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SCHISTOSOMIASIS: AN OVERVIEW OF BIOLOGY, PATHOGENESIS, DIAGNOSIS AND CONTROL

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ABSTRACT

Schistosomiasis is a serious neglected tropical disease which is caused by dioecious trematode parasites belonging to the genus Schistosoma. In man, there are five medically important species: S. mansoni, S. haematobium, S. japonicum, S. intercalatum, and S. mekongi. The importance of these parasites is not due to the adults themselves but due to the host's inflammatory reaction to the eggs which have become trapped in the host tissues. The differences between the various species involve the geographical distribution, snail intermediate hosts, definitive host range, egg morphology, major pathology, and zoonotic capability. The major pathologies of S. mansoni and S. japonicum involve the intestines and the liver/spleen while the S. haematobium is the classic cause of urogenital schistosomiasis and causes bladder pathology and squamous-cell carcinoma. The S. intercalatum and S. mekongi are less common but still of medical importance due to specific areas of infection, confusing diagnosis, and difficulties in eradication. The life cycle is based upon freshwater snails, skin penetration of cercariae, intravascular development, and the passage of eggs in feces or urine. Comparative genomics has helped in understanding lineage diversification, adaptation to intermediate hosts, and host-parasite interaction. Reference genome sequences exist for several species of Schistosoma. Although considerable control

measures have been undertaken, the only therapy that is widely used at present is praziquantel with its limitations of being ineffective against the juveniles and lack of a prophylactic action. Diagnostics is moving from microscopy to antigen detection and molecular techniques but low level infections are hard to detect. Vaccine development has progressed using defined antigens and human controlled infections but no vaccines for humans are in existence at present.

List of Abbreviations:

CAA: circulating anodic antigen, **CCA:** circulating cathodic antigen

CNS: central nervous system, **DALY:** disability-adjusted life year

DNA: deoxyribonucleic acid ,**ELISA:** enzyme-linked immunosorbent assay

HCC: hepatocellular carcinoma, **IL:** interleukin

MDA: mass drug administration, **PCR:** polymerase chain reaction

PZQ: praziquantel ,**RNAi:** RNA interference

WHO: World Health Organization

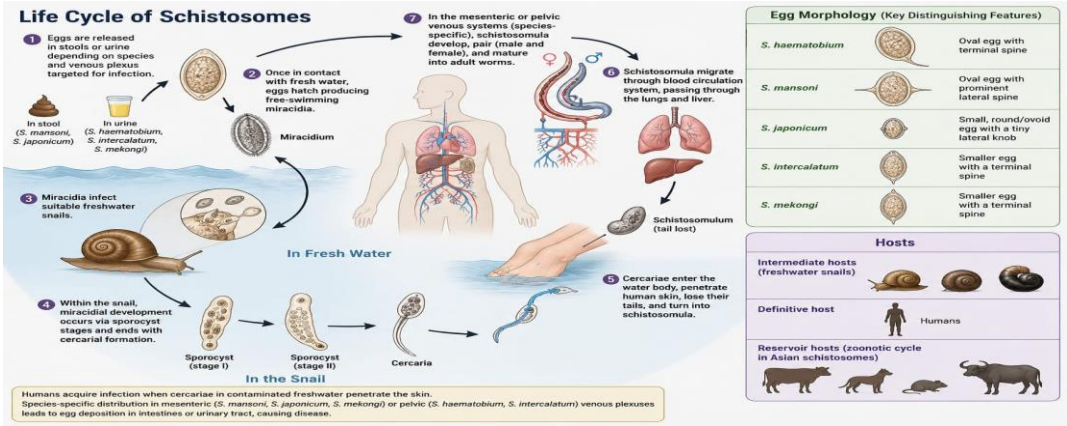
1. INTRODUCTION

Schistosomiasis is still one of the most significant diseases in humans caused by helminths and is classified as one of the important neglected tropical diseases of humans.[1] Factors that drive global prevalence of the disease include water contact, sanitation issues, suitability of environment for snails that transmit the disease, and repeated reinfections in disadvantaged communities. While there are multiple zoonotic and non-human species in the genus Schistosoma, five major human pathogenic species represent the basic clinical and epidemiological spectrum: S. mansoni, S. haematobium, S. japonicum, S. intercalatum, and S. mekongi. Burden of the disease is different for each of the species. S. mansoni is common in Africa, some regions of the Middle East and Americas, S. haematobium is the major species in sub-Saharan Africa and some regions of the Middle East, S. japonicum is limited to East and Southeast Asia, S. intercalatum exists in focal locations of Central Africa, and S. mekongi is only prevalent in the Mekong basin. In any case, pathology of the disease is mostly egg-driven, and its severity depends on both the number of parasites and the response of the host's immune system.[1,2] The public health significance of schistosomiasis is increased by the chronic nature of infection, vulnerability of children, and the interaction of the infection with anemia, poor growth, low educational performance, and organ damage. Treatment has been based on praziquantel preventive chemotherapy, but elimination cannot

be achieved with such approach due to rapid reinfections. Hybridization among schistosomes, particularly in African environments, has made the disease harder to classify and diagnose.[3] This provides a justification for comparing different schistosome species with regard to their life cycle biology, morphology, genomics, immunopathology, diagnostics, and future prospects.

2. Classification and Life Cycle

The parasite belongs to the family Schistosomatidae and is unique among trematodes due to its sexual dimorphism, dioecism, and existence intravascularly within the definitive host. Medically significant species parasitize humans, yet at times can develop within the animal reservoir hosts, primarily S. japonicum. S. mansoni and S. haematobium hybrids possess zoonotic and epidemiological significance as well.



3. The Five Major Schistosoma Species[4,5]

There are significant differences among the five human species in terms of ecology, morphology, host spectrum, pathogenicity, and required controls. While S. mansoni and S. haematobium represent the two major African schistosomes, the former is associated with intestinal-hepatic disease while the latter leads to urogenital pathology. S. japonicum is the most zoonotic, being highly adaptable to mammal hosts and very difficult to control in Asia. S. intercalatum is a geographically limited species whose taxonomy has yet to be defined, and whose relationship with S. guineensis has been historically misrepresented. S. mekongi is focal, Mekong-associated, and zoonotic in nature, despite making progress toward elimination in some regions. A useful comparative assessment of the five schistosomes must include an appreciation of the fact that the specific requirements of schistosome control relate to interactions between definitive and snail host ecology. S. mansoni uses Biomphalaria spp.,

S. haematobium uses Bulinus spp., S. japonicum uses Oncomelania spp., and S. mekongi uses Neotricula aperta. S. intercalatum is known to infect Bulinus snails in Central Africa, even though the vector specificity of this species has yet to be established in full.

4. Epidemiology

Contemporary epidemiology is influenced by focal transmission, overdispersed infection intensity distribution, and species-specific reservoir ecology. Most of the cases in the world are found in sub-Saharan Africa, while the Middle East, South America, and Asia host fewer, though consistently present, numbers of people affected. Geographically restricted species include S. mansoni predominant throughout much of Africa and America; S. haematobium in Africa; S. japonicum in China and Philippines; S. intercalatum in central Africa foci; and S. mekongi in the Mekong River basin.Infection intensity is controlled by water contact practices, snail habitats, climate favorability, agricultural practices, and sanitary facilities. Zoonotic reservoirs are of particular importance in Asian schistosomiasis, since infections in cattle, buffaloes, and rodents might maintain transmission even when the proportion of human population treated is high. The latter is one of the reasons why elimination of S. japonicum and S. mekongi was slower than in cases of African S. mansoni control.[2,6] Hybrid schistosomes become epidemiologically relevant due to findings from molecular genetics that reveal interspecific introgression and natural hybrids among species, especially between African lineages. Hybridization makes attribution of parasites on the basis of microscopy challenging, and can alter the host range, virulence or performance of diagnostic tests.

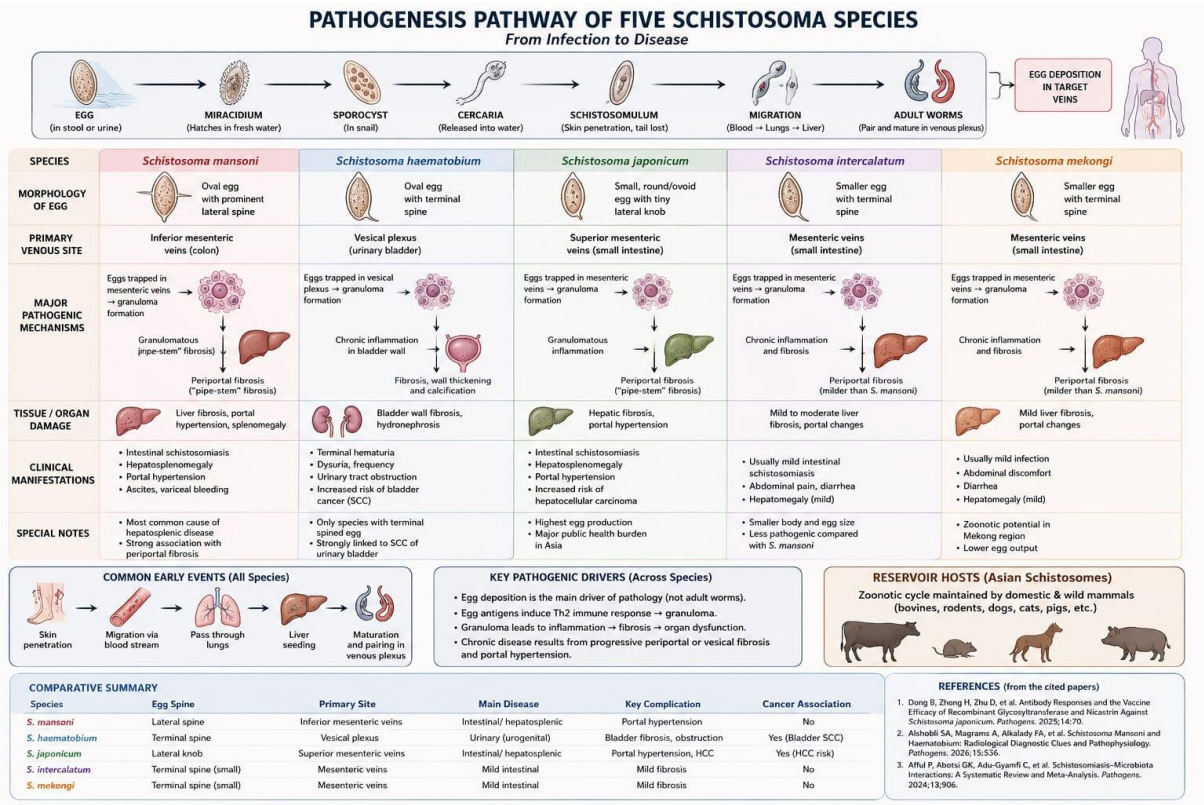
5. MORPHOLOGY[3]

Mature adult schistosomes are sexually dimorphic, with the male being wider and shorter than the female. The male possesses tubercles on the tegument, enclosing the female inside a gynecophoric canal during mating. Pairing of the sexes is necessary for the continued maturation and oviposition of the female, a feature rare among trematodes. The cercariae are fork-tailed, free-swimming stages adapted for seeking and penetrating their hosts. In S. mansoni and S. japonicum, cercarial enzymes, including elastase-related activity, assist in penetration, whereas sensory and neuroendocrine features unique to each species are highlighted by genomics. Morphology still plays a crucial role in microscopic diagnosis. The S. haematobium eggs are elongated and bear a spine on their surface, which can easily be detected in urine sediment. The S. mansoni eggs are oval, with a conspicuous lateral spine, present in stool. The S. japonicum eggs are rounder and have only a small lateral knob that

can sometimes be overlooked in routine smears, leading to misdiagnosis. The S. intercalatum and S. mekongi have smaller terminal-spined eggs which are sometimes mistaken for other species in low-intensity infections.

6. Intermediate Snail Hosts

Freshwater snails are necessary for transmission and have significant impacts on the spatial epidemiology of schistosomiasis. Biomphalaria spp. are intermediate hosts for S. mansoni; Bulinus spp. are hosts for S. haematobium and are involved in S. intercalatum transmission; Oncomelania spp. serve as definitive hosts for S. japonicum; and Neotricula aperta acts as a vector for S. mekongi.[7] Molecular recognition, immune evasion, and local ecological factors determine host specificity. For the Mekong transmission environment, N. aperta distribution and river hydrology play key roles in limiting transmission, and in East Asia, the ecology of Oncomelania has been responsible for shaping the possibilities for snail control. In Africa, Biomphalaria and Bulinus species are found in various freshwater ecosystems, making transmission possible through irrigation and peri-domestic environments. A One Health approach is required because the ecology of snails cannot be separated from human use and manipulation of the environment.



7. Molecular Biology and Genomics

Genomic approaches have taken schistosome biology from its parasitological origins to become an approach focused on mechanism. The S. mansoni genome was described at 363 Mb, and included expanded gene families, unusual intron structure, reliance on lipid metabolism, proteases, membrane receptors, and micro-exon genes.[8] The S. haematobium genome, approximately 385 Mb, helped establish urogenital tropism, interaction between the parasite and the host, and involvement in bladder cancer.[9] The S. japonicum genome brought to light the interaction between host and parasite, nutrient acquisition, and sensory adaptation, reflective of its broad range of mammalian hosts.[10] The chromosome-scale S. mekongi genome, approximately 404 Mb, further increased comparative genomic capacity and pointed to the species- or lineage-specific expansion in protease family, including M8 metalloproteases.[7] Comparative genomics across 81 parasitic worm genomes has provided a broader understanding of the evolutionary history of schistosomes, as well as potential drug targets in helminths. The most important biological finding from this research is that schistosomes are metabolically dependent on their hosts and thus vulnerable to targeting via intervention on membrane biology, signaling, and proteolysis. However, species- and lineage-specific genomics make it a mistake to assume the same molecular mechanisms are present in all human schistosomes.

8. Immunopathogenesis

The major pathogenetic event in schistosomiasis is the development of a host inflammatory reaction to trapped eggs within tissues. Egg-released antigens attract innate and adaptive immune responses, which result in formation of granulomas that first restrict tissue damage but finally lead to fibrosis, obstruction, and organ dysfunction. In animal models, the process proceeds from early Th1-skewed response towards Th2-dominated reaction with production of IL-4 and IL-13 and modulation of chronic pathology by regulatory factors IL-10 and IL-13 receptor alpha 2.[11,12] In schistosomiasis of the liver, chronic egg trapping in the liver results in the development of periportal fibrosis, portal hypertension, splenomegaly and variceal bleeding. In urogenital schistosomiasis, egg retention in the bladder wall leads to chronic inflammation and fibrosis, hematuria, hydronephrosis, and increased susceptibility to squamous-cell carcinoma.[13,14] The immunopathogenesis in these two forms of infection is tissue- and species-specific but the basic concept is similar – morbidity is associated with host attempts to isolate parasites which can not be eliminated spontaneously. Acute schistosomiasis, including Katayama fever, is caused by the systemic allergic reaction to

migratory larvae and adult worms, particularly following primary infection in immunologically naive hosts.[15,16] Chronic phenotype is caused by cumulative tissue damage and fibrosis rather than by direct cytotoxicity of parasites. It is an important point to consider during vaccine development.

9. Clinical Symptoms

The clinical course differs according to the phase and species of the pathogen. An acute disease might be accompanied by the presence of fever, malaise, cough, muscle pain, eosinophilia, and hypersensitivity reactions following the skin penetration and initial worm maturation; all this is traditionally associated with Katayama fever.[16,17] Intestinal schistosomiasis is followed by the presence of abdominal pain, diarrhea, blood in stool, and rectal disorders. Hepatosplenic schistosomiasis results in hepatomegaly, splenomegaly, periportal fibrosis, portal hypertension, and upper gastrointestinal bleeding.[18,19] Urogenital schistosomiasis, mostly caused by S. haematobium, is followed by the symptoms of dysuria, frequency, terminal hematuria, bladder wall fibrosis, ureteral obstruction, renal impairment, and increased risks of malignancies in the long run. Neuro-schistosomiasis and ectopic manifestation occur when the eggs or immune complexes affect the CNS or other organs, causing seizures, myelopathy, pulmonary lesions, or systemic diseases. The species difference has clinical importance, although it is not absolute. Intestinal disease is typical for *S. intercalatum* and *S. mekongi*, though, severe forms might develop in some localities. The clinical severity also depends on the age of the patient, infection intensity, co-infections, and access to therapy. Thus, the identification of the infecting species is important for prognosis and disease monitoring.

10. Diagnostics

Historically, microscopy has been used for diagnosis of parasitic infections, including thick Kato-Katz smear analysis of stool, urine filtration for Schistosoma haematobium, and occasionally biopsies. [15]Microscopy continues to be operationally valuable but has a poor sensitivity in case of low-intensity, post-treatment, and early stages of infection. This fact has become one of the major impediments of elimination as a reduced prevalence leads to low positive predictive value of microscopy and high proportion of light infections that escape routine diagnostics. Serological tests improve sensitivity of detection but can confuse the current infection with previous one. Antigen detection, including circulating cathodic and anodic antigens, shows the presence of active infection and ultra-sensitive CAA tests become

increasingly relevant for surveillance and elimination purposes. Molecular techniques, like PCR testing, provide high sensitivity and species identification and allow confirming low-intensity and mixed infections, 20The type of diagnostic test depends on its application. Clinical diagnosis uses microscopy or antigen tests, while surveillance during elimination campaigns involves more sensitive molecular or ultra-sensitive antigen-based tests. Hybrid infections make it necessary to use several types of tests, as morphological characteristics cannot always define species complexity. Thus, the future of diagnostics will include combination of antigen tests, PCR species-specific testing, and microscopy in some cases.

11. Treatment and Resistance

Currently, praziquantel continues to be the primary choice for treatment of all clinically significant human schistosomes. Positive aspects of this drug include its efficacy, low cost, and suitability for MDA. Drawbacks include low efficacy against young worms, no sterilizing/prophylactic activity, and potentially decreased sensitivity due to repeated mass applications. Molecular mechanism of action of the drug is poorly understood and associated with parasite membrane disturbances, increased calcium concentrations and worm paralysis or death.[21,22] MDA has led to a considerable decrease in morbidity in many locations but has failed to interrupt transmission due to reinfection after continued contact with water bodies and inability to kill immature worms. However, the potential emergence of resistance in schistosomes is biologically plausible and although there is currently no unequivocal evidence of it, like in the case of other anti-infectives, the decrease in drug efficacy in some endemic regions and the sole dependence on one drug warrant development of combination therapies, dosage optimization and discovery of new anti-schistosomal drugs.[23] In zoonotic systems of Asia, treatment alone is inadequate if reservoir hosts remain infected.

12. Vaccine Development

Vaccine development is a key unmet need since praziquantel does not offer protection against reinfection. Some of the potential antigens that have reached various levels of preclinical and clinical development include Sm-TSP-2, Sm-p80, Sm14, and Bilhvax candidates.[24,25] The controlled human infection model has also added momentum in this area as this strategy was meant to speed up efficacy assessment under ethical conditions.[26,25] The existing evidence suggests that an efficient vaccine may have to reduce either worm burden, female fecundity or egg production but not confer sterile immunity. From an immunological point of view, vaccines must be developed so that they do not increase egg-induced immunopathology. This

is especially applicable in species that cause high morbidity like S. haematobium and S. japonicum.

13. Novel Therapies

Other than praziquantel and traditional vaccine antigens, there have been advances in other potential chemotherapeutics and host-focused interventions, in addition to targeting biological molecules of the parasite. Studies of praziquantel chemistry and resistance reveal an extensive search space for derivatives and novel chemical compounds. Comparative worm genomics suggests targets like proteases, membrane proteins, ion channels and metabolic pathways.[26] RNA interference has been employed in the experimental definition of function in schistosome parasites, lending credibility to the notion that essential genes of the parasite could be targetable for treatment.[27] CRISPR-based technologies have been extensively discussed as tools for target validation, but translation into therapies has yet to be realized.[28] Monoclonal antibodies and immunomodulation have also remained promising concepts, especially when pathology is driven by the immune response and not the parasite itself. The justification for these therapeutic modalities lies in the fact that eventual elimination will entail diversification of the interventions. It is unlikely that one-drug intervention strategy will prove adequate where transmission is maintained by environmental reservoirs, reservoir hosts, and insensitive diagnostics.

14. One Health Approach

Schistosomiasis is an inherently One Health condition because it is dependent on human behavior, animal reservoirs, freshwater ecologies and biology of snails. Zoonotic reservoirs are very important in case of *S. japonicum* and *S. mekongi*, because transmission in such cases might be sustained by animals including cattle, water buffalo, rodents and other mammals.[2,6] In such cases, chemotherapy in humans is unable to eliminate transmission. Elimination through a One Health approach involves integrated surveillance, management of snails, modification of environment, sanitation and health education. In the Mekong basin, success of intervention programs has hinged upon cross-border measures and continuous surveillance.[7] This holds true for African transmission: water contact reduction, access to safe water and management of snail habitats are integral elements of MDA.

15. Research Gaps

Some gaps in research remain open. First, there is still underestimation of the actual prevalence due to the fact that microscopy is insufficient for low infections and post-

treatment carriage. Secondly, boundaries of species and hybridization need to be studied using genomics. This is especially pertinent for African ecosystems, where introgression might affect the phenotypes and epidemiology. Third, *S. intercalatum* remains relatively understudied. Fourth, the development of vaccines needs an approved product for use in humans, along with better correlates of protection, antigen prioritization, and efficacy models. Fifth, the mechanisms of praziquantel action and decreased sensitivity need further examination. Sixth, zoonotic and environmental drivers need greater integration in control models, especially in areas outside of Asia. Last, there is the need to conduct operational research in order to find out how to sustain elimination efforts when prevalence decreases and diagnosis becomes a limiting factor. These challenges go beyond mere academic interests; they are what separates programs that reduce morbidity from those that eliminate schistosomiasis.

16. Future Perspectives

In the future, schistosomiasis control will involve convergence of high sensitivity diagnostics, molecular surveillance, genomics, chemotherapeutics and vaccine success. Strategies for controlling schistosomiasis at a species level need to take into account local ecology rather than applying uniformly. For Africa, the main problem will still be human contact with water and transmission through Biomphalaria or Bulinus; in Asia, the role of the reservoir hosts and snail ecology will necessitate an integrated approach.

Genomic data will continue to advance comparative biology and possibly help in targeting interventions specifically by species. Innovation in diagnostics should be centered on rapid and field friendly antigen tests that perform well enough for low prevalence elimination efforts. The focus in vaccine development should be on reduction in worm fecundity and egg output because morbidities are egg related and transmission depends on egg excretion.

An integrated package consisting of preventive chemotherapy, targeted treatment of those at risk, reservoir control if applicable, sanitation, snail control, better access to water and sensitive surveillance is the most probable path forward. Under such circumstances, elimination becomes biologically possible although challenging from an operational standpoint.

17. CONCLUSION

There are five major schistosome species which infect humans. They have conserved life cycles but vary considerably in their geographical distribution, host ecology, morphology, genomics, and clinical presentation. *S. mansoni* and *S. japonicum* are primarily intestinal-hepatic; *S. haematobium* is urogenital; and *S. intercalatum* and *S. mekongi* are focal but very important species, which have been neglected so far, impeding the progress towards elimination.

Immunopathology based on eggs and not on the presence of adult worms accounts for the fibrotic nature of morbidities caused by the infection. Praziquantel will remain indispensable but inadequate as the single intervention tool. The diagnostic modernization, snail and reservoir control, genomic surveillance and vaccine development are necessary to achieve elimination. The comparative approach and the One Health paradigm are, therefore, crucial in understanding of this disease and its control.

REFERENCES

1. World Health Organization. Schistosomiasis (bilharzia): an acute and chronic neglected tropical disease. Geneva: WHO, 2020.
2. Impact of human schistosomiasis in sub-Saharan Africa. Pan Afr Med J / PMC9425372, 2022.
3. Genome-wide insights into adaptive hybridisation across the Schistosoma haematobium group in West and Central Africa. PLoS Negl Trop Dis, 2022.
4. Recent studies on Schistosoma intercalatum: taxonomic status, puzzling distribution and transmission foci revisited. Mem Inst Oswaldo Cruz, 2001.
5. A systematic review of Schistosoma intercalatum: an obscure causative agent of human schistosomiasis. medRxiv, 2024.
6. Schistosoma hybridizations and risk of emerging zoonosis in Africa: time to think of a One Health approach for sustainable schistosomiasis control and elimination. In: One Health. IntechOpen, 2022.
7. Zhou M, Xu L, Xu D, Chen W, Khan J, Hu Y, et al. Chromosome-scale genome of the human blood fluke Schistosoma mekongi and its implications for public health. Infect Dis Poverty, 2023; 12: 104.
8. Berriman M, Haas BJ, LoVerde PT, Wilson RA, Dillon GP, et al. The genome of the blood fluke Schistosoma mansoni. Nature, 2009; 460: 352-358.

9. Young ND, et al. Whole-genome sequence of Schistosoma haematobium. Nat Genet, 2012; 44: 221-225.
10. The Schistosoma japonicum Genome Sequencing and Functional Analysis Consortium. The Schistosoma japonicum genome reveals features of host-parasite interplay. Nature, 2009; 460: 345-351.
11. Schistosome egg migration: mechanisms, pathogenesis and host immune responses. Front Immunol, 2018.
12. Hams E, Aviello G, Fallon PG. The Schistosoma granuloma: friend or foe? Front Immunol, 2013.
13. Schistosoma "eggs-iting" the host: granuloma formation and egg excretion, 2018.
14. Circulating anodic antigen (CAA): a highly sensitive diagnostic biomarker to detect active Schistosoma infections—improvement and use during SCORE. Am J Trop Med Hyg, 2020; 103(Suppl 1).
15. Centers for Disease Control and Prevention. DPDx — Schistosomiasis infection. Atlanta: CDC.
16. History of Katayama disease: schistosomiasis japonica in Katayama district, Hiroshima, Japan. Acta Trop, 2004.
17. Characterisation of inflammatory response, coagulation, and radiological findings in Katayama fever: a report of three cases at the Medical University of Vienna, Austria, 2014.
18. International Agency for Research on Cancer. Infection with schistosomes (Schistosoma haematobium, Schistosoma mansoni and Schistosoma japonicum). IARC Monogr Eval Carcinog Risks Hum. Vol 61. 1994.
19. Urinary schistosomiasis and the associated bladder cancer: update. J Egypt Natl Canc Inst, 2020.
20. Diagnosis of schistosomiasis without a microscope: evaluating circulating antigen (CCA, CAA) and DNA detection methods on banked samples of a community-based survey from DR Congo, 2022.
21. Praziquantel for schistosomiasis, single drug revisited: metabolism, mode of action and resistance, 2017.
22. Kasinathan RS, Sharma LK, Cunningham C, Webb TR, Greenberg RM. Inhibition or knockdown of ABC transporters enhances susceptibility of adult and juvenile schistosomes to praziquantel. PLoS Negl Trop Dis, 2014.

23. Molehin AJ. Recent advances and methodological considerations on vaccine candidates for human schistosomiasis. Front Trop Dis, 2021.
24. Tebeje BM, et al. Schistosomiasis—from immunopathology to vaccines. Semin Immunopathol, 2020.
25. Tendler M, et al. Development of the Sm14/GLA-SE schistosomiasis vaccine candidate: an open, non-placebo-controlled, standardized-dose immunization phase Ib clinical trial targeting healthy young women. Front Immunol, 2022.
26. Siddiqui AA, Siddiqui SZ. Sm-p80-based schistosomiasis vaccine: preparation for human clinical trials. Parasitol Res, 2017.
27. RNA interference in Schistosoma mansoni schistosomula: selectivity, sensitivity and operation for larger-scale screening. PLoS Negl Trop Dis, 2010.
28. CRISPR-based functional genomics for schistosomes and related flatworms. Trends Parasitol, 2024.