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Out of Animals and Back Again: Schistosomiasis as a Zoonosis in Africa

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1. Introduction

Schistosomiasis is one of the world's most widely distributed and prevalent parasitic diseases, with approximately 700 million people at risk of infection. The vast majority of human cases of the disease are found in Africa, with distribution in virtually all corners of the continent, bar the Sahara and Namib deserts and the depths of the Congo jungle (Hotez et al., 2009). Pre-prubescent children, and particularly boys, are the age group most at risk from adverse clinical symptoms and are frequently targeted for treatment interventions, yet even with readily available drugs (namely praziquantel), the pervasiveness of the intermediate host snails and the ease at which re-infection occurs has hampered attempts to manage the disease in many places (Standley et al., 2009, Fenwick, 2009). Less widely recognized is that some species of *Schistosoma,* including several which commonly affect man, can also be infective in other mammalian species, and particularly in non-human primates. Given current high levels of research interest into emerging zoonotic diseases, the status of schistosomiasis as a zoonotic infection is in need of re-appraisal, especially in light of advances in application of molecular epidemiological methods; it has been 20 years since the last formal review was published (Ouma and Fenwick, 1991), with earlier appraisals fully half a century ago (Nelson, 1960, Nelson et al., 1962). By comparing historical accounts to on-going, cutting edge research using molecular tools, it will be possible to gain an insight into the dynamics of schistosomiasis in human and other hosts and whether this relationship is changing as a result of anthropogenic activities. As such, this chapter provides an overview of zoonoses involving schistosomiasis, focusing on Africa where the burden of the disease is highest, and also discusses the ways in which this information can be integrated into more effective conservation management and human disease control strategies. The emphasis will be on the most common forms of human schistosomiasis and how animals not only may suffer clinical manifestations from infection, but may also act as reservoirs for schistosomiasis, thus confounding control efforts that focus mainly on the treatment of humans.

2. Overview of schistosomiasis as a global infection of wildlife and domestic animals

There are many species of *Schistosoma* that are only known from animal infections. Out of the 22 currently recognized species, only eight have been reported from humans (Table 1),

and of these, only three are heavily implicated as diseases of public health importance. The rest of the genus *Schistosoma* is only known from animal infections, and specifically mammals; the various species have adapted to a wide variety of taxa, with some specializing on one species while others have a wide definitive host range. For the purposes of examining cross-over of parasitic infections between humans and animals and vice versa, the term 'zoonosis' is used throughout this chapter to describe transmission in both directions. Figure 1 shows a phylogeny of the genus *Schistosoma*, with main geographic distributions and primary definitive hosts marked.
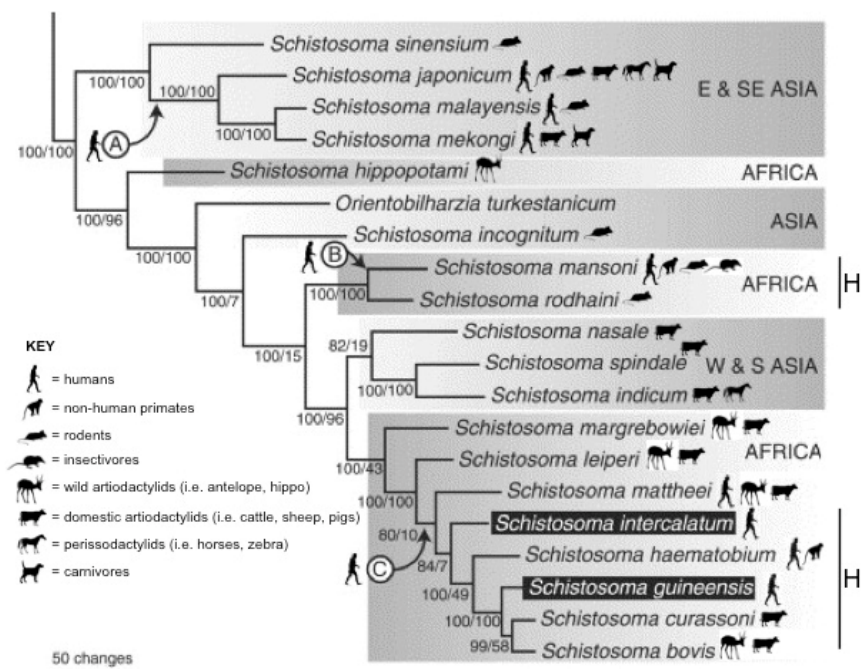

Fig. 1. Phylogeny of *Schistosoma*, as recognized in 2006 (*S. kisumuensis* was described in 2009; Hanelt et al., 2009). Known naturally infected definitive host groups are shown by the icons. The points 'A', 'B' and 'C' indicate the three suggested points where species adapted to infect humans; molecular clock estimates place the date of each divergence at roughly 3.8 MYA (millions of years ago) for point A and less than 1 million years ago for points B and C (Morgan et al., 2005, Webster et al., 2006, Attwood et al., 2008). The lines marked 'H' demonstrate clades with known hybridization between species (see section 4.1). Figure adapted from Webster et al. (2006).

2.1 *Schistosoma* infections of animals in Asia and Latin America

Although this chapter specifically focuses on the role of schistosomes as zoonotic infections in Africa, it is worth considering the distribution of the genus elsewhere in the world and the various animal definitive hosts the various species utilize, for comparison. In Asia, schistosomes from the *Schistosoma indicum* group (including *S. indicum*, *S. spindale* and *S. nasale*) are commonly found in domestic animals such as ungulates, horses, pigs and

Schistosoma species	Distribution	Natural definitive host species (excluding humans)	Human public health importance
S. mansoni	Africa, Middle East, South America, Caribbean	Non-human primates (including apes), rodents, insectivores, artiodactylids (waterbuck), procyonids (raccoon)	High
S. haematobium	Africa, Middle East	Non-human primates (not apes), artiodactylids (pigs, buffalo)	High
S. intercalatum	Central Africa (D.R. Congo only)	Possibly rodents	Low
S. guineensis	West Africa (Lower Guinea)	Possibly rodents	Low
S. mattheei	Southern Africa	Non-human primates (not apes), artiodactylids (cattle, antelope)	Low
S. japonicum	East Asia (China, Philippines, Indonesia)	Non-human primates, artiodactylids (water buffalos in particular), carnivores, rodents, perissodactylids (horses)	High
S. mekongi	SE Asia (Vietnam, Cambodia, Laos, Thailand)	Carnivores (dogs), artiodactylids (pigs)	Moderate
S. malayensis	Peninsular Malaysia	Rodents (van Mueller's rat)	Low

Table 1. The eight species of schistosome reported in humans. *Schistosoma guineensis* was only described in 2003, and so many past references to *S. intercalatum* may have actually been referring to *S. guineensis*. References include Fenwick (1969), Pitchford (1977), Loker (1983), Christensen et al. (1983), Pagès et al. (2003), and Standley et al. (2011).

possibly dogs. *Schistosoma indicum* is associated predominantly with artiodactylids, infecting a wide range of species, although perissodactylids have also been found naturally infected (Loker, 1983). *Schistosoma nasale* appears specialized to cattle, causing the veterinary condition known as 'snoring disease' (Bont et al., 1989). *Schistosoma spindale*, like *S. indicum*, appears to have a relatively low host specificity (Haas et al., 1990), though again it is mainly found in ungulates.

Species from the *Schistosoma japonicum* group are also widely recovered from different groups of animals, with *S. japonicum* itself described from perissodactylids, artiodactylids (particularly water buffalo), carnivores, rodents and primates (He et al., 2001). *Schistosoma mekongi*, conversely, is limited to humans and dogs, with pigs also possibly a natural host (Crosby and Garnham, 2009). Rodents have been successfully infected experimentally but there is no indication that these serve as natural definitive hosts (Byram and Von Lichtenberg, 1980). *Schistosoma malayensis*, the third member of the *S. japonicum* group, is rarely found in humans, with van Mueller's rat (*Rattus muelleri*) the usual definitive host in nature. Basal to this group are *S. ovuncatum* and *S. sinesium*, both of which utilize the common rat (*Rattus rattus*) as definitive hosts (Baidikul et al., 1984, Lockyer et al., 2003).

Schistosoma incognitum forms its own group (Webster et al., 2006); dogs, pigs and rats have been identified as naturally infected (Bunnag et al., 1983, Sinha and Srivastava, 1960),

while in addition, rabbits and macaque monkeys have been experimentally determined to be susceptible.

The two remaining groups of *Schistosoma* species, the *S. mansoni* group and the *S. haematobium* group, are historically confined to Africa and the Middle East. However, *S. mansoni* is also found in Latin America, introduced via the slave trade from Africa (Desprès et al., 1993). Concerted public health initiatives have eliminated schistosomiasis as a human health concern in many Latin American and Caribbean locations (Hotez et al., 2008, Steinmann et al., 2006). However, transmission of *S. mansoni* in this region remains widespread, due to the susceptibility of other animals to the infection. Specifically, it is rodents that are now the primary definitive host in many parts of Latin America and the Caribbean. An interesting effect of this host switch has been the change of cercarial shedding patterns; those adapted to infecting humans tend to have peak cercarial emergence time at midday, whereas those adapted to rodents show maximum shedding at dawn and dusk, corresponding to the times of day when rodents are most active t water sources (Alarcón De Noya et al., 1997, Theron and Combes, 1995). This behavioural plasticity may explain how schistosomes can optimize infection in a wide variety of different host species.

2.2 *Schistosoma* of animals in Africa

In Africa, species of *Schistosoma* belong either to the *S. mansoni* group, characterized by eggs with lateral spines, or the *S. haematobium* group, identified by terminal spines on the eggs. Unlike the Asian schistosomes, the eponymous species of these two groups are most commonly found in humans and exact a huge public health burden on many communities and regions. However, as in Asia, there are other species within these groups that primarily affect non-human animals; this section will outline the other species of *Schistosoma* that are found in Africa, which are known as infection of domestic and wild animals, while the rest of the chapter deals with accounts of 'human' schistosome species as infections of animals.

The other species that make up the *Schistosoma haematobium* group are *S. intercalatum*, *S. guineensis*, *S. bovis*, *S. mattheei*, *S. margrebowiei*, *S. leiperi*, *S. curassoni* and the recently-described *S. kisumusensis* (Hanelt et al., 2009, Webster et al., 2006). *Schistosoma intercalatum* and *S. guineensis* primarily infect humans (Table 1). The remaining species, with the exception of *S. kisumuensis*, usually parasitize artiodactylid ruminants, with some most commonly found in domestic ungulates whereas others are more frequently observed in wild bovids. Between them, they are distributed over most of sub-Saharan Africa. *Schistosoma bovis* and *S. mattheei* are both principally parasites of domestic cattle; *S. bovis* is located throughout Africa but primarily north of 10° south, and it is replaced by *S. mattheei* south of this latitude (Nelson et al., 1962). In addition to domestic cattle, both *S. bovis* and S. *mattheei* have been naturally found in a variety of other artiodactylids as well as horses, zebras and rodents (Hanelt et al., 2010, Pitchford, 1977). There are even reports of these species from humans and baboons, although usually alongside a mixed infection with either *S. mansoni* or *S. haematobium*. *Schistosoma mattheei* was recently confirmed using molecular methods from a free-ranging baboon troop in Zambia (Weyher et al., 2010).

Sympatric to *Schistosoma bovis* in parts of Western Africa is *S. curassoni*, which is also naturally found in cattle, as well as sheep and goats (Ndifon et al., 1988, Vercruysse et al., 2003). In sub-Saharan Africa, *S. leiperi* and *S. margrebowiei* are two broadly sympatric species known as 'antelope' schistosomes, although they both have been observed to be transmissible through a wide range of artiodactylids, including domestic livestock. Both are also reported from horses and zebras; in addition, there is one account of eggs of *S.*

margrebowiei being recovered from a human rectal biopsy in Mali, mixed with *S. haematobium* and *S. mansoni* (Pitchford, 1959a). The egg morphology of *S. margrebowiei* is unique among African schistosomes (Christensen et al., 1983); although experimental passage has never been successful, other infections have also been reported from Zambia (Giboda et al., 1988), suggesting that while humans may contract incidental infections with *S. margrebowiei*, infections are not viable in man. *Schistosoma kisumuensis* is unique among the 'non-human' *S. haematobium* group species in being exclusively an infection of small mammals, such as rodents and insectivores; it was very recently described, using molecular methods, from western Kenya, and as such is not included in the 2006 phylogeny on which Figure 1 is based (Hanelt et al., 2009).

The *Schistosoma mansoni* group has traditionally been classified to consist only of three other species: *S. hippopotami*, *S. edwardiense* and *S. rodhaini*. *Schistosoma hippopotami*, on the basis of recent molecular analysis, has since been re-classified as basal to all African schistosomes (Webster et al., 2006); *S. hippopotami* and *S. edwardiense* are also unusual in only having been found in a single species of definitive host: the African hippopotamus (*Hippopotamus amphibius*). *Schistosoma rodhaini*, on the other hand, is primarily an infection of rodents, although there are past reports of dogs and even a serval cat being naturally infected in Central Africa (Pitchford, 1977, Schwetz, 1954). More recently, insectivore species around Lake Victoria have also been observed to be infected with *S. rodhaini* (Hanelt et al., 2010); baboons have been successfully experimentally infected, but only when also co-infected with *S. mansoni* (Nelson and Teesdale, 1965). The literature only mentions one reported case of a natural infection of *S. rodhaini* in a human, from what is now DR Congo (D'haenens and Santele, 1955); however, given the age of the reference and its isolation in the literature, it may be suggested that it is a case of false diagnosis of *S. mansoni*.

3. Accounts of 'human' schistosomiasis in African animals

Of the 12 species of *Schistosoma* found in Africa, only four are regularly reported as infections of humans; these are *S. mansoni*, *S. haematobium*, *S. intercalatum* and *S. guineensis* (see Table 1). Of these, the overwhelming majority of human cases are caused by the first two; indeed, *S. guineensis* was only first described in 2003, following from a molecular appraisal and as such, many older records of infections of *S. intercalatum*, especially if reporting from the Lower Guinear region (countries such as Nigeria, Cameroon, Equatorial Guinea, São Tomé and Gabon), may actually be referring to what would now be known as *S. guineensis* (Pagès et al., 2003). As such, throughout this chapter, these two will be considered together, as *S. intercalatum/guineensis*. The following section examines both past and present records of human forms of schistosomiasis in animals, evaluates how hybridization of non-human schistosomes may result in emerging zoonotic threat, and finally describes methods for determining the extent and validity of a cross-over of schistosome infection between humans and animals or vice versa.

3.1 Historical records of *Schistosoma mansoni*, *S. haematobium* and S. *intercalatum/guineensis* in African animals

Schistosomiasis has long been reported as a human parasitic disease in Africa: eggs of *Schistosoma haematobium* have been observed from mummies in Egypt, dating back to more than a millennium BCE (Lambert-Zazulak et al., 2003). Moreover, molecular evidence has suggested a similar length and geography for the evolution of *Schistosoma* in Africa to that of

modern *Homo sapiens*, suggesting a very ancient association between humans and schistosomes (Despres et al., 1992). The distribution of the four main types of human schistosome (*S. haematobium*, *S. mansoni*, *S. intercalatum* and *S. guineensis*) covers vast swathes of Africa and Madagascar, including areas of high human density such as the West African coast, the Sahel and the southern and eastern highlands (Figure 2). High population density of humans is accompanied by large numbers of domestic livestock, putting such animals, as well as others that are associated with human activity, at risk of contracting diseases such as schistosomiasis. Moreover, many of these regions are known to possess high biodiversity of non-domesticated animals, which may also be exposed to transmission.
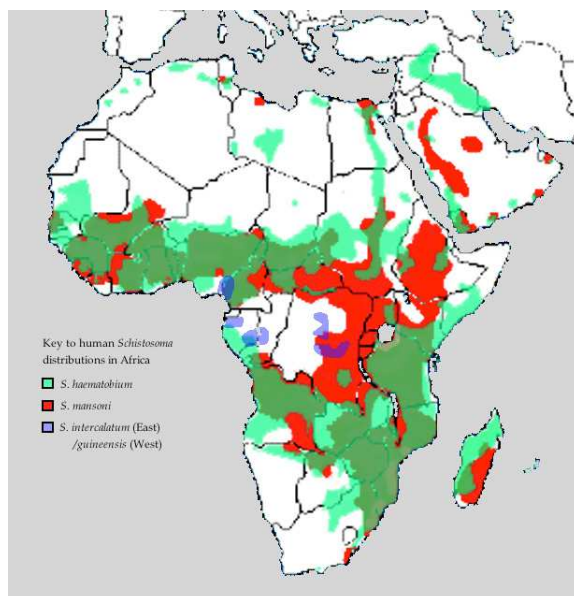

Fig. 2. Map of distribution of human *Schistosoma* species in Africa, Madagascar and the Middle East. Redrawn from www.path.cam.ac.uk (University of Cambridge, Dept. of Pathology)

Although interest in tropical medicine and parasitology had been first extensively stimulated by European troops returning home from stations in Africa after the First World War, it was the creation of the World Health Organisation after World War II which led to concerted and coordinated research programmes involving tropical diseases (Sandbach, 1976, Sturrock, 2001). These programmes included detailed surveys of human communities for incidence, prevalence and intensity of a range of infectious diseases, including schistosomiasis; in many cases, domestic and wild animals were also explicitly included in these surveys. Other cases of animal infections were reported *ad hoc*, either based on veterinary concern or commercial interest.

The explicit focus on concurrently surveying animals alongside human communities dwindled in the 1970s; the emphasis on chemotherapeutic control of schistosomiasis led to resources being targeted at mass drug administration and human treatment programmes. However, the emergence of interest in conservation issues resulted in re-energised

monitoring of wild animals populations, and the continued, if sporadic, reporting of cases of human parasites in wild animals. The modern, molecular, era has transformed the way in which zoonotic infections are identified and analysed, as will be discussed further in section 4; moreover, the status of animals as reservoirs of human schistosomiasis, as the situation was in the 1960s and 1970s, has been comprehensively covered by Nelson and colleagues (1960, 1962) and R. J. Pitchford (1977), respectively. More recently, Ouma and Fenwick (1991) reviewed schistosomiasis as a zoonosis in Africa; as such, there is little need to re-review and the following paragraphs will briefly summarise and update these earlier works regarding the main discoveries of schistosomiasis in non-human hosts in Africa in the last years of the 20th century and first decade of the 21st century.

3.2 Recent reports of *Schistosoma mansoni*, *S. haematobium*, and *S. intercalatum/guineensis* in non-human animals in Africa

Pitchford's (1977) checklist of natural hosts of *Schistosoma mansoni, S. haematobium* and *S. intercalatum* included a range of wild and domestic animals throughout Africa, although primates were considered the main mammal groups affected for all three, with *S. mansoni* also being an important infection of rodents (Table 1). These two groups will be considered separately in subsequent sub-sections.

In addition, for *Schistosoma mansoni* Pitchford lists two records of shrews (insectivores) being found naturally infected in the wild and two instances of eggs being found in artiodactylids, though the eggs were dead and thus these ruminants cannot be considered naturally viable hosts (Pitchford et al., 1974). Nelson et al. (1962) also report on a case of *S. mansoni* eggs, mixed with *S. rodhaini*, being found in a dog in Kenya; other similar discoveries of *S. mansoni* eggs in dogs has been attributed to ingestion of human feces containing parasite eggs, and hatching of the specimens in dogs does not seem to produce viable miracidia (Mango, 1971). Moreover, laboratory experiments conducted a few years earlier did not find dogs, or indeed carnivores in general, susceptible to infection, supporting the hypothesis that these incidental observations should not be the basis for considering dogs natural hosts of *S. mansoni* (Kuntz and Malakatis, 1955a, Stirewalt et al., 1951).

More recently, shrews were found naturally infected with *Schistosoma mansoni* at a marsh site in Kenya, near Lake Victoria, confirming earlier reports of their likely susceptibility (Hanelt et al., 2010). In terms of infections in artiodactylids, adult *S. mansoni* worms were recovered from a small number of cattle in Sudan during a survey in the 1980s; eggs were not recovered from the stool so viability of the infection cannot be confirmed (Karoum and Amin, 1985). The same survey failed to find signs of infection in local dogs, sheep and goats, despite 70% prevalence of infection in resident school-age children.

Schistosoma haematobium, in contrast to *S. mansoni,* has long been considered almost exclusively a primate, disease, mainly due to the paucity of observations of natural infections in other taxa (Nelson et al., 1962, Vianna Martins, 1958). Pitchford (1977) lists only a handful of reported cases from artiodactylids, including domestic pigs and sheep (the latter mixed with *S. mattheei* infection) and a single female Cape buffalo. Vianna Martins (1958) elucidates the low susceptibility of sheep and rodents to *S. haematobium*, describing comprehensive surveys of these taxa in highly endemic areas of human infection in Iraq and D.R. Congo, and finding no trace of infection. To the authors' knowledge, modern surveys have thus far not found naturally-acquired, non-hybrid *S. haematobium* infections in mammals other than primates or rodents; like *S. mansoni*, carnivores do not appear to be

readily susceptible to infection with *S. haematobium* in the laboratory so there is little reason to assume they are more permissive under natural conditions (Kuntz and Malakatis, 1955b).

Like *Schistosoma haematobium*, *S. intercalatum/guineensis* are considered primarily to be infections of man, and have rarely been reported from other taxa. Pitchford (1977) only lists primate records of natural infection, and in his review of the life history of schistosomes, Loker (1983) puts a question mark next to possible infections of rodents and artiodactylids with *S. intercalatum* (*S. guineensis* had yet to be described); Christensen et al. (1983) fully dismiss bovids as significant natural hosts of *S. intercalatum*, along, in fact, with *S. mansoni* and *S. haematobium.* Similarly, a recent review of the status of *S. intercalatum* in Central Africa fails to mention reports of this parasite in non-human mammals (Ripert, 2003); as such, as with *S. mansoni* and *S. haematobium*, it is suggested that attention should focus on rodents and non-human primates as primarily at risk from *S. intercalatum/guineensis*.

3.2.1 Schistosomiasis in African rodents

Given the broad and excellent experimental susceptibility of a range of rodent species to infection with all four of the above-mentioned 'human' schistosomes, it would come as no surprise to observe natural infections in this taxon. Moreover, the high biodiversity and abundance of rodent species especially around human settlements, lends them importance as potential reservoirs of human schistosomiasis, even if their egg excretion rates are relatively low. Understanding the role this group of mammals plays in the transmission of schistosomiasis, therefore, may be an important step towards maintaining control of the disease in human communities, as has been suggested in other locations where rodents are significant definitive hosts, such as Latin America and the Caribbean (Modena et al., 2008).

As it happens, the vast majority of reports relate to infections with *Schistosoma mansoni* alone; given that a variety of rodents have been known to be experimentally susceptible to *S. haematobium* (Gear et al., 1966), suggesting further scrutiny of this taxon be a research objective. In the literature, a single adult male worm of *S. haematobium* was reported from a Nile rat in Egypt in the 1970s (Mansour, 1973); given that the rodent was co-infected with *S. mansoni*, and no terminally-spined eggs were recovered from any of the surveyed rats, this observation may well be a misidentification (Morand et al., 2006). An earlier single report of *S. haematobium* in a rodent has likewise since been considered erroneous (Pitchford, 1959b). Similarly, there is a paucity of information on infections with *S. intercalatum* in rodents; a single historical report exists of a natural infection of a rodent with *S. intercalatum*, despite sympatric species of rodents known to be experimentally susceptible (Imbert-Establet et al., 1997).

Schistosoma mansoni, as mentioned above, is relatively commonly observed in African rodents, although usually at lower prevalence levels than seen in Latin American or Caribbean transmission settings (Hanelt et al., 2010). Historical accounts of natural infections in rodents are mainly based around a series of comprehensive surveys undertaken in D.R. Congo in the 1950s, which revealed presence of *S. mansoni* in six genera of rodents (Schwetz, 1954, 1956). At this time, the form of *S. mansoni* found in rodents was considered to be a separate variant to the human form, and was described as *S. mansoni* var. *rodentum*. More recent analyses have shown using molecular tools that there is gene flow between the parasites found in rodents and in man, suggesting that the form observed in rodents subtly changes its morphology in response to different host environments (Steinauer et al., 2008b); this work was done on rodent populations in Western Kenya, where several other reports of *S. mansoni* in rodents from recent years have originated

(Hanelt et al., 2010, Steinauer et al., 2009, Steinauer et al., 2008a). Rodents have also been found infected with *S. mansoni* throughout the rest of Africa, with more reports from Kenya (Kawashima et al., 1978, Nelson et al., 1962), South Africa (Pitchford and Visser, 1962), Senegal (Duplantier and Sène, 2000), Sudan (Karoum and Amin, 1985) and Egypt (Arafa and Massoud, 1990, Mansour, 1973).

3.2.2 Schistosomiasis in non-human primates in Africa

Whereas rodent infections with humans schistosomiasis are relatively constrained to *Schistosomiasis mansoni,* natural infections in non-human primates are known also from *S. haematobium* (Pitchford, 1977). Moreover, given the close geographical and genetic proximity of many primate species to humans, it is no surprise that these are the group of mammals most likely to be at risk from infection with human diseases of all kinds, including schistosomes, and infections with other trematode genera have been observed in free-ranging primate populations in Africa (Murray et al., 2000, Sleeman et al., 2009). In addition, as human populations grow at a rapid rate and communities push ever further into remote forest locations, they are coming into contact with relatively pristine primate habitats, thus potentially putting new species at risk of exposure to schistosomiasis infection. Given the endangered and threatened status of many of Africa's primate populations, these examples of human to wildlife transmission of parasites are of grave concern to primate conservation managers. As such, and particularly considering the vast amount of research attention awarded to wild primate populations, it is surprising that until recently, relatively little concerted effort has been undertaken to characterize and diagnose parasitic infections in non-human primates. Fortunately, the early years of the 21st century have witnessed renewed interest in questions of zoonotic transmission of diseases, and thus a number of surveys have since reported on the observation of *Schistosoma* in a variety of non-human primates. The methods for identifying these infections and confirming their transmission will be discussed in the next section; here, it suffices to outline past reports of human schistosomiasis in non-human primate species, as well as more current accounts.

It is worth mentioning initially that *Schistosoma intercalatum/guineensis* has never been recently observed as a natural infection in non-human primates. This may be because on the whole, these parasites are distributed in relatively dense tropical forest regions, where primate species tend to be arboreal and are less likely to come into contact with terrestrial infected water sources. Evidence for this hypothesis comes from the observation that several primate species, including some which are distributed in the same countries as *S. intercalatum/guineensis*, are experimentally susceptible to infection (Cheever et al., 1976, Kuntz et al., 1980, Kuntz et al., 1978b). However, these species might not be exposed to the parasite, due to habitat preference or behaviour; for example, the Patas monkey is known to be a good experimental host of *S. intercalatum* (Kuntz et al., 1978a), and is found in parts of Central and West Africa, but tends to inhabit savannah habitats which might not be suitable for *Bulinus forskalii* or *Bulinus africanus* group snails, the intermediate snail hosts of *S. guineensis* and *S. intercalatum,* respectively. Wright et al. (1978) indeed suggested that the forest/non-forest interface might be a barrier to transmission. Given that chimpanzees are also known to be susceptible (Kuntz et al., 1978b), are ground-dwelling, and are distributed in patches throughout the region where *S. intercalatum/guineensis* are found, future parasitological surveys of *Pan troglodytes* and *P. paniscus* (the bonobo) should bear in mind the possibility of encountering *S. intercalatum/guineensis.*

Schistosoma haematobium, in contrast, has been reported as a natural infection of non-human primates, although *S. mansoni* is still the more common human schistosome in this taxon. Based on the collated records presented by Ouma and Fenwick (1991), by the early 1990s both parasites had been observed in vervet monkeys (*Cercopithecus aethiops*, also known as grivet monkeys), Sykes monkeys (*C. mitis*) and baboons (*Papio* spp.). These accounts have spanned Africa; they include surveys from Kenya, Tanzania, Uganda, Zimbabwe, Senegal and Ethiopia. In addition, a chimpanzee imported into the USA from Senegal was diagnosed with *S. haematobium* (De Paoli, 1965), although at the time of Ouma and Fenwick's review (1991) no *S. mansoni* had ever been observed as a natural infection of any ape other than humans. It is no coincidence that all of these localities are known areas with high endemic prevalence of schistosomiasis in human communities, suggesting that a combination of environmental transmission suitability and high levels of infection in humans is putting non-human primates at risk of exposure to schistosomiasis.

As such, it should come as no surprise that human-mediated landscape change and population growth may explain the increasing number of observations of human schistosomiasis in non-human primates in recent years. By far the most common reported non-human primate host has been the baboon, and the dominant parasite in these instances has been *Schistosoma mansoni*, although one observation of a baboon infected with *S. haematobium* was made from South Africa in the 1990s (Appleton and Henzi, 1993). Observations have been equally as widespread in the last two decades as in earlier years, with accounts of infection from Kenya (Hahn et al., 2003, Munene et al., 1998, Muriuki et al., 1998), Tanzania (Muller-Graf et al., 1997, Murray et al., 2000), Ethiopia (Legesse and Erko, 2004, Phillips-Conroy, 1986), Senegal (Howells et al. 2011, Mcgrew et al., 1989) and Nigeria (Weyher et al., 2006); baboons have also recently been implicated as potential reservoir hosts for *S. mansoni* in parts of the Arabian peninsula (Ghandour et al., 1995, Zahed et al., 1996). In several of these cases, as well as other incidences of parasite transmission between humans and non-human primates, it has been suggested that forest fragmentation, increased proximity of humans to wild habitats and the emerging reliance of wild primates on human settlements for food (such as through crop-raiding) is at least partially responsible for increased exposure and risk of these animals contracting 'human' diseases (Gillespie and Chapman, 2008, Weyher et al., 2006). A worrying trend is that national park and forest reserve areas, which might have been expected to afford a degree of protection against zoonotic transmission of infections, also seem to show signs of human to animal transfer of parasites, as has been seen in Mahale Mountains National Park and Gombe Stream National Park, to name but two examples.

Of note is the observation that while baboons in many locations have been shown to be infected with *Schistosoma mansoni*, other sympatric non-human primate species were described as free of the parasite. This is particularly interesting given that in several cases, these sympatric primate species are known to be susceptible to *S. mansoni* infection, and have even been observed naturally infected in the wild. For example, in their survey of three species of wild primate in Kenya, Munene et al. (1998) positively identified *S. mansoni* infections in baboons but not in local vervet or Sykes monkeys, despite earlier accounts of these species being infected, also in East Africa (Nelson, 1960). Similarly, Legesse and Erko (2004) observed schistosomiasis infection in baboons in Ethiopia, but not in sympatric vervet monkeys. Infected baboons have also been reported from two localities, Fongoli in Senegal and Gombe Stream National Park in Tanzania, which are also inhabited by troops of chimpanzees; despite extensive parasitological surveys, these chimpanzees have never

convincingly displayed positive infection with *S. mansoni* (Bakuza and Nkwengulila, 2009, Howells et al., 2011, Muller-Graf et al., 1997, Murray et al., 2000). There is an isolated, unpublished account, from the early 1990s, of *S. mansoni* eggs being recovered from chimpanzee stool in Gombe Stream NP (Nutter, 1993); however, since both earlier and ensuing examinations failed to reconfirm the finding, it may be that this report is a case of mislabeled samples, and the stool had actually belonged to a baboon.

Likewise, there are locations where chimpanzees are known to inhabit areas that have high levels of schistosomiasis transmission to humans, and yet appear not to have been exposed to the disease; one such location is Rubondo Island, where prevalence in humans in island communities nearby is very high, and snails shedding *Schistosoma mansoni* cercariae have been observed in the shallow waters fringing the island itself (Standley et al., 2010). However, despite extensive parasitological surveys, the chimpanzees, vervet monkeys and guerezas (*Colobus guereza*) that inhabit the island have not been reported as infected (Petrášová et al. 2010, Petrzelkova et al., 2006), based on stool examinations; it would be interesting to also include serological tests for exposure, which offer much greater levels of sensitivity.

The relative absence of natural infections of *Schistosoma* species in chimpanzees has long suggested that despite their close phylogenetic relationship to humans, chimpanzees are perhaps not naturally susceptible to the parasite, or do not access infected water sources in ways which would expose them to infection. This assumption has been resolutely refuted through the confirmation of naturally acquired infections of *S. mansoni* in wild-born, semi-captive chimpanzees on Ngamba Island, a sanctuary for rescued and orphaned chimpanzees (Standley et al., 2011). Over the course of four surveys in three years, 11% of chimpanzees tested for *S. mansoni* infection were stool-positive for eggs, which were later hatched and used to infect *Biomphalaria* snails, proving their viability. Chimpanzees were also observed close to the water's edge on a number of occasions, indicating behavioural risk of exposure (Figure 3). Of more concern is recent evidence of significant liver pathology in these chimpanzees, comparable to humans progressing towards chronic infection status; this observation was made by using ultrasound imagery, a technology never before used, to the authors' knowledge, for diagnosis of clinical schistosomiasis in naturally-infected
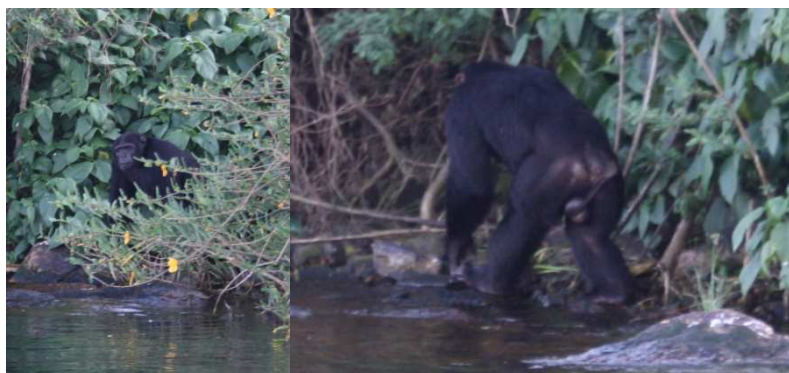

Fig. 3. The above photographs show Kalema, a chimpanzee resident on Ngamba Island. These chimpanzees are regularly observed walking through shallow water; snails shedding *Schistosoma mansoni* cercariae have been collected from near this location, indicating the exposure risk of these chimpanzees to schistosomiasis (photographs taken by C. J. Standley).

non-human primates (C. J. Standley and J. R. Stothard, manuscript in preparation). These new discoveries of infections in semi-wild animals indicate the importance of continued surveys in order to catch new and emerging cases of transmission of parasites between humans and wild animal populations. In addition, there may be cases in which schistosomes themselves change in ways in which enables them to infect a wider variety of hosts; examples of this, along with a further analysis of the methods for diagnosing and evaluating risk of zoonotic transmission of schistosomiasis, will be considered in the following section.

4. Emerging zoonotic risk of schistosomiasis: Causes, diagnosis and analysis

A consideration of past reports of schistosomiasis in animals in Africa would not be complete without an evaluation of potential risks of emerging zoonotic infections, including methods for researchers to determine the origin, transmission direction and causes of infections found both in humans and wildlife. In order to do so, scientists should be encouraged to employ the same up-to-date technology on animal populations as is used in humans, for consistency of results. Finally, research on zoonotic parasitic infections should embrace the use of a multidisciplinary tools in order to analyse their results and thus produce conclusions that can be used to inform other interested parties across different fields, from public health to conservation medicine and encompassing biogeography, molecular epidemiology and mathematical modeling (Daszak et al., 2004, Morens et al., 2004, Stephens et al., 1998, Wilcox and Gubler, 2005).

4.1 Hybridization of schistosomes: Risk of emerging zoonotic schistosomes

While it is beyond the scope of this chapter to review comprehensively the literature on hybridization of schistosomes, it is worth mentioning a few key examples of how interbreeding between human and non-human schistosome species has been reported as infections of novel hosts, and thus how these parasites might constitute risk of an emerging zoonotic disease, either from humans to wildlife or vice versa. Similarly, there are examples where hybridization may also protect against transmission of disease.

The two main instances of hybridization that involve so-called 'human' species of schistosome are those between *Schistosoma haematobium* and *S. bovis* and between *S. mansoni* and *S. rodhaini*. Natural hybrids between *S. haematobium* and *S. bovis* have been documented from children living in the Senegal River Basin (Huyse et al., 2009). In this example, the construction of the Diama Dam led to the creation of suitable habitat for the snail intermediate hosts of *S. mansoni*, *S. haematobium* and *S. bovis*, which spread rapidly through the region (De Clercq et al., 1999). Individuals co-infected with all three genotypes are relatively common; 4 out of 15 children infected with hybrids also excreted *S. mansoni* and *S. haematobium* eggs (Huyse et al., 2009). While to the authors' knowledge, accounts of these hybrids in cattle have yet to be reported from this region, given the presence of cattle schistosome hybrids in humans and the close phylogenetic relationships between these species (see Figure 1), searching for hybrids in bovine species should also be recommending in this setting, as well as other locations where known *S. haematobium/bovis* hybrids occur in humans (Coyne and Orr, 1998).

In contrast to the situation with *Schistosoma haematobium/bovis* hybrids, natural occurrence of hybridization between *S. mansoni* and *S. rodhaini* has thus far only been reported from snail intermediate hosts and rodents, and not mammals (Morgan et al., 2003, Steinauer et al., 2008a). In this case, the concern is that such infections could pass from rodent hosts into

humans; these natural hybrids from the Kisumu region of Kenya have similar cercarial emergence times as *S. mansoni*, thus putting humans more at risk of exposure than if *S. rodhaini*-like emergence behaviour were the dominant phenotype (Steinauer et al., 2008a).

There are also examples of hybridization involving the relatively rare *Schistosoma intercalatum/guineensis* species, both primarily infections of humans. These hybridize successfully with both *S. haematobium* and *S. bovis* in areas where their ranges and intermediate hosts overlap (Southgate et al., 1976, Tchuenté et al., 1997); *S. guineensis*, being transmitted by *Bulinus forskalii* snails, can come into contact with *S. bovis* in the snail host, as can *S. intercalatum* and *S. haematobium* in snails of the *Bulinus africanus* complex. All four may also come into contact in various definitive hosts, depending on susceptibility. It has actually been suggested that the process of hybridization is responsible for the limited distribution range of *S. intercalatum* and *S. guineensis*; given that males of *S. haematobium* and *S. bovis* are more reproductively successful, gene flow in the hybrids tends to be in the direction of the loss of *S. intercalatum/guineensis* genome and dominance of genetic material from *S. haematobium/bovis* (Tchuenté et al., 1997). In the case of hybrids with *S. bovis*, this might actually result in the reduction of exposure risk of schistosomiasis infection caused by human schistosomes, but at the same time it may increase the distribution and extent of animal species of the parasite. In both instances, a danger is that changes to the genome could result in enhanced pathology or virulence, either in humans or animals, which could then exacerbate the public health, veterinary and conservation burden of the hybrid infection.

4.2 Diagnosis, identification and analysis of zoonotic schistosomiasis infections and risk

The observation and identification of forms of schistosomiasis passing between humans and animals is often a non-trivial matter, given the wide variety of definitive host species at risk of infection as well as morphological similarities between different schistosome species across several life stages. This section will briefly outline some suggestions for new methods of diagnosis of infection for use in non-human settings, ways in which direction of transmission can be confirmed and also alternative, cross-disciplinary tools which should be employed by parasitological researchers in order to maximize the analyses which can be achieved from their data.

A crucial obstacle facing researchers in terms of the observation and diagnosis of schistosomiasis in non-human hosts is the difficulty in accessing samples from populations of wild animals. Given that primates and rodents are suspected to be the main animal groups at risk of infection with human schistosomes, and therefore the most likely reservoirs of infection (Nelson et al., 1962, Ouma and Fenwick, 1991), standardized protocols for sampling and data collection of these animal groups should be employed, to ensure consistency of results between surveys. Such protocols have been developed for primate parasitology in the field (Gillespie, 2006); however, for rodents, it might be prudent to follow methods established by field surveys in the literature, for example that of Hanelt et al. (2010) in their rodent surveys in Kisumu, Kenya. Another approach should also be to increase surveying effort of non-primate and non-rodent mammals which are known to be naturally susceptible to schistosomiasis infection, or which have never before been sampling extensively; for example, insectivore species are known from recent surveys to be susceptible and naturally infected with *Schistosoma mansoni* and *S. kisumuensis* (Hanelt et al., 2010). Given their constant exposure to water and abundance through water bodies, such as Lake Victoria, where schistosomiasis is highly endemic, it is also suggested that African otters should be targeted for parasitological surveys, as a high-risk group of mammals.

Once the target definitive host group has been identified, the next question involves the type of sample and the methods used for diagnosing infection. The traditional method is to observe eggs passed either in the stool, for gastro-intestinal species (such as *Schistosoma mansoni*, *S. rodhaini*, *S. intercalatum* and *S. guineensis*) or urine, for *S. haematobium*. In non-threatened species, trapping and dissection for observation of adult worms is also an option; similarly, for domestic livestock that are routinely slaughtered, surveys of abattoirs can be performed. While these methods are cheap, simple and relatively effective, they are not in line with current diagnostic efforts in human populations. For example, the CCA dipstick utilizes a tiny drop of urine, but since only feeding adult worms produce circulating cathodic antigen, is more indicative than eggs in stool of an active infection. This method has been tested on Ngamba Island's semi-captive chimpanzee population (Standley et al., 2011), and was shown to have greater sensitivity than any stool-based diagnostic (apart from PCR), and so may be especially useful in animals that are not efficient egg excretors.

Similarly, blood samples can be used to test for antibodies (IgG/M) against schistosome egg antigen enzyme-linked immunosorbent assay (SEA-ELISA), which is highly sensitive in diagnosis of humans (Stothard et al., 2009). This method has also been tested on Ngamba Island, showing over 90% prevalence in the chimpanzees (Standley et al., 2011); given that antibodies may persist in the bloodstream up to several years after the infection has been cleared, this method may be particularly effective in gauging exposure to *Schistosoma*, especially where host antibodies are sufficiently similar to human IgG/M to allow cross-specific binding, but is not accurate in measuring current infection status. In order to ensure that surveys of animals are comparable and consistent with on-going and parallel human studies, the inclusion of these new, field-reliable and highly sensitive rapid diagnostic tests should be incorporated into future sampling efforts (see Figure 4). It should be noted the SEA-ELISA test does not work on bovids as their IgG does not bind with the protein conjugate; a bovine IgG/M conjugate is needed.
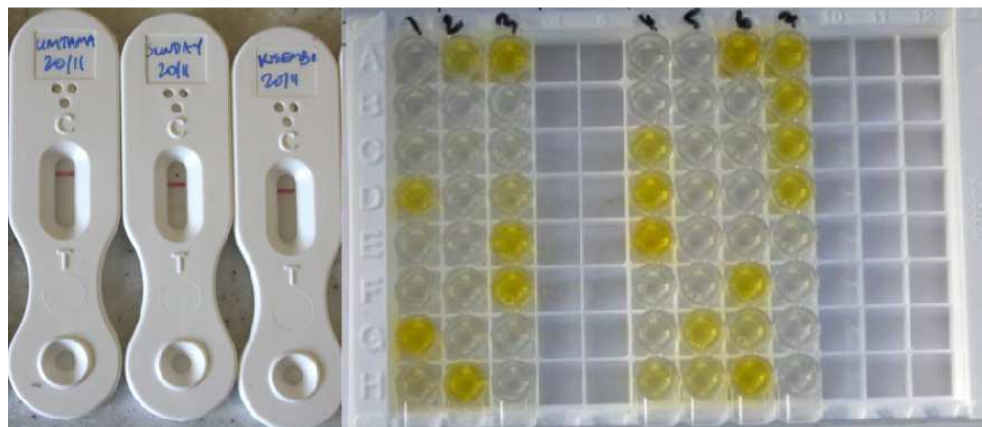

Fig. 4. Examples of the urine CCA lateral flow test (left) and SEA-ELISA serological diagnostic, both as used on chimpanzee urine and blood samples, respectively. In the CCA picture, a second pink line underneath the control band indicates a positive infection, as indicated with the central test. For the SEA-ELISA, a yellow test well indicates a sample positive for antibodies against schistosome egg antigen (photos taken by C. J. Standley).

One disadvantage with these rapid diagnostic tests is that they only diagnose schistosome infection to genus rather than species level. Morphology has traditionally been the first method for species identification; the shape, size, and spine location on schistosome eggs is often sufficient. Adult worms too have interspecies variations in body form and behaviour; cercarial identification is more difficult, but is aided by the type of intermediate snail host used and emergence behaviour. However, there have been observations of intraspecific variations in egg shape, perhaps due to host morphology; moreover, hybrids are difficult to detect through morphology alone. In these cases, the advent of molecular tools has revolutionized researchers' ability to confirm species identification (Webster et al., 2006), hybrids (Webster et al., 2007) and even the direction of transmission, in this setting as well as with other parasitic diseases (Graczyk et al., 2002, Standley et al., 2011). Moreover, monitoring changes in parasite genotype over time and comparing variation between human and animal populations can determine the source and maintenance of the infection (Nejsum et al., 2010). As such, when investigating purported cases of zoonotic transmission, it is recommended that conclusions are supported by these forms of additional evidence.

In addition to molecular tools, there are other methods that should be employed alongside traditional parasitological surveys for analyzing the zoonotic potential of parasitic diseases. For example, there is a growing movement to integrate spatial epidemiological data with human and animal population distribution information using geographical information systems (GIS), in order to evaluate high risk areas for the cross-over of infectious diseases (Eisen and Eisen, 2007). While geospatial models have been applied to schistosomiasis epidemiology in humans (Clements et al., 2010), and to human-animal schistosomiasis transmission in Asia (Ishikawa et al., 2006, Williams et al., 2002), it would be useful to integrate animals into these models within an African setting. These can also be informed by classic models of disease transmission, as developed by Anderson and May (1991), and used to gauge the risk of emergence of infection in particular areas, as well as evaluate the effect of control interventions.

5. Conclusions: Implications for public health initiatives and wildlife conservation management

As this chapter has demonstrated, species of the genus *Schistosoma* are widespread across the globe, causing infections in wildlife as well as in humans. In Africa, the public health burden of schistosomiasis, caused primarily by *S. mansoni*, *S. haematobium* and *S. intercalatum/guineensis*, is enormous (Hotez and Fenwick, 2009); less well recognized is the risk imparted on animal populations by these parasites. Human control interventions have been established across the Africa; usually coordinated at the national level and involving mass drug administration of praziquantel, such programmes have been effective at reducing the prevalence and intensity of schistosomiasis infection in a number of regions (Fenwick et al., 2009). However, it may be that in some settings, control will be confounded without a thorough understanding of the role animal reservoirs play in maintaining transmission; moreover, there are clear examples of how endangered non-human mammals, such as chimpanzees, will profit from a specific consideration of schistosomiasis as part of their conservation strategy. As such, human public health initiatives and wildlife monitoring groups should work synergistically together to produce disease control strategies that are beneficial to all animals, including humans, at risk of contracting diseases such as schistosomisias.

6. References

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In the wake of the invitation by InTech, this book was written by a number of prominent researchers in the field. It is set to present a compendium of all necessary and up-to-date data to all who are interested. Schistosomiasis or blood fluke disease, also known as Bilharziasis, is a parasitic disease caused by helminths from a genus of trematodes entitled Schistosoma. It is a snail-borne trematode infection. The disease is among the Neglected Tropical Diseases, catalogued by the Global Plan to combat Neglected Tropical Diseases, 2008-2015 and is considered by the World Health Organization (WHO) to be the second most socioeconomically devastating parasitic disease, next to malaria. WHO demonstrates that schistosomiasis affects at least 200 million people worldwide, more than 700 million people live in endemic areas, and more than 200.000 deaths are reported annually. It leads to the loss of about 4.5 million disability-adjusted life years (DALYs).

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