Trends in Parasitology

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Review

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 gastropod-borne helminths, predominantly flatworms and roundworms, whose life cycles are characterized by a diversified ecology and epidemiology. Despite the plethora of data on these parasites, very little is known of the fundamental biology of their gastropod intermediate hosts, or 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, together 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.

Trends

Gastropod-borne parasites are agents of illness in animals and humans. The number of case reports is likely to increase in the near future owing to global travel and climate change.

A wealth of data is currently available on the relationships between key trematode parasites and their snail hosts. Conversely, the fundamental biological relationships between gastropods and nematode parasites are increasingly being elucidated.

The application of advanced omics technologies, together with data on snail–helminth fundamental biology, could lead to the development of integrated strategies for the control of gastropod-borne diseases.

Gastropods, Parasites, and Vertebrates

The Mollusca, one of the largest phyla of living creatures, includes gastropod species able to colonize 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 several parasites, including nematodes and trematodes [2]. Indeed, gastropods act as **intermediate hosts** (see Glossary) 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 within the superfamily **Metastrongyloidea** [4,5]. Currently, diseases caused by gastropod-borne helminths (GBHs) are estimated to affect more than 300 million people worldwide [6]. Some of these GBHs, such as the zoonotic liver flukes *Fasciola hepatica* and *Fasciola gigantica*, significantly affect the livestock industry [7], while others (e.g., *Angiostrongylus vasorum* and *Aelurostrongylus abstrusus*) have long been in the spotlight as causes of significant concern for companion animal health [8,9]. Despite major global efforts to control GBHs, many of these diseases are still endemic in vast areas of the world [6]. 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 [2,10].

To date, the majority of studies on gastropod-borne parasitic diseases have involved trematodes of the families Schistosomatidae and Opisthorchiidae [10–12]. Nonetheless, other GBHs may

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potentially represent a public health threat in the near future, as a consequence of climate change and/or enhanced movement of people and goods [13]. The rat lungworms *Angiostrongylus cantonensis* and *Angiostrongylus costaricensis* represent two key examples of such GBHs [3,14]. The life cycles of these helminths are strictly associated to the biology of their gastropod intermediate hosts [15], which makes improvement of current knowledge of snail–parasite interactions a priority. Over the past few years, a range of studies have explored the fundamental biology of snail intermediate hosts of GBHs, as well as key molecular and immunological interactions occurring at the snail–parasite interface [16–19]. 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, focusing 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 to support the design of integrated strategies to combat these diseases [2].

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 [6], which translated into losses estimated at ~3.3 million **disability-adjusted life years** (DALYs) [20]. Schistosomiasis, also known as **bilharziasis**, is endemic among poor communities of tropical and subtropical areas, where sanitation conditions are below standards and snail intermediate hosts are endemic [21]. 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 [22]. The distribution of these species of *Schistosoma* overlaps with 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 [23]. 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 [24,25].

The density of snail populations in **lentic** and **lotic** ecosystems fluctuates with the availability of several abiotic and biotic environmental factors (e.g., temperature of the water, conductivity, pH, presence of suitable vegetation) [26,27]. 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 certain to play key roles in the epidemiology of these diseases, and it affects 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 characterized by hard water and stony river beds close to karst springs [28]. Therefore, given the specific ecological requirements of this snail species, eradication of disease based on control of *N. aperta* is a feasible option [29].

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 mountainous regions [25]. Similarly, *Biomphalaria* snails, responsible for the transmission of *S. mansoni* in the Caribbean, South America, Egypt, and sub-Saharan Africa [30–32] are adapted to a large

Glossary

Bilharziasis: synonymous to schistosomiasis, named after Theodor Bilharz (1825–1962), a German parasitologist who described in 1851 the adult worms of *Schistosoma haematobium* during the autopsy of an Egyptian patient with a clinical history of hematuria.
Dead-end host: a host from which the parasite is not transmitted to other susceptible hosts, thus blocking the parasite life cycle.
Disability-adjusted life years (DALYs): a measure of overall disease burden, expressed as the number of healthy years lost owing 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 characterized by stationary or still water, including lakes, wetlands, or ponds, whereas lotic involves flowing terrestrial waters, such as rivers, streams, or springs, characterized by unidirectional flow and continuous physical change.
Metastrongyloidea: superfamily within the order Strongylida, which includes the so-called lungworms of vertebrates. At the adult stage, metastrongylids can localize to the pulmonary arteries, the right ventricle, the mesenteric veins, or the bronchioles of the lung. All first-stage larvae pass through the gastrointestinal tract before being shed in the feces. Most 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 but in which no dramatic development of the parasite occurs.