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EDITORIAL

Schistosomiasis treatment in young children: a welcome step towards deployment of the paediatric praziquantel formulation

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It is an awkward fact that effective public health control of schistosomiasis in Africa has yet to deliver a fully comprehensive intervention for appropriate anthelmintic treatment of those preschool-age children and infants with active infection(s) and/or insidious disease. Over the last decade, despite the steady progress of the Pediatric Praziquantel Consortium in developing a monoenantiomeric oral dispersible tablet, future challenges remain in securing its deployment and implementation at scale. This commentary provides a forward-looking critique for the international community, reminding us of this unfortunate treatment gap, and seeks to encourage commensurate action on ameliorating this overlooked medical inequity.

Keywords: anthelminthic, health systems, medical inequity, paediatrics, preventive chemotherapy.

For those unfamiliar with the control of schistosomiasis, it may come as an unpleasant surprise, even a shock, that today millions of African preschool-age children (PSAC) and infants still receive no appropriate anthelmintic medication.[1,2] Set within a chronic public health blind spot of international and national unfairness (see Figure 1), such infected young children remain burdened with progressive disease.[3] This is soon to change upon the fruition of actions spearheaded by the Pediatric Praziquantel Consortium (PPC) (see https://www.pediatricpraziquantelconsortium.org/),[4] upon the completion of their slow but steady march towards ending this poignant inequity within international child health.[5]

The PPC's roadmap was originally launched in 2012, harnessing an international public–private partnership between TI Pharma, Merck KGaA, Astellas Pharma and the Swiss Tropical and Public Health Institute.[5] Their activity milestones were well conceived and the article by Kurscheid et al.[6] is another careful step forward towards implementation and embedding their paediatric praziquantel formulation (PPF) into the primary healthcare system in Africa. By conducting this valuable and seminal consultation, using an online questionnaire in English and French, the forthcoming public health workforce of drug distributers has now been better engaged, technically consulted and, more importantly, provided a 'bottom-up' perspective to voice putative implementation concerns.[6]

Preventive chemotherapy (PC) remains the foundational tool for public health control of schistosomiasis,[7] achieved by offering donated praziquantel tablets to those infected or at risk from intestinal and/or urogenital schistosomiasis. Anthelmintic tablets are typically administered with food, at a recommended single dosing of 40 mg/kg.[7] Owing to resource-constrained settings where weighing scales are absent, the appropriate number of praziquantel tablets is estimated using a height or dosing pole.[7] This pole's performance has a good linear relationship between patients' height and weight over several childhood years, although it can be confounded by increasing obesity in older children.[8] To streamline programmatic costs, which is often gauged in millions of dollars per country per year, PC typically includes the co-delivery of other medications such as albendazole (ALB) for intestinal worms and/or Zithromax (AZM) for trachoma, a cost-effective justifying rationale for the coordinated delivery of 'integrated' PC for neglected tropical diseases (NTDs). This public health strategy has been endorsed by the World Health Assembly for >2 decades.[9] Since 2022, the World Health Organization (WHO) guideline on control and elimination of schistosomiasis has recommended that younger children, ≥2 y of age, should benefit from PC, using crushed and/or broken tablets, ahead of PPF deployment.[7]

The WHO's realignment of PC towards PSAC and infants provides some umbrella support, but the PPF cannot closely follow it, as new pharmacokinetic considerations and species-specific dosing are required. Unlike the standard donated 600-mg praziquantel tablet, novel features of the PPF include a small circular (not oblong) 150 mg orally dispersible tablet (ODT). These ODTs are moulded without any subdivision scorings and each ODT contains the more palatable monoenantiomer (not racemate) of laevo-(R-)praziquantel. The recommended dosing is

Figure 1. An aquatic shoreline in Malawi, typical of Africa more widely, where schistosomiasis is common and today continues to expose a blind spot of international and national unfairness. While all members of this local community are at daily risk from exposure to schistosome larvae infesting freshly drawn water, infected younger children have insufficient access to praziquantel treatment and, as of yet, no treatment access to the PPF. For younger children unable to swim or wade in water, schistosome exposure typically takes place through passive water contacts, where their (infected) mothers or guardians bathe or wash them with water drawn directly from environmental sources. These at-risk young children have increasing levels of infection through time with progressing disease, until receipt of their first praziquantel treatment.

50 mg/kg for intestinal schistosomiasis (i.e. infection with *Schistosoma mansoni*) and 60 mg/kg for urogenital schistosomiasis (i.e. infection with *Schistosoma haematobium*). Knowing these ODT specifics and upon structured questioning of their drug distribution stakeholders, Kurscheid et al.[6] revealed that future PPF deployment will need both solid training and careful communication among communities, caregivers, healthcare workers and decision-makers to ensure acceptance and future uptake of treatment.

Although they do not specifically mention its implied cost, this will not be a trivial future financial consideration, as the PPF will not be donated gratis. Similarly, paediatric schistosomiasis is not just a health problem confined to endemic areas, e.g. within Europe there are numerous reported infections within migrants and returning travellers.[7] Essentially, Kurscheid et al.[6] very adeptly explored the 'who', 'when' and 'how' of future deployment of the PPF to those young children with proven or at-risk infection(s). Certainly the PPF can mitigate several critical challenges related to the dosing and administration of other paediatric drugs in common use in Africa. A forgivable weakness of their approach, however, was that it was an analysis based on theory and interviews and not upon actual practice or experiential observation, although the latter was bolstered by a literature survey of published experiences in the operational deployment of other paediatric medicines.[6] Clearly their investigative findings and analyses stand, that the use of an ODT is preferrable and superior to that of crushing or splitting tablets (see Table 1 in Kurscheid et al.[6]), however, they did not consider the confusions that could arise within health centres or treatment outposts during actual large-scale programmatic implementation. We must remember that 'vertically focused' disease control programs, even when delivered from more 'horizontal focused' infrastructures, interact

across several health system dimensions, sometimes gaining external and/or internal tensions.[1]

Kurscheid et al.[6] clearly demonstrated that many drug distribution stakeholders were cognisant in the delivery of malaria medicines or nutritional supplements to young children (see Figure 1 in Kurscheid et al.[6]), but they did not explore whether these ODT tablets could be jumbled up with other PC medicines, e.g. the 3-mg Mectizan tablet, if not always held within appropriate packaging. A common problem of PC is that NTD medications are often repackaged in-country then transported to more convenient drug distribution points, thus mixing similarly shaped white tablets within bottles is all too easy. Other mistakes include future muddling of drug-specific height poles, particularly as each form of schistosomiasis (intestinal or urogenital) has different PPF recommendations. Additionally, the generic PC praziquantel tablet pole carries different divisions and, like all paper tablet poles, degrades. Therefore, without sufficient quality control and replenishment, several implementation bottlenecks and errors will likely accrue.

Since there is no medical autonomy of the younger child, praziquantel treatment must be administered with a child's parent or guardian present. Kurscheid et al.[6] side-stepped the debate about which healthcare facilities and/or community treatment platforms are most suitable for their (infected) mothers.[1] It would be singularly odd if an infected mother and her infected child were compelled to receive praziquantel treatment from different age-specific siloed drug delivery platforms. Some of these overlooked or more nuanced on-the-ground specifics were likely captured during key informant discussions, benefiting from expert opinions honed from years of experience with paediatric drugs and large-scale PC programs, but were not formally mentioned in their report.[6] Hopefully these were kept in mind for further PPC deliberations.

Looking ahead towards improving international child health, all of us wish this PPF to succeed and reach those vulnerable children who need it.[10] Kurscheid et al.[6] made an admirable effort to secure a well-grounded consultation from end-user perspectives, carefully documenting advice and opinions of those who had some first-hand experience and sharing their real-life knowledge. At a different and equally important level, however, it falls short of addressing the 'who', 'when' and 'how' of future international PPF deployment, e.g. upon selection of those countries that can afford to use it, perhaps first securing their long-term interest and commitment in paediatric schistosomiasis control.

This raises a different set of questions, engaging a different set of stakeholders, but perhaps all still in good time according to the PPF's roadmap.[5] Following Kurscheid et al.'s investigation,[6] that time is nigh. Indeed, several rather thorny questions need airing now to obtain opinions that could well yield disappointing answers formally. For example, a disease-endemic country, although willing, may simply be unable to mobilise sufficient in-country resourcing. Yet, these broader directed consultations are currently vital, for without them, encouraging international agencies such as UNICEF or Save the Children Fund to bring their collective might to reduce this unfortunate medical inequity will remain elusive.

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