible for affecting over 300 million individuals globally. This figure is expected to increase in the foreseeable future due to the expansion of these diseases beyond their endemic regions, facilitated by global travel and climate change. Additionally, the persistent disregard for these diseases as a significant global health concern contributes to their escalating impact (Giannelli et al., 2016). Furthermore, these diseases not only have detrimental impacts on the well-being of those residing in these regions but also impose significant economic burdens, particularly within the cattle sector. The effective implementation of control methods for any illness is contingent upon a comprehensive comprehension of the biology, ecology, and epidemiology of the pathogen. When considering parasites that have indirect life cycles, it is crucial to possess a comprehensive understanding of the intermediate hosts (Williams & Bunkle., 2019).

## Schistosomiasis

Schistosomiasis is a parasitic disease caused by infection with blood flukes. Schistosomiasis is a prevalent tropical disease that is frequently underestimated, mostly attributable to parasitic flatworms of the *Schistosoma* genus (Rey et al., 2021). The species under consideration demonstrates the biological phenomenon of gonochorism, which refers to the separation of individuals into distinct male and female sexes (Fusco and Minelli, 2019). Additionally, this genus displays significant sexual dimorphism, wherein the physical characteristics between males and females differ noticeably. Furthermore, this genus indicates a predisposition for residing within the circulatory system of various vertebrates that serve as definitive hosts. The life cycle of schistosomes, like that of other trematodes, is characterized by its complexity (Figure 3). To summarize, the snail functions as an intermediary host that is actively invaded by an invasive larval creature referred to as Miracidium. The larva rapidly emerges from the ejected egg upon its immersion in water. After successfully infiltrating the snail, the parasite undergoes a quick transformation into the second stage, referred to as the mother sporocyst. This stage commonly has a predisposition to remain in close proximity to the initial invasion site. Based on the findings of, it has been observed that the mother sporocyst triggers the generation of daughter sporocysts approximately two weeks after the infection occurs. The aforementioned procedure has the potential to persist for a period of up to seven weeks. It is worth mentioning that the offspring sporocysts frequently have a proclivity to migrate towards specific anatomical locations inside the host organism's body that provide greater access to nutritional resources, such as the gonads or hepatopancreas. Based on the findings of (Walker, 2011), it has been noted that each sporocyst possesses the ability to produce a significant quantity of cercariae, with numbers varying from several dozen to several hundred.

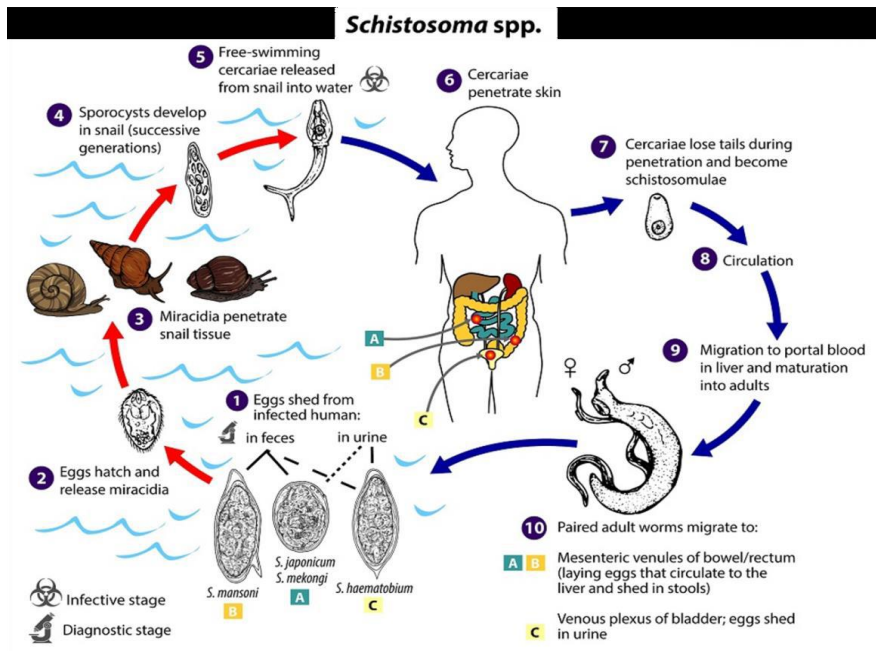
The cercariae have been identified as an invasive life stage capable of infecting the definitive host, which may include humans. It is noteworthy that the expulsion of these cercariae from the gastropod's body occurs approximately 4 to 5 weeks following the initial infection. After the selection of an appropriate host, whether it is a particular or non-specific one, cercariae proceed to adhere to the epidermis of the host's skin. When the cercariae come into contact with fatty acids found in the host's epidermis, such as linoleic acid and linolenic acid, they undergo a mechanism in which their penetration glands are depleted. The presence of proteolytic material in the glands leads to eventual tissue damage in the host. Subsequently, the larva undertakes the process of shedding its tail and subsequently infiltrates the body of the host organism. Within the host's body, the larva undergoes a series of quick and substantial physiological changes, ultimately resulting in its transformation into a migratory larva known as the schistosomulum, which lacks a tail (Juhász et al., 2022).

Infiltration of the dermal lymphatics and venules is how the schistosomulum first gets into the circulatory system. In this particular ecosystem, it maintains its sustenance through the consumption of blood and subsequently eliminates the heme component in the form of hemozoin. The schistosomulum undergoes a migratory phase, typically taking around 5 to 7 days, in order to reach the lungs following penetration. Afterward, it undergoes a process of circulation, notably through the left side of the heart, in order to reach the hepatportal circulation, which requires

duration of more than 15 days. When the schistosomulum comes into contact with a mate of the opposite sex, it proceeds to undergo additional developmental stages until it reaches sexual maturity. Subsequently, the pair engage in a collective migration. Schistosomes typically establish their residence in certain anatomical sites, such as the tiny inferior mesenteric arteries in the case of *S. Schistosoma mansoni* or the venous plexuses surrounding the urinary bladder in the context of *Schistosoma* infection. The parasitic organism *Schistosoma haematobium* demonstrates the distinctive behavior of cohabitating in couples and possesses the ability to produce a significant quantity of eggs on a daily basis (Goto and Sato, 2021).

The eggs endeavor to navigate through the arteries and infiltrate the walls of the intestines or bladder, ultimately reaching the inner cavity of these organs. Subsequently, these parasites are eliminated from the host's body through the process of defecation or urination, ultimately entering the aquatic ecosystem. Within this environment, the parasites have the potential to come into contact with their intermediate hosts, namely snails. A fraction of the eggs is not efficiently eliminated from the host organism, while roughly fifty percent of them are transferred from the mesenteric veins to the portal veins of the liver and thereafter disseminated to the surrounding organs. It is the eggs that are found in the tissues of the host organism that cause serious health problems, like splenomegaly and hepatomegaly, fibrosis near the portal area, high portal vein pressure, urinary system obstruction, cancer growth, infertility, poor nutrition, and slow growth. Chronic infections have the capacity to endure for prolonged durations, potentially resulting in the demise of the host organism (Elbaz & Esmat, 2013).

The process of identifying the parasite in a certain place and the intermediate host is simplified when a specific intermediate host is found at the site. The snails were collected, individually placed into separate containers, and subjected to direct sunlight. The invasive stages, referred to as cercariae, exhibit a response to these stimuli and subsequently leave the intermediate host. These events are observable with the naked human eye. But it's important to get the right fluke species by looking at the shape of cercariae, because these snails are important intermediate hosts for many parasites (Civitello et al., 2018). A significant limitation of this detection technique is the prepatent period, which denotes the interval between the introduction of the parasite into the host and the subsequent detection of the parasite within the host's body, specifically upon the recovery of the infectious stage. The prepatent period is the temporal interval that includes the introduction of the miracidium into the snail and the following maturation of the first cercariae. In a recent publication by the World Health Organisation (WHO, 2020), it was reported that schistosomiasis transmission has been observed in 78 countries. As a result, preventive treatment was deemed necessary for at least 240 million individuals in the year 2018.



**Figure 3. The life cycle of three key schistosomes (CDC, 2019)**

### Angiostrongyliasis

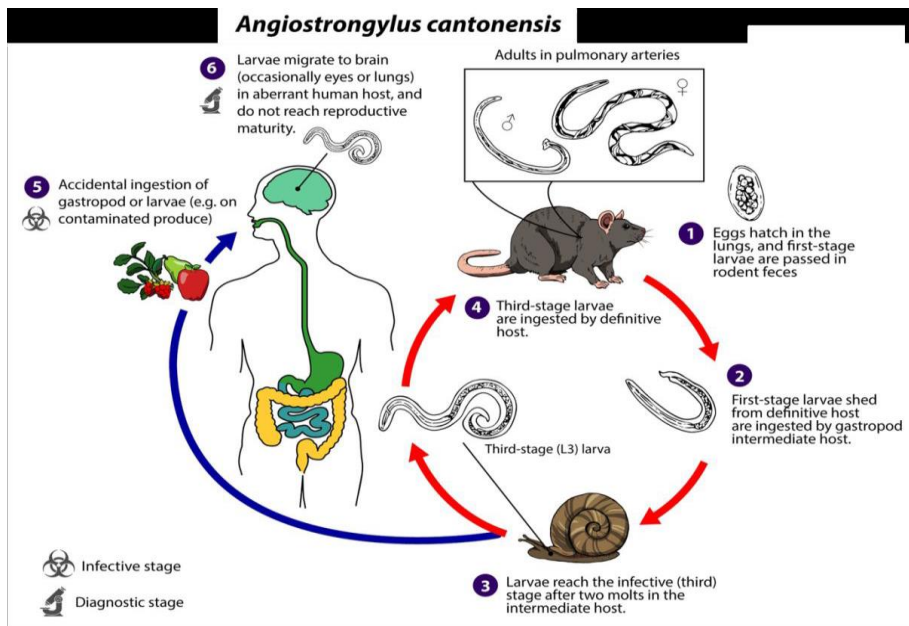
Angiostrongyliasis refers to an infectious condition caused by a species of roundworm belonging to the genus *Angiostrongylus* (Lu et al., 2018). The life cycle of these parasites has been extensively documented (Figure 4). The initial phase of larval worms is expelled through the feces of rats, which act as the ultimate host. These contaminated feces are consumed by snails or slugs, which function as intermediate hosts. However, it is also feasible for the larvae to infiltrate the snail's body either by penetrating the body wall or through the breathing pore. The larvae progress through three distinct stages, namely the first larval stage (L1) to the third larval stage (L3), within the snail host and persist in this state until the snail is consumed by a definitive or dead-end host, or until the snail perishes. Upon ingestion by the host, the third instar larval stage snails proceed to the small intestine, where they actively breach the intestinal wall and subsequently get access to the bloodstream. Subsequently, these entities undergo passive transportation within the circulatory system, ultimately reaching the central nervous system and subsequently the brain. Upon entering the brain, the larvae undergo development and transition into the subadult stage. Upon reaching the subadult stage, the worms undergo a transition where they exit the brain and migrate into the venous circulation. Subsequently, they proceed to enter the right ventricle of the heart and subsequently colonize the pulmonary arteries. In this environment, the worms undergo growth and maturation, engage in reproductive activities, and the females deposit eggs. The eggs are transported via the circulatory system to the pulmonary tissue, where they undergo hatching and develop into first-stage larvae (L1) (Cowie, 2013).

The extent of infection can lead to notable arterial damage in rats due to the high presence of adult worms, as well as lung damage resulting from inflammatory responses to the larvae. The



initial-stage larvae subsequently penetrate the bronchial and pulmonary walls, migrate into the trachea via respiratory secretions, and are subsequently ingested and excreted in the stool. The duration of this cycle is around 45 days. The acquisition of infection in humans can occur through the ingestion of infected hosts, which serves as a terminal point in the parasite's life cycle. This phenomenon primarily occurs through the deliberate consumption of raw or undercooked snails, or other paratenic hosts that are infected, or through the consumption of raw fruits or vegetables that have been contaminated by small gastropods carrying the infection (Cowie, 2013).

In the case of an inadvertent human host, the infective larvae undergo migration to the cerebral region and undergo maturation into juvenile worms or maybe adult forms. However, their lifespan is brief, leading to the development of eosinophilic meningitis, which is characterized by symptoms including intense headache, stiffness in the neck, abnormal sensations, as well as episodes of vomiting and nausea. In due course, the occurrence of a serious infection frequently results in the progression of ascending weakness, quadriparesis, areflexia, respiratory failure, muscle atrophy, and ultimately mortality if left untreated (Wang et al., 2012). The frequent occurrence of these infections can be attributed to the small size of the L1, L2, and L3 larvae, measuring a maximum of 0.5 mm in length and 0.03 mm in width, which renders them virtually invisible to the naked eye.



**Figure 4. The life cycle of *Angiostrongylus cantonensis* (CDC, 2019).**

### Snail control

As previously mentioned, the management of parasitic infections involves a multifaceted approach that encompasses preventive strategies. In the context of gastropod-borne helminth diseases, these strategies primarily involve the timely identification and treatment of infected individuals using efficacious medications or potentially vaccines, enhancing overall quality of life, and promoting health education initiatives. Notwithstanding the extensive endeavors made in these regards, there has been limited progress in mitigating the prevalence of these diseases in regions

where they are endemic. It is increasingly evident that achieving a successful reduction in transmission or complete eradication of these diseases necessitates the implementation of effective snail control measures. This entails disrupting the parasite cycle by restricting the population of its intermediate snail host (Diakité et al., 2018).

A recent meta-analysis conducted by (Lo et al., 2018) examined the existing observational data on the effectiveness of snail management in the control of schistosomiasis. The analysis revealed that snail control measures were indeed efficient in reducing both the prevalence of current cases and the incidence of new cases over time. Subsequently, a more recent study by (Jones et al., 2018) provided further evidence for this result. The study found that nations implementing a control plan at the national level, specifically targeting intermediate snail hosts, achieved greater decreases in infection prevalence compared to countries that did not employ such a strategy. The control of snails has been notably successful in the efforts to control and eliminate GBDs in several regions of Asia in recent years (Rollinson et al., 2013). It is apparent from the aforementioned statement that the management of snail populations is a crucial component of an integrated approach aimed at combating parasitic diseases and hence should be vigorously pursued. According to (Konecny, 2022), there are three basic strategies for managing snail populations:

### **1. Chemical agents for snail control**

Chemicals are usually used to get rid of snails. These chemicals are called molluscicides, and they can be synthetic chemicals or plant-based extracts that are specially made to kill snails. The application of molluscicides has been the predominant approach employed for the management of GBDs during the past century, demonstrating its effectiveness and efficiency in rapidly lowering or eradicating disease transmission.

### **2. The controlling of snail populations by environmental control mechanisms**

An alternative approach for mitigating the population size of intermediate hosts is to modify the ecological habitat in which these hosts are found. Nevertheless, it is important to note that the majority of parasitic worms exhibit a high degree of host specificity. In fact, nearly every parasite, including those within the same genus, needs a distinct intermediate host in order to successfully complete its life cycle. For instance, the species *Schistosoma mansoni* relies on the genus *Biomphalaria* as its intermediate host, whereas *S. haematobium* depends on the genus *Bulinus*, and *S. japonicum* requires the genus *Oncomelania*.

### **3. Biological control methods for snails**

The concept of biological snail control refers to the deliberate decrease or eradication of intermediate hosts through the utilisation of their natural predators, competitors, or parasites. This approach has been extensively examined, and numerous papers have highlighted its potential as a viable strategy for alleviating the prevalence of GBDs in regions where they are endemic.

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