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Schistosomiasis control in Africa: 8 years after World Health Assembly Resolution 54·19

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INTRODUCTION

The authors welcome the publication of a special issue in *Parasitology* pertaining to the control of schistosomiasis in Africa. In this editorial, we summarize the key features of the visionary World Health Assembly Resolution 54·19, passed some 8 years ago. Indeed, this resolution endorsed large-scale distribution of anthelminthic drugs for morbidity control of schistosomiasis and soil-transmitted helminthiasis, which should become the wider, global strategy of preventive chemotherapy in 2006. Looking into the future, the authors propose to further foster effective partnerships bringing to fruition field-level implementation and health policies adaptable to different epidemiological and socio-economic settings of the developing world, and conclude that a scale-up and an upgrade in the fight against schistosomiasis are feasible and mandatory for the international community.

WORLD HEALTH ASSEMBLY RESOLUTION 54·19

In May 2001, the World Health Assembly (WHA) Resolution 54·19 set a milestone for schistosomiasis control and placed this disease firmly back on the international health agenda. Recognizing the experience of large-scale programmes in Brazil, China, Egypt and Morocco in proving that chemotherapy with praziquantel was an effective way to control schistosomiasis-associated morbidity, the WHA urged member states to follow these examples to scale-up control of the disease throughout endemic regions. Resolution 54·19 was the global endorsement of a strategic approach that had been developed and presented in two scholarly articles published in the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, the first one in the early 1990s (Savioli, Bundy and Tomkins, 1992) and the second one a decade later in 2002 in its present strategic format and the necessary supporting scientific evidence (Savioli *et al*. 2002).

WHA Resolution 54·19 advocated for the control of schistosomiasis morbidity in highly endemic areas, and urged countries to attain a target of regular treatment of "*at least 75% and up to 100% of all school-age children at risk of morbidity by 2010*".

Regular administration of single-dose, safe anthelminthic drugs was the first key point of the above strategy: administration of praziquantel at regular intervals – so as to keep the worm burden in individuals low and confined – was identified as the most effective tool to control morbidity rapidly in spite of continued high schistosomiasis transmission. Coverage was the second key point: setting a coverage goal ensured that treatment interventions were not isolated and focal, but full public health interventions which could be implemented at the national level. The third key point was the target population: the resolution recommended a focus on children of school-age, as they represent the group at highest risk of heavy worm burden and, in a context of low availability of resources, the easiest one to reach (through school-based drug distribution interventions), and consequently the group in which the highest impact of treatment both in terms of coverage and likelihood to reverse the pathology would occur.

With this policy firmly set in place, and technical guidance ensured by WHO, progress has been made since 2001; several governments – thanks to backing from a number of international organizations, donor foundations, bilateral institutions and non-governmental organizations (NGOs) – responded to the call for action. The most significant, perhaps, was a major commitment of the Bill and Melinda Gates Foundation to kick-start control activities at the national level. With a grant of US$ 30 million, the Schistosomiasis Control Initiative (SCI) was launched in 2002 that aided the scale-up of schistosomiasis and soil-transmitted helminthiasis control in six selected African countries (Garba *et al*. 2006; Kabatereine *et al*. 2006). As a consequence, the number of schistosomiasis treatments increased in those countries from 530 000 in 2003 to 12·84 million by the end of 2005 (Frost and Reich, 2008). As summarized

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by Fenwick and colleagues in their Schistosomiasis Control Initiative (SCI) review published in this special issue of *Parasitology*, another 8·17–10·72 million treatments have been administered annually from 2006 to 2008 (Fenwick *et al*. 2009). Several additional sub-Saharan African countries have also embarked on large-scale treatment for schistosomiasis with the availability of donated praziquantel. While much still needs to be done, activities against schistosomiasis are a reality in many endemic countries, and several least developed countries, including Burkina Faso and Uganda (Gabrielli *et al*. 2006; Zhang *et al*. 2007; Touré *et al*. 2008), have already attained the 2010 target.

STEPS TOWARDS INTEGRATION OF HELMINTHIASES CONTROL

A possible fourth key point of WHA Resolution 54·19 was the integration of disease control interventions. Recognizing that geographical overlap of schistosomiasis and soil-transmitted helminthiasis is the rule rather than the exception, the resolution addressed the two diseases together. Even though co-administration of praziquantel with either of the two benzimidazole drugs, albendazole and mebendazole, was not overtly recommended in the resolution, the scientific and ethical justification for this was already available and an opportunity for synergy existed (Olds *et al*. 1999). Indeed, Olds and colleagues showed that co-administration was both safe and potentially more cost-effective, as it took advantage of a single drug delivery channel, thereby better streamlining resources. It therefore became the responsibility of WHO to advocate and encourage countries on the need to concurrently control morbidity due to schistosomiasis and soil-transmitted helminthiasis.

Today, in most countries where praziquantel is distributed, albendazole or mebendazole are also included in the intervention package, thus potentially enhancing the impact in terms of improved health status. Albendazole is the most widely used anthelminthic drug, since it is recommended for use in interventions against soil-transmitted helminthiasis (as an alternative to mebendazole), and against lymphatic filariasis (in combination with ivermectin or diethylcarbamazine). When given alone, albendazole or mebendazole can be distributed from one year of age onwards and, in 2007 over 170 million preschool-age children and school-age children were administered with at least one dose of these drugs (WHO, 2009). It is likely that the number of children treated with either albendazole or mebendazole will further increase.

The idea that one drug can combat more than one disease, and conversely, that an intervention can be used to distribute more than a single drug, was one of the key concepts that inspired, in October 2006, the launch of a new global strategy against helminthic diseases (WHO, 2006). The term 'preventive chemotherapy' was coined and the strategy for helminthiasis was reviewed and endorsed by experts during an Informal Consultation held in March 2006, at the WHO headquarters in Geneva. The key message was for a broader, co-ordinated, and more rational use of anthelminthic drugs in control interventions: the new strategy does not supersede or replace the recommendations of WHA Resolution 54·19, rather puts the control of schistosomiasis within a broader picture, promoting integrated control of helminthic diseases in areas of co-endemicity, so as to optimize resources and maximize public health impact (Brady, Hooper and Ottesen, 2006; Hotez *et al*. 2006, 2007; Lammie, Fenwick and Utzinger, 2006).

By advocating for a co-ordinated use of anthelminthic drugs and promoting a further integration among disease control programmes, preventive chemotherapy reiterates the key message of WHA Resolution 54·19 and expands its domain of application to two additional diseases, thus covering all the four major human helminthiases (in addition to schistosomiasis and soil-transmitted helminthiasis, also lymphatic filariasis and onchocerciasis). The decision-making process for treatment (what drugs to use, how frequently) relies on algorithms that take into account the endemicity and co-endemicity of diseases, such that medicines can be given alternatively and safely (WHO, 2006). Drugs against three of the four diseases currently covered by preventive chemotherapy have also been safely co-administered in co-endemic areas of Zanzibar and Nigeria (Eigege *et al*. 2008; Mohammed *et al*. 2008). However, due to the risk of side-effects and the difficulties of administering a large number of tablets to individuals, triple drug administration with ivermectin, albendazole and praziquantel should be accompanied by precaution measures before scale-up is fully rolled out (WHO, 2006).

Preventive chemotherapy is an adaptable tool that could also include one of the elements of the SAFE strategy against blinding trachoma, namely the distribution of azithromycin (note: the SAFE strategy consists of eyelid surgery (S), antibiotics to treat the community pool of infection using azithromycin (A), facial cleanliness (F) and environmental change (E)), as well as the distribution of vaccines, micronutrients and commodities such as insecticide-treated nets, etc. Coordinated implementation of programmes has also been given impetus and momentum by the advocacy for the control of neglected tropical diseases (Hotez *et al*. 2006, 2007), leading to significant pledges of support from the American and British governments, as well as the Bill and Melinda Gates Foundation, working through the Global Network for Neglected Tropical Disease Control (GNNTDC), the pharmaceutical industry, and

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many not-for profit organizations. With more resources for disease control and many potential actors, coordinated implementation becomes imperative.

AN EVOLVING TARGET OF CONTROL

But what is the present evolution – with respect to control of schistosomiasis – from recommendations generated by the WHA resolution set forth in May 2001 (WHO, 2002) to the recommendations of the 'preventive chemotherapy' guidelines published in October 2006? Thresholds of prevalence for implementation of large-scale interventions remain unchanged. What has evolved is a further expansion, where necessary, of the target population, so as to include additional high-risk groups such as older preschool children (over 4 years of age and $\geqslant$94 cm high), and adults considered to be at risk, from special groups (pregnant and lactating women; individuals with occupations involving contact with infested water), to entire communities living in highly-endemic areas (WHO, 2006). Children of school-age (enrolled and non-enrolled) continue to be the major target group, to be reached not only through schools, but through a multiplicity of delivery channels and because of the association between genital schistosomiasis and HIV infection, adolescent girls in areas endemic for urinary schistosomiasis, are also an important group to be targeted for treatment (Kjetland *et al*. 2006, 2008).

The rationale for such an expansion of the target population was the recognition that population groups other than school-age children are also at risk of developing morbidity. Young adults have active inflammatory lesions that should be treated while still reversible, so as to prevent further development of morbidity, and older preschool-age children in high transmission areas may have already built up significant worm burdens that require treatment (Stothard and Gabrielli, 2007). It is also a matter of unperceived burden of disease: even if overt, disease-specific pathology cannot be readily appreciated, many individuals infected with schistosomiasis will suffer from 'subtle morbidity', such as anaemia, chronic pain and exercise intolerance, negatively affecting their productive and social life (King and Dangerfield-Cha, 2008).

An additional reason for expanding the target population is linked to the increased affordability of praziquantel on the international market; the commitment by Merck KGaA to provide free of charge 200 million tablets through the Merck Praziquantel Donation Program (MPDP), in partnership with WHO, is a remarkable example in this regard. However, the current supply of praziquantel is not sufficient to treat all those at risk of morbidity due to schistosomiasis. More needs to be done to ensure the availability of praziquantel either through increased donations or through purchase with the additional resources pledged for the control of neglected tropical diseases.

With respect to delivery channels, it is up to national governments and their implementation partners to identify the best way to make health services available to citizens. School-based distribution, the main channel currently used for delivery of praziquantel, is an excellent option where school enrolment is high, but might not be sufficient where less than 50% of children attend school, and where an expansion of the target population beyond the school-age population is the case. Moreover, in areas where drug administration campaigns against onchocerciasis and lymphatic filariasis are in place through community-based interventions, it may be more rational to add praziquantel to these delivery channels rather than to advocate for an additional system for distributing drugs. Some countries have used various delivery channels in a complementary manner to successfully reach high coverage of at-risk populations.

FORGING SUSTAINABLE CONTROL INTERVENTIONS

Benefits resulting from control and the eventual elimination of schistosomiasis and the other neglected tropical diseases far exceed the costs of implementing public health measures against them, with cost-benefit ratios showing that regular anthelminthic treatment delivered through the health and educations system and other existing or new innovative delivery channels is possibly the 'best buy' available today in public health.

The WHO will continue to advocate for the control of neglected tropical diseases, as well as to collect scientifically sound and up-to-date information that can be translated into feasible and adaptable guidelines for field use. In this rapidly-changing scenario, WHO endeavours to foster partnerships that seek solutions for field-level implementation and translation into policies adaptable to different epidemiological and socio-economic settings.

Recommendations and strategies would remain a pure theoretical exercise without substantial investment. Even if the 75% target set for 2010 by WHA Resolution 54·19 will most likely be missed, we are convinced that the overall balance is not negative, because the purpose of setting a threshold is not only that of reaching such a threshold, but rather that of fostering mobilization of resources and involvement of committed partners around a common objective. This indeed has happened, and the 'spirit' of the resolution has therefore not been betrayed: today, an increasing number of governmental institutions and NGOs, with expanding support from the private sector, are recognizing that neglected tropical diseases, including schistosomiasis, are a serious obstacle to the economic development of endemic

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countries. This inequity of health in sub-Saharan Africa is becoming more widely known and in so doing is fostering a greater international willingness to alleviate these intolerable burdens.

In our view, the future of the fight against schistosomiasis comprises two major steps. On the one hand, a *quantitative* step, that is, a marked expansion of treatment coverage of populations in need through a global access to praziquantel, i.e. more tablets and more financial resources to distribute them, with the aim of reaching the target set by WHA Resolution 54·19 as soon as possible. The involvement of the private sector will be crucial in this regard, and we hope that the example given by Merck KGaA will be instrumental in rallying other 'men of good will' around this cause. The other step is the *qualitative* upgrade of the combat: the successful achievement of control of morbidity and mortality through preventive chemotherapy in many endemic foci opens the way to a more ambitious objective, that of producing a significant impact on transmission rates and therefore achieving elimination of schistosomiasis. In order to do so, we need to build on the experiences of Cambodia, China, Morocco, Tunisia and a number of Caribbean countries and territories that significantly managed to curb transmission rates by upgrading their control arsenal and gearing it up for elimination. In other words, we need the proof-of-principle that transmission of schistosomiasis – especially that due to *Schistosoma haematobium* and *S. intercalatum* – can indeed be interrupted in settings such as São Tomé and Príncipe, Zanzibar or the Sahelian plateaus of West Africa. WHO is ready to face this challenge and is happy to welcome new and old travel companions wishing to embark on this journey. We see control and elimination of schistosomiasis in Africa as the core of the expansion of the fight against neglected tropical diseases worldwide: if the battle is won here, all other continents are doomed to follow.

REFERENCES

Brady, M. A., Hooper, P. J. and Ottesen, E. A. (2006). Projected benefits from integrating NTD programs in sub-Saharan Africa. *Trends in Parasitology* **22**, 285–291.

Eigege, A., Pede, E., Miri, E., Umaru, J., Ogbu Pearce, P., Jinadu, M. Y. and Njepuome, A. N. (2008). Triple drug administration (TDA), with praziquantel, ivermectin and albendazole, for the prevention of three neglected tropical diseases in Nigeria. *Annals of Tropical Medicine and Parasitology* **102**, 177–179.

Fenwick, A., Webster, J. P., Bosque-Oliva, E., Blair, L., Fleming, F. M., Zhang, Y., Garba, A., Stothard, J. R., Gabrielli, A. F., Clements, A. C. A., Kabatereine, N. B., Touré, S., Dembélé, R., Nyandindi, U., Mwansa, J. and Koukounari, A. (2009). The Schistosomiasis Control Initiative (SCI): rationale, development and implementation from 2002–2008. *Parasitology*, **136**, 1719–1730.

Frost, L. J. and Reich, M. R. (2008). Access: how good health technologies get to poor people in poor countries. Harvard Series on Population and International Health. Cambridge, Massachusetts, pp. 249.

Gabrielli, A. F., Touré, S., Sellin, B., Sellin, E., Ky, C., Ouedraogo, H., Yaogho, M., Wilson, M. D., Thompson, H., Sanou, S. and Fenwick, A. (2006). A combined school- and community-based campaign targetting all school-age children of Burkina Faso against schistosomiasis and soil-transmitted helminthiasis: performance, financial costs and implications for sustainability. *Acta Tropica* **99**, 234–242.

Garba, A., Touré, S., Dembelé, R., Bosque-Oliva, E. and Fenwick, A. (2006). Implementation of national schistosomiasis control programmes in West Africa. *Trends in Parasitology* **22**, 322–326.

Hotez, P. J., Molyneux, D. H., Fenwick, A., Kumaresan, J., Ehrlich Sachs, S., Sachs, J. D. and Savioli, L. (2007). Control of neglected tropical diseases. *New England Journal of Medicine* **357**, 1018–1027.

Hotez, P. J., Molyneux, D. H., Fenwick, A., Ottesen, E., Ehrlich Sachs, S. and Sachs, J. D. (2006). Incorporating a rapid-impact package for neglected tropical diseases with programs for HIV/AIDS, tuberculosis, and malaria. *PLoS Medicine* **3**, e102.

Kabatereine, N. B., Fleming, F. M., Nyandindi, U., Mwanza, J. C. and Blair, L. (2006). The control of schistosomiasis and soil-transmitted helminthes in East Africa. *Trends in Parasitology* **22**, 332–339.

King, C. H. and Dangerfield-Cha, M. (2008). The unacknowledged impact of chronic schistosomiasis. *Chronic Illness* **4**, 65–79.

Kjetland, E. F., Ndhlovu, P. D., Gomo, E., Mduluza, T., Midzi, N., Gwanzura, L., Mason, P. R., Sandvik, L., Friis, H. and Gundersen, S. G. (2006). Association between genital schistosomiasis and HIV in rural Zimbabwean women. *AIDS* **20**, 593–600.

Kjetland, E. F., Ndhlovu, P. D., Kurewa, E. N., Midzi, N., Gomo, E., Mduluza, T., Friis, H. and Gundersen, S. G. (2008). Prevention of gynecologic contact bleeding and genital sandy patches by childhood anti-schistosomal treatment. *American Journal of Tropical Medicine and Hygiene* **79**, 79–83.

Lammie, P. J., Fenwick, A. and Utzinger, J. (2006). A blueprint for success: integration of neglected tropical disease control programmes. *Trends in Parasitology* **22**, 313–321.

Mohammed, K. A., Haji, H. J., Gabrielli, A. F., Mubila, L., Biswas, G., Chitsulo, L., Bradley, M. H., Engels, D., Savioli, L. and Molyneux, D. H. (2008). Triple co-administration of ivermectin, albendazole and praziquantel in Zanzibar: a safety study. *PLoS Neglected Tropical Diseases* **2**, e171.

Olds, G. R., King, C., Hewlett, J., Olveda, R., Wu, G., Ouma, J., Peters, P., McGarvey, S., Odhiambo, O., Koech, D., Liu, C. Y., Aligui, G., Gachihi, G., Kombe, Y., Parraga, I., Ramirez, B., Whalen, C., Horton, R. J. and Reeve, P. (1999). Double-blind placebo-controlled study of concurrent administration of albendazole and praziquantel in schoolchildren with

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schistosomiasis and geohelminths. *Journal of Infectious Diseases* **179**, 996–1003.

Savioli, L., Bundy, D. and Tomkins, A. (1992). Intestinal parasitic infections: a soluble public health problem. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **86**, 353–354.

Savioli, L., Stansfield, S., Bundy, D. A. P., Mitchell, A., Bhatia, R., Engels, D., Montresor, A., Neira, M. and Shein A. M. (2002). Schistosomiasis and soil-transmitted helminth infections: forging control efforts. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **96**, 577–579.

Stothard, J. R. and Gabrielli, A. F. (2007). Schistosomiasis in African infants and preschool children: to treat or not to treat? *Trends in Parasitology* **23**, 83–86.

Touré, S., Zhang, Y., Bosqué-Oliva, E., Ky, C., Ouedraogo, A., Koukounari, A., Gabrielli, A. F., Sellin, B., Webster, J. P. and Fenwick, A. (2008). Two-year impact of single praziquantel treatment on infection in the national control programme on schistosomiasis in Burkina Faso. *Bulletin of the World Health Organization* **86**, 780–787.

WHO (2002). Prevention and control of schistosomiasis and soil-transmitted helminthiasis. Report of a WHO Expert Committee. *WHO Technical Report Series* No. 912. Geneva, World Health Organization.

WHO (2006). Preventive chemotherapy in human helminthiasis. Coordinated use of anthelminthic drugs in control interventions: a manual for health professionals and programme managers. Geneva, World Health Organization.

WHO (2009). WHO PCT databank (http://webitpreview.who.int/entity/neglected_diseases/preventive_chemotherapy/sth/en/index.html) [accessed 15 May 2009].

Zhang, Y., Koukounari, A., Kabatereine, N., Fleming, F., Kazibwe, F., Tukahebwa, E., Stothard, J. R., Webster, J. P. and Fenwick, A. (2007). Parasitological impact of 2-year preventive chemotherapy on schistosomiasis and soil-transmitted helminthiasis in Uganda. *BMC Medicine* **5**, 27.

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