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Current Opinion

Schistosomiasis elimination by 2020 or 2030?

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ABSTRACT

Schistosomiasis has been a public health burden in a number of countries across the globe for centuries and probably beyond. The World Health Organization and partners are currently preparing to move towards elimination of this disease. However, given the historical challenges and barriers to ridding areas of this water-borne parasite infection, we question whether the current targets for eliminating schistosomiasis as a global health problem can be achieved.

Three species of schistosomiasis have been a health scourge globally; in China, the Philippines and Japan (*Schistosoma japonicum*), in Egypt, Sudan and in sub-Saharan Africa (*Schistosoma haematobium* and *Schistosoma mansoni*), and in parts of the Caribbean and South America, particularly Brazil (*S. mansoni*) (Gryseels et al., 2006). By 2001, however, the World Health Organization (WHO) was calling for countries to be implementing programmes to control morbidity caused by schistosomiasis, and by 2012, the World Health Assembly (WHA) endorsed the elimination of schistosomiasis as a public health problem (http://www.who.int/neglected_diseases/mediacentre/WHA_65.21_Eng.pdf). This was in part motivated by the fact that Japan had already eliminated schistosomiasis, and that China, Egypt and parts of South America had greatly reduced prevalence by a combination of treatment and improved socio-economic conditions (Rollinson et al., 2013). Additionally however, this was based on findings that show that treatment reduces common serious complications of schistosomiasis such as periportal fibrosis and hepatomegaly in intestinal schistosomiasis (Homeida et al., 1988; Wu et al., 2015) and vesico-urethero-nephropathy in urogenital infection (Rasendramino et al., 1998; Subramanian et al., 1999) in both children and adults (Hatz et al., 1998; Magak et al., 2015). The effect of anti-schistosomal treatment on genital morbidity in men and women is still not yet well understood (Leutscher et al., 2000; Kjetland et al., 2006).

For other neglected tropical diseases (NTDs), lymphatic filariasis (LF), onchocerciasis and trachoma in particular, the year 2020 was seen as a feasible target to reach elimination of transmission (WHO, 2012) (http://www.who.int/neglected_diseases/NTD_RoadMap_2012_Fullversion.pdf). Whereas this might be achievable for those diseases, most scientists involved with promoting control programmes believe that 2020 is an unachievable target for the elimination of schistosomiasis as a public health problem, and indeed for the three soil-transmitted helminth infections (STHs) or intestinal worms, *Ascaris* spp., *Trichuris* spp. and hookworm (*Necator* and *Ancylostoma* spp.), even 2030 might be too ambitious a target (Ross et al., 2015a).

In fact, because schistosomiasis (and STHs) are highly focal in distribution and the power of transmission depends on so many factors, different target dates could and should be set for different countries, districts and ecological zones (French et al., 2015).

Some of the factors that determine the prevalence and intensity of infection in a given ecological setting include, but are not necessarily limited to, the following (in no particular order of importance) (Gryseels et al., 2006): (i) human population density; (ii) human fresh water contact (fishing, agriculture, livestock, domestic activities, leisure); (iii) the presence or absence of piped water (school, health centre, village and household levels); (iv) the presence or absence of sanitation facilities, including quality and cleanliness; (v) the type of habitat for intermediate hosts (snails) and

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distance from human habitation (lakeshore, river, stream, pond, irrigation canal, drain, etc); (vi) snail density and seasonal variation in snail population linked to vegetation and temperature; and (vii) snail control methods which might be effective (vegetation clearance, competitive snails, predators such as ducks, fish, crustaceans, canal lining, molluscicide).

WHO currently recommends preventive chemotherapy (PC) or mass drug administration (MDA) for the control of schistosomiasis, combined with access to safe water, improved sanitation, hygiene education and snail control (WHO, 2015). http://www.who.int/neglected_diseases/NTD_RoadMap_2012_Fullversion.pdf Praziquantel (PZQ) is the drug of choice; not only is it safe and effective, but since 2003, increasing quantities of drugs have been made available free of charge through generous donations by pharmaceutical companies. In 2002, the Schistosomiasis Control Initiative (SCI) was established at Imperial College London, UK (http://www3.imperial.ac.uk/schisto) with the aim of providing treatment with PZQ to infected and at-risk children in sub-Saharan African countries to improve their immediate health and to protect them from the chronic consequences of disease (Fenwick et al., 2009). However, the increase in PZQ demand led to a scarcity of PZQ supply becoming a constraint in controlling schistosomiasis at the global level.

In 1988, PZQ was marketed by Bayer (pharmaceutical) at a price of USD 1.00 per tablet, but by 2003, PZQ was available at a price of approximately USD 0.08 per tablet, which equates to USD 0.20 cents a dose per school-age child treated. However, the market was not stable or predictable because it depended on the regular availability of funding to purchase the drug, and this funding was itself scarce and variable. Other NTDs have benefitted from pharmaceutical company donations, onchocerciasis treated with Mectizan (ivermectin) donated by Merck in the USA since 1986; LF from treatment with Mectizan (Merck) and albendazole from GlaxoSmithKline (GSK) donations since the late 1990s, and trachoma donated by Zithromax (azithromycin) from Pfizer since 1998. The Bill & Melinda Gates Foundation (BMGF) first awarded a grant for NTD control in 2001, and by 2003 BMGF had invested their funds in NTDs and really led the way towards implementation of control programmes. For schistosomiasis, BMGF funds were awarded to SCI, Imperial College London, and used to purchase generic PZQ for six countries in sub-Saharan Africa. Initially, PZQ was not donated by any pharmaceutical company until Merck KGaA stepped up with a relatively small donation of 20 million tablets annually of PZQ through WHO from 2007 to 2010 (Table 1). At about the same time, Johnson and Johnson, followed by GSK, targeted STHs for the first time with donated mebendazole and albendazole, respectively. In 2010, the major breakthrough came for schistosomiasis with several milestone announcements. The first was the expanded commitment by Merck KGaA to incrementally increase their donation from 20 million tablets of PZQ per year to reach 250 million tablets by 2016 and beyond; the second was an increase by the governments of the UK and USA in funds targeting the control of NTDs, in particular for the purchase and delivery of PZQ to infected and at-risk individuals in sub-Saharan Africa. The third event was the World Bank agreement to fund the treatment of schistosomiasis in Yemen. A fourth event was the arrival of a philanthropic organisation willing to support NTD control (Legatum, which led to the launch of the EndFund), and the final event was the launch of the Global Network for NTDs which has become a major global advocacy organisation (Molyneux, 2014). Looking forward, the development of an appropriate formulation of PZQ for treatment of preschool children may further improve treatment coverage of younger populations at risk of schistosomiasis (Trastullo et al., 2015).

In 2012, Bill Gates convened a meeting in London which led to the London declaration against NTDs and WHO taking a massive initiative to encourage every endemic country to develop a national plan for NTD control (UK Coalition against Neglected Tropical Diseases, 2012. London Declaration on Neglected Tropical Diseases) (http://ntd-coalition.org). So from a situation in 2000, where only Egypt, Brazil, China and the Philippines were implementing schistosomiasis control, by 2015, every endemic African country had developed a national plan for control of NTDs including schistosomiasis and many had at least started implementation of their schistosomiasis control programmes. The WHA resolutions, together with funding from the BMGF, USAID and UK all played their part, as has additional funding from the newly created ENDFUND, and the support for deworming by independent charity evaluators (Liese et al., 2014).

Despite this massive support for NTD and schistosomiasis control, the question remains whether all this is enough to allow us to even move toward elimination of schistosomiasis as a public health problem. And if not, what is missing? In our opinion, there are a number of barriers still preventing us from eliminating schistosomiasis as a public health problem in the near future.

Governmental commitment is still insufficient to permit the elimination of schistosomiasis, and while many governments welcome the implementation of NTD control programmes in their countries, domestic financial support is still too limited to implement sustainable control programmes, and schistosomiasis remains a neglected tropical disease. This applies both to single-disease programmes, and to integrated programmes targeting multiple diseases through the same programme structure. Several countries in Africa are suffering from political instability and civil

Table 1
Past, current and future praziquantel (PZQ) commitments for mass treatment of schistosomiasis.

PZQ producer	Past 30 years	Current donations	Next 10 years[a]
Bayer	Sell PZQ at USD 1.00 per tablet	None	Unlikely to donate
Merck	Donated 20 million PZQ tablets per year 2007/2010	20 million PZQ tablets in 2007, rising to 103 million tablets in 2015	Pledged to donate 250 million PZQ tablets per year through 2020
MedPharm	Donated 13 million PZQ tablets in 2004	None	Unlikely to donate
Shin Poong Pharm	Reduced the price of PZQ to USD 0.08 a tablet by 2000	None	Sells PZQ to WHO for Yemen, unlikely to donate
Micro Labs Limited	Started selling PZQ in 2010 at USD 0.08 a tablet	None	Will be a competitive bidder for selling PZQ, unlikely to donate
Cipla Limited	Started selling PZQ in 2002 at USD 0.08 a tablet	None	The first registered PZQ with WHO - the price is likely to rise to about 12 US cents, unlikely to donate

WHO, World Health Organization.
[a] Authors' predictions based on current situation and trends.

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