Opinions

Can Specialized Pathogens Colonize Distantly Related Hosts? Schistosome Evolution as a Case Study

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Parasites that live in intimate contact with the immune system of their hosts require specialized adaptations to survive in such exposed environments. Once adapted to these demanding environments, it seems such parasites could not easily switch to distantly related hosts [1], and, thus, would be good candidates to diversely congruently with their hosts, i.e., cospeciation. One of the best-known parasite groups is the schistosomes, digenetic (having alternating sexually and asexually reproducing generations in their life cycle) trematodes that live in the vascular system of their vertebrate hosts. Schistosomes achieve notoriety because six of the roughly 100 described species [2,3] cause schistosomiasis, a disease that afflicts 200 million people, mostly in tropical Africa.

Schistosomiasis is usually chronic and debilitating in its course, with most of the pathogenesis caused not directly by the adult worms but by the eggs they produce. Eggs become lodged in the viscera and incite tissue responses, often causing pronounced enlargements in the liver and spleen, and abnormalities in blood flow through these organs. If worms colonize the urinary system, hematuria (blood in the urine) and kidney and bladder damage often result.

Schistosomiasis negatively affects growth and productivity, and has largely underestimated, insidious effects on the people with this disease. Adult worms can be killed by drugs, but the limited availability and high cost of these drugs and the potential for emergence of drug resistance are important concerns. Immunity is slow to develop, though hope for an effective vaccine remains high.

Schistosomes infect birds or mammals, but one species, *G. amoena*, often considered the missing link in schistosome evolution, is known to infect freshwater crocodiles [4]. Schistosomes share the habit of living in a vascular habitat with other trematodes, including the Spirorchidae of turtles and the Sanguinicolidae of fishes. Worms in these three families have two-host life cycles—a snail host and a vertebrate host—and also share a distinctive tegument, or body covering, consisting of two lipid bilayers instead of the typical single bilayer. The double bilayer is believed to be an adaptation for survival in the immunologically hostile environment of the blood [5]. Schistosomes differ from the other two families of blood flukes, though, by being dioecious (having separate male and female worms) and dimorphic (with the two sexes different in morphology), and by having specialized habitat requirements. The remarkable biology of schistosomes has precipitated considerable discussion regarding their origins and their evolution of dioecy (the change from the typical state in trematodes of being hermaphroditic to a state with separate males and females) [2,4,6–10].

The discovery of *G. amoena* [4], the only species of schistosome known in an ectotherm, gave rise to a hypothesis that schistosomes arose in early ectothermic archosaurs, for example, ancestors of modern crocodiles, and radiated into endothermic archosaurs (birds). This view was supported by a phylogenetic analysis of adult morphology, which placed *G. amoena* as basal, or ancestral, among schistosomes [11], and challenged the role of endothermy as the pivotal factor driving schistosome diversification [10–12]. Molecular phylogenetic studies to date [7,13,14] have been hampered by an incomplete sampling of the 13 widely recognized schistosome genera, including the provoking and putatively basal *G. amoena*. The molecular phylogeny in Figure 1 includes representatives of all the commonly recognized genera of schistosomes, and spirorchiids from both freshwater and marine turtles [7]. Included in this molecular phylogeny is *G. amoena*, specimens of which were recovered from the Australian freshwater crocodile, *Crocodylus johnstoni*, obtained near Darwin, Australia.

Our analysis shows that *G. amoena* is, in fact, not a basal schistosome, but is more closely related to spirorchiids from freshwater turtles. This expands the host range of spirorchiids to include reptiles other than turtles, and suggests that schistosomes parasitize only endotherms. Our analysis confirms that the sister group to the schistosomes are the spirorchiids from marine turtles [7], and that the basal schistosomes are parasites of marine birds and snails (Figure 1). This pattern supports the idea that a long-range host switch from turtles to avian hosts occurred in marine habitats, and that schistosomes subsequently colonized birds, mammals, and freshwater snails. This argues against a hypothesis of a long-term association between schistosomes and archosaurs (crocodilians), and suggests that exploitation of endotherms has been the key factor leading to the emergence of schistosomes and their dioecious condition [2,8]. We speculate that the transferal of a spirorchiid protoschistosome to an...
endothermic host was favored by the partial endothermy of their ancestral marine turtle hosts.

Endotherms have metabolic rates that are roughly one order of magnitude higher than those of ectotherms of comparable size, and they consequently ingest more food [17]. Nutrients are then conveyed to the liver via the hepatic portal system. Most species of schistosomes live in the hepatic portal system. We argue that schistosomes colonized this specific habitat in the endothermic host was favored by the partial endothermy of their ancestral marine turtle hosts.

Figure 1. Maximum Likelihood Estimated Tree from the Combined Data Partitions of 6,335 Bases Derived from 18S and 28S Ribosomal DNA and Partial Cytochrome Oxidase I Mitochondrial DNA Genes

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References

1. Adamson ML, Caira JN (1995) Evolutionary factors influencing the nature of parasite specificity. Parasitology 109: 585–595.

2. Basch PF (1991) Schistosomes: Development, reproduction and host relations. Oxford: Oxford University Press. 248 p.

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3. Khalil LF (2002) Schistosomatoida. In: Gibson DI, Jones A, Bray RA, editors. Keys to the Trematoda. Wallingford: CABI Publishing. pp. 419–432.

4. Platt TR, Blair D, Purdie J, Melville L (1991) *Griphobilharzia amoena* n. gen., n. sp. (Digenea: Schistosomatidae), a parasite of the freshwater crocodile *Crocodylus porosus* (Reptilia: Crocodylia) from Australia, with the erection of a new subfamily, *Griphobilharziinae*. J Parasitol 77: 65–68.

5. McLaren DJ, Hockley DJ (1977) Blood flukes have a double outer membrane. Nature 268: 147–149.

6. Carmichael AC (1984) Phylogeny and historical biogeography of the *Schistosomatidae* [PhD thesis]. East Lansing (Michigan): Michigan State University. pp. 1–246.

7. Snyder SD (2004) Phylogeny and paraphyly among tetrapod blood flukes (Digenea: Schistosomatidae and Spirorchiidae). Int J Parasitol 34: 1385–1392.

8. Short RB (1983) Sex and the single schistosome. J Parasitol 69: 3–22.

9. Despres L, Maurice S (1995) The evolution of dimorphism and separate sexes in schistosomes. Proc R Soc Lond B Biol Sci 262: 175–180.

10. Platt TR, Brooks DR (1997) Evolution of the schistosomes (Digenea: Schistosomatidae): The origin of dioecy and colonization of the venous system. J Parasitol 83: 1035–1044.

11. Morand S, Muller-Graf CD (2000) Muscles or testes? Comparative evidence for sexual competition among dioecious blood parasites (Schistosomatidae) of vertebrates. Parasitology 120: 45–56.

12. Combes C, Despres L, Establet D, Fournier A, Jourdane J, et al. (1991) Schistosomatidae (Trematoda): Some views on their origin and evolution. Res Rev Parasitol 51: 25–28.

13. Snyder SD, Loker ES (2000) Evolutionary relationships among the *Schistosomatidae* (Platyhelminthes: Digenea) and an Asian origin for *Schistosoma*. J Parasitol 86: 283–288.

14. Locker AE, Olson PD, Ostergaard P, Rollinson D, Johnston DA (2003) The phylogeny of the Schistosomatidae based on three genes with emphasis on the interrelationships of *Schistosoma* Weil & Land, 1898. Parasitology 126: 203–224.

15. Spotila JR, Stantclor EA (1985) Environmental constraints on the thermal energetics of sea turtles. Copeia 3: 694–702.

16. Paladin FV, O’Connor MP, Spotila JR (1990) Metabolism of leatherback turtles, gigantothermy, and thermoregulation of dinosaurs. Nature 344: 856–860.

17. Pough FH, Janis CM, Heiser JB (2005) Vertebrate life. 7th edition. Upper Saddle River (New Jersey): Prentice Hall. 752 p.

18. Platt TR (2002) Spirorchiidae. In: Gibson DI, Jones A, Bray R, editors. Keys to the Trematoda. Wallingford: CABI Publishing. pp. 453–467.

19. Ulmer MJ (1959) Studies on *Spirorchis salmonis* (Stunkard, 1922) Price, 1954 (Trematoda: Spirorchiidae) in the definitive host. Trans Am Microsc Soc 78: 81–89.

20. Blair D, Davis GM, Wu B (2001) Evolutionary relationships between trematodes and snails emphasizing schistosomes and paragonimids. Parasitology 123: S229–S243.

21. Oliver L (1953) Observations on the migration of avian schistosomes in mammals previously unexposed to cercariae. J Parasitol 39: 237–243.

22. Horak P, Dvorak J, Kolarova L, Trefil L (1999) *Trichobilharzia regenti*, a pathogen of the avian and mammalian central nervous systems. Parasitology 119: 577–581.

23. Baysade-Dufour C, Vuong PN, Rene M, Martin-Loehr C, Martins C (2002) Lesions viscerales de mammiferes et oiseaux, exposes aux agents de dermatite cercarienne humaine. Bull Soc Pathol Exot 95: 229–237.

24. Platt TR, Islam KS (1983) The life cycle and morphology of *Trichobilharzia australis* n.sp. (Digenea: Schistosomatidae) from the nasal blood vessels of the black duck (*Anas superciliosa*) in Australia, with a review of the genus *Trichobilharzia*. Syst Parasitol 5: 89–117.

25. Johnson KP, Clayton DH (2003) Coevolutionary history of ecological replicates: Comparing phylogenies of wing and body lice to columbiform hosts. In: Page RDM, editor. Tangled trees: Phylogeny, cospeciation, and coevolution. Chicago: University of Chicago Press. pp. 262–296.

26. Criscione C, Blouin M (2004) Life cycles shape parasite evolution: Comparative population genetics of salmon trematodes. Evolution 58: 198–202.

27. Swofford DL (2000) PAUP*. Phylogenetic Analysis Using Parsimony* and other methods, Version 4 [software]. New York: Sinauer Associates.

28. Huebner JP, Ronquist F (2001) MrBayes: Bayesian inference of phylogenetic trees. Bioinformatics 17: 754–755.