Gastropod-borne helminths: a look at the snail-parasite interplay

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More than 300 million people suffer from a range of diseases caused by snail-borne helminths, predominantly flatworms and roundworms, whose life cycles are characterised by a diversified ecology and epidemiology. Despite the plethora of data on these parasites, very little is known on the fundamental biology of their gastropod intermediate hosts, and of the interactions occurring at the snail-helminth interface. In this article, we focus on schistosomes and metastrongylids of human and animal significance and review current knowledge of snail-parasite interplay. Future efforts aimed at elucidating key elements of the biology and ecology of the snail intermediate hosts, along with an improved understanding of snail-parasite interactions, will aid to identify, plan and develop new strategies for disease control focused on gastropod intermediate hosts.

Gastropods, parasites and vertebrates
The Mollusca, one of the largest phyla of living creatures, includes gastropod species able to colonise every humid corner of the planet [1]. Given their adaptability to a range of diverse ecosystems, molluscs have been long known to serve as ideal hosts for a number of parasites, including nematodes and trematodes [2]. Indeed, gastropods act as intermediate hosts for a range of helminth parasites of medical and veterinary concern [2,3], including more than 18,000 digenean trematodes and about 50 roundworm species ranked into the superfamily Metastrongyloidea [4,5]. Currently, diseases caused by gastropod-borne helminths (GBHs) are estimated to affect more than 300 million people worldwide (http://www.who.int/mediacentre/factsheets/fs115/en). Some of these GBHs, such as the zoonotic liver flukes Fasciola hepatica and Fasciola gigantica, significantly affect the livestock industry [6], while others (e.g., Angiostrongylus vasorum and Aelurostrongylus abstrusus) have long been in the spotlight as causes of significant concern for companion animal health [7,8]. In spite of major global efforts to control GBHs, many of these diseases are still endemic in vast areas of the world (http://www.who.int/mediacentre/factsheets/fs115/en). Therefore, there is a constant need to discover novel strategies to effectively reduce the burden of disease caused by these parasites, in both humans and animals. The development of adequate control strategies against any disease heavily relies on a thorough understanding of the pathogen biology, ecology and epidemiology. In the case of parasites with indirect life cycles, this includes a profound knowledge of the intermediate hosts. Accordingly, for GBHs, current and future efforts aimed at controlling the diseases they cause must take into account measures to reduce the burden of infections in snails [2,9].

To date, the majority of studies on gastropod-borne parasitic diseases have involved trematodes belonging to family Schistosomatidae and Opisthiorchiidae [9-11]. Nonetheless, some GBHs may potentially threaten a larger number of people in the near future, as a consequence of climate change and/or enhanced movement of people and goods [12]. The rat lungworms Angiostrongylus cantonensis and Angiostrongylus costaricensis represent two key examples of such GBHs [3,13]. The life cycles of these helminths are strictly associated with the distribution of their gastropod intermediate hosts [14], which makes improvement of current knowledge of snail-parasite interactions a priority. Over the last few years, a range of studies has explored the fundamental biology of snail intermediate hosts of GBHs, as well as key molecular and immunological interactions occurring at the snail-parasite interface [15-18]. This improved understanding provides a solid basis for the development of future strategies of disease intervention based on control of infected gastropods.

In this article, we provide an account of recent advances in knowledge of snail-parasite interactions, focussing in particular on schistosomes and zoonotic metastrongylids and, in line with the principles of the One Health Initiative (www.onehealthinitiative.com), we emphasize the need for enhanced communications amongst research groups investigating human and animal GBHs, in order to support the design of integrated strategies to combat these diseases.

A snail for each schistosome
Recent estimates provided by the World Health Organization (WHO) indicate that, in 2013, at least 260 million people required preventative treatment for schistosomiasis (http://www.who.int/mediacentre/factsheets/fs115/en), which translated into losses estimated at ~3.3 million disability-adjusted life years (DALYs) [19]. Schistosomiasis, also known as bilharziasis (see Glossary), is endemic amongst poor communities of tropical and subtropical areas, where sanitation conditions are below standards and snail intermediate hosts are endemic [20]. Most human infections are caused by Schistosoma mansoni, S. haematobium, or S. japonicum, with the latter known to infect 46 species of animals, which therefore serve as reservoir hosts for human infections [21]. The distribution of these species of Schistosoma overlaps that of the snail intermediate hosts; S. mansoni, transmitted by aquatic snails of the genus Biomphalaria, is estimated to infect >80 million people, mainly in the sub-Saharan Africa, isolated Middle East areas, southern America and the Caribbean, whereas S. haematobium, transmitted by Bulinus freshwater planorbids, is widespread throughout sub-Saharan Africa and the Eastern Mediterranean countries, where it affects >110 million people [22]. Conversely, the distribution of Oncomelania snails, the intermediate hosts of S. japonicum, is limited to Southeast Asia and China, where ~1.8 million people are infected by this flatworm [23,24].

The density of snail populations in lentic and lotic ecosystems (see Glossary) fluctuates along with the availability of several abiotic and biotic environmental factors (e.g., temperature of the water, conductivity, pH and presence of suitable vegetation) [25,26]. In addition, the adaptability of snail species serving as intermediate hosts of GBHs to changing environments, as a consequence of climatic variations and/or human-driven modifications of ecosystems, is bound to play key roles in the epidemiology of these diseases, as well as on the robustness of intervention strategies based on the control of snail populations. For example, Neotricula aperta, implicated in the transmission of Schistosoma mekongi in Cambodia, Laos and Thailand, where ~140,000 people are at risk of infection, occupies exclusively shallow areas characterised by hard water and stony river beds, close to karst springs [27]. Therefore, given the specific ecological requirements of this snail species, eradication of disease based on control of N. aperta is a feasible option [28]. Conversely, the control of schistosomiasis japonica in China, the Philippines and Sulawesi Island is challenged by the resistance to silting and amphibious nature of Oncomelania hupensis snails, which may inhabit ditches, wetlands and marshy ground in both hilly and mountains regions [24]. Similarly, Biomphalaria snails, responsible for transmission of S. mansoni in the Caribbean, South America, Egypt and sub-Saharan Africa [29-31] are adapted to a large number of ecosystems (e.g., lakes, fish ponds and rice fields) and benefit from the presence of controlled water flows, dams and irrigation networks [30]; in addition, planorbids of the genus Bulinus are known to successfully breed in a range of environmental conditions and can be detected in several regions of Africa (i.e., the Nile River valley, Maghreb, most of southern and sub-Saharan Africa, including Madagascar) [32], and the Middle East (e.g., Iran, Malawi, Sudan) [33], where they are efficient intermediate hosts of S. haematobium.

Therefore, given the ability of these gastropods to colonise a range of different habitats, their control and that of the GBHs they transmit presents inevitable challenges. For this reason, gaining a profound knowledge of snail-parasite interactions will represent a key arrow in our quiver of potential weapons against GBHs, as it will allow researchers to identify parasite ‘Achille’s heels’ on which to address future efforts aimed at developing disease intervention strategies based on parasite control.

**Gastropods and trematodes**

The majority of studies performed to explore snail-parasite relationships have been focused on schistosomes and their intermediate hosts, primarily because of the availability of experimental systems that allow maintenance of these parasites in several species of mollusces in the laboratory [9]. As a consequence, a plethora of information has been collected over the last few years on the biological and molecular interactions occurring between schistosome parasites and their gastropod
intermediate hosts (Box 1) [34-37], including the intramolluscan life cycle of those flatworms.

Miracidia of S. mansoni infect Biomphalaria gastropods through the exposed mantle epithelium, and frequently through the antennae or the head-foot. In the fibromuscular tissue of the cephalopodal region, the parasite undergoes morphological and physiological changes, developing into a primary or mother sporocyst; this stage generates several secondary or daughter sporocysts, which migrate to the digestive glands or the hepatopancreas of the mollusc. Finally germinative cells of the daughter sporocyst produce water-living furcocercous cercariae (Figure 1) [38].

Infections by trematodes inevitably impact on snail longevity and fitness, with variable outcomes [39]. For instance, accelerated shell growth or gigantism has been observed in Lymnaea snails infected by plagiorchids, whereas retarded development or stunting has been recorded in Biomphalaria planorbids exposed to S. mansoni [39]. The occurrence of these changes is often associated with impairment of the snail fecundity, an event also referred to as parasitic castration [40], during which the trematode gradually redirects the host metabolism towards its own needs [41]. Although the exact mechanisms that lead to the snail castration are currently unknown, it has been suggested that the parasite may act as a ‘competitor’ for nutrients required for reproduction (e.g., vitelline glands), or may directly interfere with selected physiological processes of the gastropod [41]. For instance, preliminary studies in the Lymnea stagnalis-Trichobilharzia ocellata system had pointed towards a role of schistosomin, a host-derived host factor, in the occurrence of parasitic castration [42]; however, recent data indicate that changes in expression levels of this neuropeptide in B. glabrata snails are not directly linked to active development of schistosomes [43].

Clearly, the availability of basic parasitological information on snails-schistosome interactions has assisted scientists in the acquisition of a better understanding of GBHs epidemiology. However, substantial gaps still exist in our knowledge of the cascade of molecular events that regulate the development of nematodes within their mollusc intermediate hosts. Such gaps are particularly pronounced for snail hosts of metastrongylid parasites of humans and animals, as illustrated in the following section.

Zoonotic Angiostrongylus infection: the state of the art

The superfamily Metastrongyloidea includes several GBHs of veterinary concern and two zoonotic species of public health interest, namely A. cantonensis and A. costaricensis. The former is the causative agent of eosinophilic meningitis, which affects ~3000 people throughout Southeast Asia, Australia, Pacific Islands and the Caribbean [3,44,45], whereas A. costaricensis is emerging in the New World, causing life-threatening human abdominal angiostrongyliasis [13,46]. Although gastropods serve as intermediate hosts for both parasites, a range of paratenic hosts (e.g., shrimps, prawns, crabs, toads, planarians) act as vehicles of the infection to humans [47]. In particular, the completion of the life cycle of Angiostrongylus relies on rats as definitive host, which shed first-stage larvae (L1s) in the environment with their faeces. As for most metastrongylids (Figure 2), L1s infect gastropods (for A. cantonensis, more than 160 snail or slug species under natural or experimental conditions; [3]), in which they moult twice before developing to infective third stage larvae (L3s). Rats and other dead-end hosts become infected when they ingest gastropod molluscs or paratenic hosts [47]. While studies on Angiostrongylus-gastropod interactions are currently limited (Table 1), a number of surveys have investigated the main factors involved in the distribution and possible expansion of eosinophilic meningitis from endemic regions to geographical areas previously considered ‘parasite-free’ [48-50]. For instance, the spreading of A. cantonensis via newly-introduced gastropod species [3] has been investigated in the Hawaiian Islands, where the parasite was detected in 16 snail species (2 native, 14 non-native), four of which were acknowledged as intermediate hosts for the first time [3]. Similarly, this parasite has also been newly-introduced via terrestrial snails (i.e., Achatina fulica, Zachrysia provisoria, Bradybaena similaris and Alcadia striata) imported in the Gulf Coast region of the United States [51].

Above all, global travel, climate change and globalization act as major drivers for the emergence of
Angiostrongylus infection worldwide. For instance, molluses consumed as food or kept as domestic pets (e.g., Achatina fulica), along with the expansion of the distribution range of some invasive species (e.g., Pomacea canaliculata) are considered key determinants of the increasing prevalence of infections by A. cantonensis in Mainland China and South America [52]. Nonetheless, the detection of this roundworm in European native gastropods (e.g., Cornu aspersum or Theba pisana) [50], together with the availability of predictive models based on climatic factors suggesting an increase in suitable habitats for this pathogen in Europe [12], is worrisome. For this reason, preventative measures should be developed to face a potential introduction of rat definitive hosts to non-endemic areas. To achieve these goals and accurately identify risk factors for disease transmission in Europe, comprehensive investigations of the complex interactions occurring at the gastropod-angiostrongylid interface are needed.

Delving into the great unknown: zoonotic metastrongylid-snail interactions

Thus far, knowledge of snail-Angiostrongylus interactions is limited to reports dating back to the ‘70s and ‘80s. For instance, the detection of A. cantonensis larvae in the kidney and rectum of B. glabrata, suggested that these might represent the main routes of larval migration to the snail mantle collar and head-foot, i.e. the ‘exit doors’ to the outer environment [53]. In the same study, angiostrongylid larvae were encapsulated by the snail 24-48 hours post-infection following a two-phase process, consisting of an initial infiltration and aggregation of basophilic haemolymph cells around the parasite, followed by encasement in fibrous-appearing nodules [53]. As a likely consequence of the increasing interest towards GBHs [2], recent studies have focussed on the metabolic responses of gastropods infected by A. cantonensis. For instance, the energetic balance and oxidative metabolism of B. glabrata infected by A. cantonensis under experimental conditions, displayed a sharp decline in glucose content immediately following infection, likely as a consequence of the competition for nutrients between the nematode and the snail which, in turn, is forced to activate its anaerobic metabolism (i.e., increased activity of enzymes involved in the glycolytic pathway mediated by lactate dehydrogenase), in order to survive [54]. The angiostrongylid also promote the protein metabolism of snails, as demonstrated by the increased production of nitrogen catabolites such as urea, and particularly the conversion of uricotelic into ureotelic acid, probably as a detoxification strategy, thus favouring the vital functions of the snail and, indirectly, parasite development [55]. Similarly, co-infections by Echinostoma paraensei, a trematode of wild rodents, and A. cantonensis [56] trigger a progressive depletion of the carbohydrates reserves in B. glabrata snails, which, in turn, increase the rate of deamination of amino acids. Moreover, the enhanced demand for nutrients by the parasites modifies the kinetic behaviour of A. cantonensis and E. paraensei in the gastropod tissues, inducing the former to pursue new migration routes [56]. Indeed, the intense cellular disorganization induced by E. paraensei in the digestive gland-gonad complex of the snail (i.e., the site for A. cantonensis moulting) forces the nematode to continue its development into the kidneys [56]. Further immune-molecular studies on the fundamental Angiostrongylus-gastropod interplay are crucial to implement strategies for the control of the infection. Even though a suitable experimental snail model is currently unavailable, such a system would provide a ready-to-use infrastructure for in-depth studies of biological pathways specifically involved in snail-parasite interactions, as recently proposed for the Bithynia-Opisthorchis complex [57]. Until that, research on phylogenetically-related animal parasites (e.g., A. vasorum or A. abstrusus) [46] may represent a useful way to overcome these gaps, thus opening new opportunities for a thorough investigation on GBHs of medical and veterinary concern.

Opening new fields in GBHs research

Over the past couple of years, a few fundamental studies have opened new and exciting avenues for research on gastropod hosts of parasites, that may pave the way towards much needed comparative studies between trematode- and nematode-bearing snail intermediate hosts. For instance, new scientific evidence now points towards the occurrence of an alternative mode of transmission of the
cat lungworm *A. abrusus* among gastropods. Indeed, after being shed in the mucus trails of the land snails or in the water where gastropods had died [58], L3s of this metastrongylid are able to infect new intermediate hosts, in a mechanism referred to as intermedesis. This phenomenon may represent a dynamic survival-and-transmission strategy for nematodes, allowing spread of parasites to other susceptible intermediate hosts [59]. While it is tempting to speculate on the potential advantages that intermedesis may present for spreading and survival of snail-borne nematodes, a clear understanding of this phenomenon can only be achieved via in depth studies of snail-nematode interactions. Indeed, while a plethora of information is available on the molecular and immunological interactions occurring at the snail-schistosome interface (mainly as a consequence of the availability of suitable experimental systems, including a draft genome sequence for *B. glabrata* [http://www.vectorbase.org]), its embryonic cell lines (Bge) [60], and schistosome genomes [61-63], studies of the immune-molecular mechanisms that govern the snail-metastrongylid interplay are minimal (Table 1). Beside a single attempt to cultivate *A. cantonensis* from L3s to fourth-stage larvae in a defined culture medium [64], the development of metastrongyloid *in vitro* is still un unexplored field; progress in this area is required to provide essential information on the physiology of helminths, as well as for the advancement of parasitological and biomedical research on GBHs. Therefore, an improved knowledge of snail-parasite interactions will not only result in a better understanding of the ecology, epidemiology and basic biology of GBHs, but will also represent the necessary infrastructure for hypothesis-driven studies aimed at interrupting the spreading of the diseases they cause.

### Biological control of snails: a feasible option?

Nowadays, the control of GBH infections is based on a combination of preventative measures, which, in the case of schistosomiasis, include early diagnosis and treatment of infected people, improvement of life quality and implementation of health education [65]. Nonetheless, the monitoring of susceptible snail populations, through wide-scale malacological surveys, will provide basic essential data towards planning adequate strategies to reduce the transmission risk of GBHs. For instance, in areas where schistosomiasis is endemic, campaigns involving gastropod control measures are mandatory to achieve a long-term effect on disease transmission [66]. In line with the agenda of the World Health Assembly, which endorsed an integration of non drug-based interventions to prevent parasite transmission [67], the scientific community is now seeking alternative means for interrupting the life cycles of snail-borne parasites [66]. For example, the introduction of gastropod intermediate hosts resistant to the infection, as opposed to the spreading of molluscsicides (e.g., niclosamide) in the water, has been proposed as an effective and environmentally friendly strategy to reduce the burden of disease [68,69]. The impact of biological control of snails on the epidemiology of GBHs has long been debated (reviewed by [70]), with a number of reports documenting how competitors and snail predators might be exploited to reduce populations of molluscs in the environment [70]. For instance, fishes of the family Cichlidae or Cyprinidae are natural predators of gastropods, and their introduction may result in a significant reduction of schistosome intermediate hosts [70]. However, due to the broad-spectrum diet of these fishes and their low population density, this method is considered unfeasible [70]. Conversely, rhabditid nematodes of the genus *Daubyalia* (e.g., *D. potomaca*) [71, 72] and bacteria such as *Candidatus* Paenibacillus glabrata [73] could provide a means to the control of schistosome snail hosts, although the potential efficacy of this approach remains to be clearly demonstrated [72]. Competing and predatory snails have been considered a valid, promising and relatively inexpensive option for the control of gastropods. For example, the ampullarids *Marisa cornuarietis* and *Pomacea australis* have been successfully employed to reduce the populations of *Biomphalaria* and *Bulinus* under natural condition [70]; however, these species are considered economically-important agricultural pests [52]. Similarly, the re-introduction of the prawn *Macrobrachium vollenhoveni*, a predator of snails, was effective for the control of *Bulinus* planorbids, and ultimately resulted in a detectable reduction of the number of urinary schistosomiasis in a village of Senegal [74].

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However, caution is required when hypothesising the use of snail predators (e.g., other snails or prawns) for the control of certain GBHs, as they may serve as hosts for lung flukes (e.g., *Paragonimus* spp.), lungworms (*Angiostrongylus* spp.) and other foodborne helminths (*Clonorchis* and *Opisthorchis* spp.)[70]. Fly larvae of the genus *Sciomyzidae* are strictly malacophagous and harmless to humans and vertebrates; however, their use is made impractical by the different degrees of vulnerability displayed by snails [70]. Finally, trematode predators, including annellids of the genus *Chaetogaster*, mosquito larvae and Hydrozoa, may provide effective means to reduce the burden of GBHs. Also, guppies (*Lebistes reticulatus*) are highly cercariophagous, with up to 1000 cercariae ingested per hour, but only in cases of densely established fish populations [70]. These key examples suggest that, today, the control of GBHs cannot solely rely on the use of biological agents, mainly because of the unfeasibility of such approaches on a global scale. Therefore regular administrations of praziquantel remain the most effective strategy to reduce the burden of schistosomiasis in exposed populations [65].

**Concluding remarks**

Given the well-known issues with widespread anthelmintic resistance involving a number of parasites of livestock, and the realistic possibility that such mechanisms may eventually emerge in human helminths, we advocate for the development of an integrated approach to combat diseases caused by GBHs. This could include i) information campaigns on GBHs and on their prevention in endemic areas, ii) reduction of the molluscicide dispersal, which often negatively affects organisms that may interfere with the helminth transmission; iii) implementation of research programs on alternative/novel ways to reduce the gastropod burden in the environment; iv) enhanced circulation of information among physicians, veterinarians, parasitologists and malacologists.

In conclusion, further data on snail-parasite biology is needed to enhance our knowledge of host-parasite interactions, and ultimately to provide new potential tools for GBH control. In particular, the application of so-called -omic technologies (e.g. genomics, transcriptomics, proteomics, metabolomics) to large-scale explorations of snail-nematode interactions is bound to accelerate this progress, ultimately leading to the development of integrated strategies of GBHs control, based on extensive knowledge of snail biology and immunology. Altogether, these efforts will be determinant in the near future to identify the parasite ‘Achille’s heel’, thus translating these fundamental discoveries into potential control measures.
Gastropods can activate mechanisms of innate immunity to cope with *Schistosoma* development [17,75], modulated by the activity of the mollusc internal defence system (IDS). The snail IDS includes two populations of haemocyte effector cells (granulocytes and hyalinocytes) [75] and a range of soluble factors in the hemolymph, which are involved in pathogen recognition and inflammatory responses [17]. Among these molecules, fibrinogen-related proteins (FREPs) are of major interest to the scientific community, due to their conserved structure throughout animal evolution; in addition, gastropod FREPs are the only known proteins, which combine immunoglobulin superfamily domains (IgSF) with their fibrinogen domain [18,76]. Fourteen subfamilies of FREPs have been described thus far, and eight more have been detected using RNA-seq (reviewed by [18]). Some of these molecules (i.e., FREP3) may act as opsonins [77] for a number of monosaccharide and mucin antigens expressed on the surface of schistosome larval stages [18]. In addition to FREPs, several cytokines, such as the macrophage migration inhibitory factor [78], and other proteins (e.g., biomphalysin) [79] have been hypothesized to be involved in the immune defence of *B. glabrata* against schistosomes. Once stimulated by the presence of miracidia, the haemocytes undergo enhanced mitosis within 24-72 hours, and produce reactive oxygen species (ROS), including hydrogen peroxide and hypochlorous acid, or phagocytise portions of *Schistosoma* tegument, leading to mechanical damage and destruction of the invader [17]. The expression of immunological factors that regulate snail resistance to trematode infection (e.g., production of FREPs, cathepsins, actins, heat-shock proteins) varies according to snail species, strain and age [80]. Studies on snail immunology [16-18], along with new insights on snail gene regulation and expression [81], are essential for elucidating the interactions between GBHs and their intermediate hosts, including those that result in unsuccessful infections. For instance, the *Biomphalaria tenagophila* Taim/RS strain is resistant to *S. mansoni* challenge, due to the clustering of haemocytes in a thick layer which surrounds, encapsulates and destroys the *S. mansoni* miracidium, soon after its penetration [82,83]. Considering that the resistance factor is transmitted as a dominant character with Mendelian inheritance [69,84,85], the identification of other genes linked to schistosome resistance (e.g., the guadeloupe resistance complex [GRC] in *B. glabrata*) and the genetic manipulation of snails might pave the way towards the insertion of such genes in susceptible gastropod populations [81]. Altogether, this approach could potentially help reducing the burden of infection in endemic areas of disease.
References


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**Glossary**

**Bilharziasis**: synonymous of schistosomiasis, named after Theodor Bilharz (1825–1962), German parasitologist who described in 1851 the adult worms of *Schistosoma haematobium* during the autopsy of an Egyptian patient with a clinical history of haematuria.

**Dead-end host**: a host from which the parasite is not transmitted to other susceptible hosts, thus blocking the parasite life cycle.

**DALY**: the disability-adjusted life year measures the overall disease burden, expressed as the number of healthy years lost due to ill-health, disability or early death.

**Intermediate host**: a fundamental host for the parasite life cycle that supports the immature or asexual developmental stage of a parasite.

**Lentic and lotic habitat**: lentic refers to an aquatic ecosystem featured by stationary or still water, including lakes, wetlands or ponds, whereas lotic involves flowing terrestrial waters, such as rivers, streams, or springs, featured by unidirectional flow and continuous physical change.

**Metastrongyloidea**: superfamily ranked into the order Strongylida, includes the so-called lungworms of vertebrates. Metastrongylids show a wide range of definitive anatomical localization, ranging from the pulmonary arteries and right ventricle to the mesenteric veins and the bronchioles of the lung. All first-stage larvae pass through the gastrointestinal tract, before being shed in the faeces. Most of species display an indirect life cycle, which requires the presence of gastropods as intermediate hosts, and some species may also use paratenic hosts.

**Paratenic host**: a host that may be important for the maintenance of a parasite life cycle and in which no dramatic development of the parasite occurs.
Figure 1. Intramolluscan cycle of schistosomes. Miracidia of infect gastropods (1), developing into a primary or mother sporocyst (2), which generates secondary or daughter sporocysts after 2-3 weeks (3). The latter stage migrates to the digestive glands or the hepatopancreas of the mollusc, where its germinative cells give birth to furcocercous cercariae (4). Drawing by Viviana Domenica Tarallo.

Figure 2. Life cycle of the cat lungworm *Aelurostrongylus abstrusus* with new insights on its biology in the gastropod intermediate host. Infected cats shed L1 larvae through their faeces (1) that may be ingested by susceptible gastropod intermediate hosts or may penetrate through the snail tegument. Within the host tissues, L1 moult to L3 (2). Infected gastropods may be ingested by a new felid host (3) or by a range of paratenic hosts (e.g., rodents, birds, lizards) (4-5), thus closing the biological life cycle when predated by cats (6). Alternatively, metastrongylid L3 can be released with the snail mucous trails (7), potentially contaminating the cat food (8) or infecting other intermediate hosts (also referred as to intermediesis, 9), thus broadening the number of gastropod hosts available to the paratenic and definitive hosts. Drawing by Viviana Domenica Tarallo.
Table 1. Summary of our current understanding on gastropod-borne nematodes.

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