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PREVENTION AND CONTROL OF SCHISTOSOMIASIS AND SOIL-TRANSMITTED HELMINTHIASIS

Report of a
WHO Expert Committee

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WHO Expert Committee on the Prevention and Control of Schistosomiasis and Soil-Transmitted Helminthiasis

Geneva, 8–14 October 2001

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1. Introduction

The WHO Expert Committee on the Prevention and Control of Schistosomiasis and Soil-Transmitted Helminthiasis met in Geneva from 8 to 14 October 2001. The meeting was opened on behalf of the Director-General by Dr M. Neira, Director, Communicable Diseases Control, Prevention and Eradication.

Dr Neira recalled that the WHO Expert Committee on the Control of Schistosomiasis had last met in 1991, and that a WHO Expert Committee on Prevention and Control of Intestinal Parasitic Infections had met in 1986. Since those earlier meetings, many milestones have been reached in both fields, and WHO – together with Member States and other partners – has methodically addressed and clarified the technical issues related to control of helminth infections.

It has now been accepted that infections caused by soil-transmitted nematodes are a major public health concern in many parts of the world, particularly among the poorest of the poor in all developing countries. It has also become clear, however, that cost-effective solutions to the problem are available.

The endemicity of schistosomiasis presents a dual picture. Many control programmes have been, and continue to be, successful in reducing mortality, morbidity, and transmission, to the extent that it is now possible to contemplate elimination of the disease. However, schistosomiasis remains a major cause of mortality and morbidity in a number of countries, notably those of sub-Saharan Africa.

WHO's Member States have proposed a combined approach to morbidity control in both schistosomiasis and soil-transmitted helminthiasis, since the tools and the target groups are similar. The price of praziquantel and other anthelminthics has now decreased to a level at which it should no longer deter Member States from making these drugs available to people in endemic areas. Regular treatment is affordable and can be delivered in a sustainable manner through existing channels. This strategy, designed to reach those at highest risk of morbidity due to schistosomiasis and soil-transmitted helminthiasis, was endorsed by the World Health Assembly in resolution WHA54.19 (see Annex 1) in May 2001. The Expert Committee's task was thus to provide clear and strategic guidance on how implementation should proceed.

A glossary of the key terms and abbreviations used in this report is provided in Annex 2.

2. Estimates of the disease burden due to soil-transmitted helminthiasis and schistosomiasis

The burden of disease resulting from infection with soil-transmitted helminths (*Ascaris lumbricoides*, *Trichuris trichiura*, and the hookworms *Necator americanus* and *Ancylostoma duodenale*) has been calculated by classifying the spectrum of possible consequences of infection into defined disease states. The classification is based on two worm-burden thresholds – a lower threshold above which there are detrimental effects on physical fitness and school performance, which may be temporary or permanent, and a higher threshold above which there is a risk of clinically overt illness. Mathematical modelling makes it possible to calculate the total DALYs (disability-adjusted life years) lost to soil-transmitted helminthiasis: available epidemiological estimates are extrapolated to the national, regional, or global level (*1*).

Table 1 provides a comparison of global figures for DALYs lost as a result of soil-transmitted helminth and schistosome infections and other selected infections. The estimated global figures for infections, mortality,

Table 1
Global DALYs lost to soil-transmitted helminth and schistosome infections and selected other infections

Infection	DALYs lost[a] (millions)
Total intestinal helminthiasis	39.0[b]
Hookworm disease	22.1[b]
Ascariasis	10.5[b]
Trichuriasis	6.4[b]
Schistosomiasis	4.5
Measles	34.1
Malaria	35.7
Tuberculosis	46.5

[a] 1990 estimates.
[b] Source: reference *1*.

Table 2
Estimated global number of soil-transmitted helminth infections, and related morbidity and mortality

Helminth	No. of infections (millions)	Morbidity (cases, millions)	Mortality (deaths per year, thousands)
Ascaris lumbricoides	1450	350	60
Hookworms	1300	150	65
Trichuris trichiura	1050	220	10

and morbidity due to soil-transmitted helminth infections are summarized in Table 2.

For schistosomiasis, the disease burden was originally calculated by estimating the prevalence of infection and associating a low disability weight (0.005–0.006) with infection. The calculation took into account no clinical sequelae and only directly attributable mortality (then assumed to be 7000 per year (2)). It is widely believed that the calculated figure for DALYs lost to schistosomiasis represents a significant underestimate and should be revised. Estimating disease burdens is particularly complicated where control programmes are in progress, but it is clear that schistosomiasis remains a serious public health issue in the countries of sub-Saharan Africa and in Brazil and Egypt.

In 1993, the World Bank (3) reported that, within the global burden of disease "league", soil-transmitted helminth infections ranked first among children aged 5–14 years; 16.7 million DALYs were lost, which represents 11.3% of the total burden in this age group. In the same report it was also noted that controlling these diseases is both efficient and cost-effective. Using mathematical modelling, it has been estimated that 70% of the total burden of disease due to soil-transmitted helminth infections can be prevented in high-prevalence communities by treating only school-age children (1).

In 1998, WHO estimated that schistosomiasis and soil-transmitted helminthiasis were responsible for more than 40% of the disease burden due to tropical diseases (excluding malaria) (2). A fresh assessment of the global burden of disease is now being carried out. A new list of 14 sub-regions has been defined in relation to adult and child mortality, including that due to HIV/AIDS. Once completed, it will allow a comparison, in each country group, of disease burden and consequent public health priorities, against a similar disease background.

This new assessment will focus on estimating the burden related to clinical complications and indirect mortality due to schistosomiasis, particularly in sub-Saharan Africa. Modern techniques, such as mathematical modelling and geographical information systems (4), are being used to obtain more precise epidemiological estimates, and this is also generating additional information on hookworm and hookworm-related anaemia. The estimates of the burden of disease due to hookworm may have to be updated accordingly.

3. New knowledge, developments, and tools

3.1 Clinical morbidity and recalculation of the burden of disease due to schistosomiasis

To achieve a better and more disease-oriented estimate of the burden of disease due to *Schistosoma mansoni* and *S. haematobium*, a study has been carried out to quantify clinical morbidity and its relationship to prevalence and intensity of infection (5). However, this estimate of disease burden does not yet include subtle morbidity, such as nutritional impairment and reduced working productivity. In its first stage, the study has been confined to sub-Saharan Africa (including Somalia and Sudan) where much of the disease burden is currently concentrated and for which recent epidemiological estimates are available.

A mathematical expression representing the prevalence of morbidity as a function of the prevalence of infection in a community was developed by collecting both published and unpublished information on schistosomiasis infection and morbidity. Since this information included different ways of expressing the same kind of morbidity, a selection had to be made of the most reliable or characteristic conditions for which sufficient information was available. To ensure the comparability of data from different sources and to reduce bias, it was also necessary to process prevalences of infection in two ways:

— standardization to a default sensitivity of parasitological diagnosis (e.g. a single, 41.7-mg, Kato–Katz stool examination for *S. mansoni*) by means of a stochastic model of egg-count variation;
— adjustment of the relationship between prevalence of infection and disease for differences in the infection levels of communities within the countries concerned.

Estimates of the number of individuals with specific morbidity due to infection with *S. haematobium* and *S. mansoni* are given in Table 3. Although further studies are necessary to validate mortality estimates, which have fluctuated widely over recent years, it can be inferred from these estimates that the annual number of deaths resulting from schistosomiasis in sub-Saharan Africa may be as high as 200 000. There is no doubt that people die from schistosomiasis. Historical data from Brazil, for example, in areas where there was no anthelminthic intervention, revealed that 1% of infected people died from schistosomiasis. Nevertheless, it must be remembered that the major impact of all forms of schistosomiasis worldwide continues to be chronic morbidity.

Even these evaluations fail to consider the impact of subtle morbidity induced by schistosomiasis. Among the principal reasons for the high estimates of DALYs lost to soil-transmitted helminthiasis are the links

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between hookworm and anaemia, ascariasis and stunting of growth, and trichuriasis and impaired school performance. With the recent demonstration of a causal relationship between schistosomiasis and anaemia, stunting, and cognitive impairment, it becomes clear that these morbid sequelae of the infection should be included in the DALY calculation.

Table 3
Current estimated total number of individuals with morbidity and mortality due to *Schistosoma haematobium* and *S. mansoni* infection in sub-Saharan Africa[a]

Schistosome species	Estimated morbidity and mortality (millions)[b]
S. haematobium	
At risk of infection	436
Infected	112
Haematuria during previous 2 weeks	71 (52–89)
Dysuria during previous 2 weeks	32 (17–55)
Minor bladder morbidity (detected by ultrasound)	76 (67–92)
Major bladder morbidity (detected by ultrasound)	24 (15–31)
Moderate hydronephrosis	9.6
Major hydronephrosis	9.6
Non-functioning kidney	[1.7]
Non-functioning kidney (deaths/year)	[0.15]
Bladder cancer (deaths/year)	
Males	[0.011]
Females	[0.0023]
S. mansoni	
At risk of infection	393
Infected	54
Diarrhoea during previous 2 weeks	0.78 (0.0–7.8)
Blood in stool during previous 2 weeks	4.4 (3.0–8.3)
Hepatomegaly (mid-sternal line)	8.5
Splenomegaly	[6.3]
Ascites	[0.29]
Haematemesis (ever)	[0.93]
Haematemesis (deaths/year)	[0.13]

[a] Source: reference 5 and M.J. van der Werf & S.J de Vlas (personal communication).
[b] 90% confidence interval in parentheses.
  Figures in square brackets should be interpreted with caution.

3.2 Age-related impact of treatment of schistosomiasis-related pathology, and prevention of late-stage sequelae

The severity and complexity of the pathology of schistosomiasis are related to the fate of the eggs that become trapped in the tissues. It has been shown repeatedly that treatment with the anthelminthic drugs recommended by WHO reverses the morbidity resulting from

schistosomiasis. Quantitative improvements in periportal fibrosis, hepatomegaly, and splenomegaly have been observed, as well as improvements in physical fitness, appetite, and school performance. Deterioration in iron status is arrested by anthelminthic treatment; iron supplementation improves iron status.

More information on the timing of pathological improvements has become available in recent years. Reversal of organ damage follows 6 months after cure of urinary schistosomiasis, and resurgence occurs after another 6 months or more. Retreatment in less that one year is generally unnecessary. Intestinal schistosomiasis appears to regress promptly after treatment. The sooner treatment is given, the higher are the chances of reversing the organ damage. Regression of periportal fibrosis and subsequent resurgence (as detected by ultrasonography) occur between 7 months and several years after cure. Regular retreatment will ensure that hepatic morbidity is reduced in the community until the transmission rate of the infection declines.

School-age children (including those who are not enrolled at school), adolescents, women of childbearing age, and any other high-risk groups should be the major targets for systematic regular treatment. Repeated treatment during childhood reduces the risk of urinary morbidity developing in adulthood, and may have a long-term effect on reinfection intensities and the development of severe morbidities even in areas where control has been interrupted for many years.

3.3 Consequences of soil-transmitted helminthiasis and impact of treatment on the health and development of children and women

Intensity of infection with *Ascaris lumbricoides* and *Trichuris trichiura* generally reaches its peak in school-age children. Hookworm infections may also reach a considerable intensity in children but commonly remain high throughout adulthood. Children with high-intensity *A. lumbricoides* infection are at high risk of intestinal obstruction (6), while adults may experience a range of acute complications when adult *A. lumbricoides* migrate from the lumen of the small intestine (7). There may be as many as 135 000 deaths a year that are directly due to soil-transmitted helminth infections (8), but the principal public health significance of these infections lies in their chronic effects on health and nutrition.

3.3.1 *Ascariasis*

It has only recently been observed that, following deworming of children with *A. lumbricoides* infection, food intake improves. In India, Indonesia, Kenya, Myanmar, and the United Republic of Tanzania, it has also been repeatedly shown that nutritional status improves (weight

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and height gain, increased skinfold thickness) following deworming treatment. Treatment probably has an impact on the impaired fat digestion, reduced vitamin absorption, and temporary lactose intolerance that are known consequences of ascariasis.

3.3.2 *Hookworm disease*

Hookworms cause blood loss. Thus, hookworm disease is associated with poor iron status and iron-deficiency anaemia and has adverse consequences for childhood growth, school performance, pregnancy, and worker productivity (*9*).

The effect of a hookworm infection on the individual depends on iron intake and body iron stores as well as on the intensity and duration of the infection. A threshold effect is sometimes seen in the development of anaemia, although the threshold worm load in affected communities or population subgroups will differ according to iron intake levels and body iron stores. Where iron status is very poor and body iron stores therefore too low to buffer the losses caused by hookworms, a fall in haemoglobin levels may be apparent even at the lowest intensities of hookworm infection. Several controlled trials have demonstrated a positive impact of deworming treatment on the iron status of schoolchildren

Iron deficiency is particularly prevalent among preschool children, and it has been suggested that hookworm infection contributes to the problem. There is thus an urgent need for investigation of the effect of deworming on the iron status of this age group in communities where hookworm infection is endemic.

Hookworm infection is also recognized as a major threat both to the health of women of reproductive age and to the course and outcome of pregnancy, especially in developing countries. Poor iron status, and consequent iron-deficiency anaemia, affects most people in developing countries and is the world's most common nutritional deficiency. Iron-deficiency anaemia is most frequent and most severe in adolescent girls and women of childbearing age. More than half the pregnant women in developing countries are believed to suffer iron-deficiency anaemia, which contributes to maternal morbidity and mortality, increases the risk of fetal morbidity and mortality, and is associated with low birth weight.

Studies in pregnant women with hookworm infection have shown that deworming treatment is beneficial for the course of pregnancy. Anthelminthic drugs recommended by WHO (albendazole, levamisole, mebendazole, and pyrantel) should be used, although as a general rule no drugs should be given during the first trimester. Anthelminthics alone halt the iron loss, or reduce the rate of loss, and the addition of iron–

folate supplements improves iron status; the effects of combining deworming treatment and iron–folate supplements are additive.

In conclusion, where hookworm infections are prevalent, deworming can improve the iron status of populations with poor iron intake, particularly by reducing the occurrence of moderate to severe anaemia. Although deworming alone is not an adequate strategy for anaemia control, it should be included in programmes designed to improve iron status and reduce anaemia.

3.3.3 *Trichuriasis*

Trichuriasis is a threat to the healthy growth and development of the millions of preschool children in countries where the infection is endemic. The consequences of high-intensity infection include *T. trichiura* dysentery syndrome, chronic dysentery, reduced iron status and iron-deficiency anaemia, and poor growth rate (*10*).

Although blood loss can be a feature of *T. trichiura* infection, it is less prominent than in hookworm infection. However, it may occasionally take the form of gross haemorrhage (associated with dysentery or rectal prolapse), which can lead to severe and even life-threatening anaemia. Trichuriasis often occurs concurrently with hookworm infections and so may well accelerate the onset of iron-deficiency anaemia.

3.4 School performance

Schistosomiasis and soil-transmitted helminthiasis have an adverse effect on cognitive development. Although assessing the impact of interventions on this effect is methodologically complex, there is no doubt that poor iron status and iron-deficiency anaemia are closely linked to diminished educational performance. Since hookworm disease, trichuriasis, and schistosomiasis all cause blood loss and lead to iron deficiency and anaemia, it is reasonable to conclude that the educational performance of infected schoolchildren will be impaired unless a programme of regular deworming is introduced to keep infection intensities low.

A clear illustration of the detrimental effects of helminth infection on educational performance was provided in Jamaican schoolchildren aged 9–12 years. Treatment of *T. trichiura* infection was followed by significant improvements in the results of tests of auditory short-term memory and of scanning and retrieval of long-term memory. Nine weeks after treatment, previously infected children performed as well as uninfected (and therefore untreated) children. Absenteeism was more frequent among infected than uninfected children: the heavier the intensity of infection, the greater the absenteeism, to the extent that

some infected children attended school for only half as much time as their uninfected peers.

3.5 Treatment of pregnant and lactating women and of children under 24 months for soil-transmitted helminthiasis and schistosomiasis

Infections with hookworms (*Ancylostoma duodenale* and *Necator americanus*), whipworm (*T. trichiura*), and schistosomes involve blood loss and are determinants of poor iron status, leading to iron-deficiency anaemia. Hookworm-induced anaemia is now recognized as a serious threat to the health of pregnant women and unborn children, but concerns about the safety of anthelminthic drugs for both have limited efforts to control hookworm infection as a cause of iron-deficiency anaemia in women.

The Informal Consultation on Hookworm Infection and Anaemia in Girls and Women, held in Geneva in 1994, concluded that the use of WHO-recommended drugs was appropriate in view of the serious effect of hookworm infection on iron status and the consequent likelihood of iron-deficiency anaemia (*11*). During puberty and in the reproductive years, girls and women will be much healthier if their iron status is good. On the basis of the available information, the Consultation concluded that the use of good-quality benzimidazole drugs (albendazole and mebendazole) in women of childbearing age should be regarded as safe. Their pharmacological characteristics are such that these drugs, used in the recommended dosages, should not represent a risk to pregnant and lactating women or to breastfed babies. Under experimental conditions, neither levamisole nor pyrantel appears to have teratogenic or genotoxic effects; these drugs may therefore be safer to use in women and infants.

A comparative study of more than 7000 women, most of whom had taken mebendazole, provided reassurance that the use of anthelminthic drugs during pregnancy does not represent a risk to the fetus (*12*). Birth defect rates among the children of treated women were not statistically different from those among the children of untreated women.

3.5.1 *Use of praziquantel during pregnancy and lactation*

Recognizing that pregnant and lactating women with schistosomiasis are currently left untreated for up to a year and that the disease has serious effects both on their health and on pregnancy outcomes, the Committee expressed its concern that urgent attention be given to treating such women with praziquantel. The results of a risk–benefit analysis indicate that treatment should be recommended (*13*).

The common practice of not treating lactating women for schistosomiasis can result in their remaining untreated for years: in some

countries, women are either pregnant or lactating for a substantial proportion of their reproductive years. Current practice in China, Egypt, and the Philippines is to treat women and have them stop breastfeeding for 24 hours. However, it is unlikely that the small amount of praziquantel present in breast milk would be toxic for infants.

On the basis of published results of animal studies and considerable experience of the clinical use of praziquantel in humans, the Committee proposed that WHO hold an Informal Consultation, as soon as possible, to assess all aspects of the use of praziquantel during pregnancy and lactation. The agenda of the Consultation should include a literature review, a prospective analysis, toxicology, pharmacovigilance, and use of the drug – including generic versions – under public health conditions. The Committee would support, in principle, the recommendations of the Informal Consultation.

3.5.2 *Use of benzimidazoles in children under 24 months*

There is growing evidence of the detrimental effects of soil-transmitted helminthiasis on the growth and development of children under 24 months of age. What little published information there is about the use of anthelminthic drugs in children of this age offers no clear reason to exclude them from treatment. In view of the need to strengthen health care for this age group, the Committee urged WHO to convene an Informal Consultation to examine the various aspects and consequences of using benzimidazoles to treat children under 24 months for soil-transmitted helminthiasis.

3.6 Price and quality of, and access to, anthelminthic drugs

Four drugs for the treatment of intestinal nematode infections – albendazole, levamisole, mebendazole, and pyrantel – and two for the treatment of schistosome infections – praziquantel and oxamniquine – are included in WHO's Model List of Essential Drugs (*14*). Ivermectin, listed as an antifilarial drug, has recently been registered in Australia, France, and USA for the treatment of strongyloidiasis; it has also been shown to be effective against ascariasis and, to a lesser extent, trichuriasis. The choice of the most cost-effective drugs for use in helminth control is guided principally by considerations of quality, efficacy, safety, and cost.

For many years, the high cost of good-quality anthelminthic drugs meant that efforts to control morbidity had to rely on substantial support from donors, even in small-scale and time-limited programmes. Financial sustainability was rarely an option, and drug availability depended almost entirely on the extent and duration of external donor

support. At the end of a programme, the many individuals whose health had been substantially improved would inevitably become reinfected and the original levels of morbidity would be re-established.

With the expiry of patents, generic versions of anthelminthic drugs are now available at low cost. For example, good-quality generic albendazole (400-mg single-dose tablets) and mebendazole (500-mg single-dose tablets) can now be obtained at a cost of less than US$ 0.02 per tablet. Praziquantel (600-mg tablets) is currently available from manufacturers of the generic preparation for as little as US$ 0.065 per tablet; on average, treatment of school-age children in Africa requires 2½ tablets.

Drug quality is critical, especially in developing countries where anthelminthics may be imported or produced locally as generic drugs. Tablets may vary not only in their content of active ingredient but also in properties such as purity, disintegration, dissolution, and bioavailability, which affect therapeutic efficacy. Substandard preparations are best avoided by procuring drugs only from certified suppliers. In countries where a widely developed private sector is used for drug distribution, quality should be ensured by establishing an appropriate control system. Most countries have a drug regulatory authority that monitors quality; where there is no such authority, or the authority cannot guarantee quality, standard checks should be performed for evaluation of all aspects of drug quality.

Praziquantel has been the subject of some recent reports on drug quality control (15, 16). Thirty-four praziquantel samples from different manufacturers were collected at the user level in various countries and subjected to quantitative analysis of active ingredient, purity, disintegration, and dissolution in accordance with established pharmacopoeial standards. Most results were reassuring, with both generic and proprietary products meeting the standards. Two samples, however, both from the same manufacturer, were found to contain no praziquantel (17): certain anomalous features of the packaging of these samples might provide warning of their spurious nature.

On the basis of these results, the use of generic preparations can generally be encouraged, but strict vigilance must be exercised to prevent the purchase of drugs of suspicious appearance. If drugs are obtained other than through the regular national drug purchasing and distribution system, health managers should check their quality rigorously to avoid counterfeit preparations. This is best done through an independent analysis (18). The WHO certification scheme Good Manufacturing Practice provides a mechanism for qualitative and quantitative analysis, assessing the quality of pharmaceutical products moving in international

commerce. Recently, a number of kits have become available that permit rapid screening for drug quality, even under field conditions.

The low cost of currently available generic anthelminthics of good quality does not implicitly ensure good access to these drugs in affected communities. The WHO medicines strategy has defined four key elements for good access to drugs – affordable prices, reliable supply systems, sustainable financing, and rational selection and use of drugs. However, further development of these elements is essential if all those in need are to have adequate access to regular anthelminthic treatment: in many developing countries, drug supply systems are still inadequate to meet essential demands at the peripheral level.

With the reduction in drug prices, the cost–benefit ratio of helminth control has significantly improved. However, donor support may still be needed for control programmes, especially school-based or community-based interventions in the poorest areas of developing countries. In the quest for good access to drugs, it is important not to underestimate the importance of rational selection and use. For example, better symptom-based diagnosis of schistosomiasis at most peripheral health care levels can substantially improve access to treatment for those most in need: treatment compliance is increased and the cost of treating each patient is 5–7 times lower (19). Similarly, the targeted treatment of school-age children for schistosomiasis and soil-transmitted helminthiasis in areas above a certain level of endemicity is probably the most rational approach to offering optimal access to treatment.

3.7 Efficacy and effectiveness of, and resistance to, anthelminthic drugs

3.7.1 Efficacy and effectiveness

Comprehensive evaluation of the impact of anthelminthic drugs in community-based treatment campaigns is a complex process. It is important to draw the subtle distinction between the terms *efficacy* and *effectiveness* as applied to anthelminthics. Efficacy refers to the effect of a drug against an infectious agent, in isolation and under ideal conditions; effectiveness is the effect of the drug against an infective agent under operational conditions. Thus, effectiveness may be influenced by variables such as patient compliance with treatment, and by ecological, immunological, or epidemiological factors such as confounding by ongoing disease transmission. For the public health planner, the key measure of the effectiveness of large-scale deworming is the general improvement in the health status of the at-risk population in relation to other important considerations, such as the cost of drug delivery, accessibility and acceptability of treatment, and sustainability.

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Most studies have evaluated the impact of treatment on direct or indirect measures of helminth infections, such as prevalence and intensity of infection, number of adult worms expelled, or number of eggs passed in urine or faeces. These parasitological indicators are relatively easy to measure, using standardized methods. However, results depend on the parasitological techniques used and on the time after treatment at which prevalence and intensity of infection are assessed. They do not always reflect changes in morbidity (which may occur much later), and they may vary with the study population, the intensity of infection, levels of ongoing transmission, and various environmental factors. At present, diagnosis is more expensive than treatment.

Increasingly, effectiveness is being evaluated in terms of improvements in aspects of morbidity, including iron-deficiency anaemia, impaired growth, malnutrition, lowered school performance, and impaired social development. These insidious effects of helminth infection can be reversed by periodic treatment – with obvious benefits for health. Benefits assessed in terms of such indicators are appealing, because they can stimulate political commitment in endemic countries and are likely to mobilize resources and funds from donor agencies. However, the assessment is relatively difficult, partly because of the lack of standardized methodology.

Efficacy and effectiveness are measured using qualitative and quantitative tests for eggs or larvae in excreta at an optimal time – which depends on the helminth species – after treatment. Cure rates and egg reduction rates are used to measure the reduction in prevalence and intensity of infection but may vary widely, even in efficacy trials in which the same drug is given at the same dosage under optimal conditions.

The need for more standardized guidelines to ensure the direct comparability of study results was stressed in the report of a WHO Informal Consultation held in 1998 (20). Factors that may account for an observed "poor" efficacy of an anthelminthic drug include the following:

— the drug–patient interaction (poor drug quality, reduced absorption and bioavailability, poor patient compliance);
— the host–parasite relationship (heavy intensity of infection before treatment, variability of egg laying and excretion, intense transmission resulting in a preponderance of immature worms that are less susceptible to the drug);
— the diagnostic method (timing of parasitological examination after treatment, lack of standardized techniques);
— genetic variations between parasite strains, leading to poor drug susceptibility (tolerance) or selection of resistant strains.

3.7.2 *Resistance*

Drug resistance is defined as a genetically transmitted loss of susceptibility to a drug in a parasite population that was previously sensitive to the appropriate therapeutic dose (*18*). Anthelminthic drug resistance among the nematodes of livestock, such as sheep and goats, is now a widespread problem with economic implications in many countries (*21*). The World Association for the Advancement of Veterinary Parasitology has recommended standardized methods for the detection of anthelminthic resistance in nematodes that are of veterinary importance. These simple and effective tests can be used in parasitological laboratories and may prove useful for surveillance in human treatment programmes.

Growing understanding of the mode of action of anthelminthic drugs against nematodes has encouraged the development of molecular biological techniques for the detection of resistance. Sensitive and specific probes for the detection of levamisole, morantel, and ivermectin resistance have yet to be developed, but studies of the mechanism of benzimidazole resistance have recently led to the design of DNA probes that specifically identify benzimidazole susceptibility/resistance in individual worms, larvae, or eggs. There are no such probes for praziquantel. Relatively inexpensive laboratory methods exist for investigating the presence of drug resistance in nematodes and yield information quite quickly. However, extrapolation of results to the field situation may be problematic, since schistosome and nematode populations studied in the laboratory have a small gene pool, often representing only a small fraction of the genetic repertoire of the field population. Field studies, on the other hand, focus on a given type of host/helminth combination under certain specific environmental conditions, and this is their shortcoming. Selection for drug resistance depends on the genetic variation in the worm population and on the selection pressure applied to it.

With regard to resistance to broad-spectrum anthelminthics for use in humans, there have been two reports of failure in the treatment of human hookworm infection, involving mebendazole in Mali and pyrantel in north-west Australia. In both studies, the anthelminthics were observed to be of low efficacy, but this may have been related to factors other than resistance; the suggestion of emerging drug resistance should therefore be treated with caution (*21*).

Praziquantel is the drug of choice for the treatment of schistosomiasis caused by any of the schistosome species that infect humans. Oxamniquine is equally safe and effective for the treatment of *S. mansoni* infections, but its higher price makes it a less attractive

option today. The diminished demand for oxamniquine raised the concern that production might be halted, but reassurances from the producer now indicate that the drug is likely to remain available. For *S. haematobium* infections, the only alternative to praziquantel is metrifonate, currently available as a generic preparation. No viable alternative drug exists for the control of *S. japonicum*. Artemisinin derivatives are effective against all schistosome species but only in the early stages of infection; these drugs are therefore generally indicated only in specific circumstances, i.e. known recent exposures. In addition, artemisinin derivatives are commonly used as antimalarials, and their widespread use might favour the development of drug-resistant plasmodia. However, praziquantel and artemether act synergistically, targeting two different stages of the schistosome, so that combination therapy could be useful in certain circumstances in areas endemic for schistosomiasis but not for malaria.

In 1994 and subsequently, very low cure rates were reported for praziquantel in an intense focus of *S. mansoni* in Senegal. Epidemiological data collected at this site suggested that these low rates were probably a consequence of the extremely high intensity of infection (so that even killing 90–95% of the worms would not produce complete parasitological cure) and of the intense transmission, which would result in the presence of recently acquired (immature) parasites in a number of treated patients. Since praziquantel is known to be effective only against mature schistosomes, some parasites would survive and mature to the egg-producing stage. A protocol was suggested for screening for suspected instances of praziquantel resistance; this consisted of administering two doses of the drug, 2–3 weeks apart, so that the second dose would eliminate any schistosomes that had matured in the interval (*22*). Use of this protocol in Senegal achieved the expected high cure rates. However, although most of the evidence suggests that praziquantel-resistant schistosomes were not involved in the Senegalese focus of infection, the possibility cannot be entirely ruled out.

An intensive investigation of possible praziquantel resistance has been carried out in the Nile delta region (*23*). Patients who were still passing *S. mansoni* eggs after drug treatment were given a second dose and, if necessary, a third. If eggs were still excreted, an isolate was established in the laboratory and the drug susceptibility of the resulting schistosomes was tested in mice. Despite some problems of stability and reproducibility, a few isolates showed a somewhat reduced susceptibility to praziquantel: ED_{50} values were 2–6 times higher than for isolates derived from patients who had been cured with a single dose of praziquantel. Praziquantel resistance, albeit of limited magnitude, was thus demonstrated.

In another investigation, a laboratory strain of *S. mansoni* has been subjected to increasing doses of praziquantel in successive mouse passages of the life cycle (*23*). At the seventh passage, the parasites were demonstrably less sensitive to praziquantel than unselected schistosomes, although the differences were again small, with ED_{50} values some 2–3 times higher than "normal". Data on the relative fitness, or vitality, of sensitive and resistant schistosomes are being collected in an effort to determine the chances of their prevailing in the parasite population.

While it is highly unlikely to have any substantial clinical significance, this insensitivity to praziquantel should be acknowledged as a warning of the need for continuous monitoring of the drug's efficacy. It must be emphasized that, even in patients in whom praziquantel did not effect parasitological cure, egg excretion was drastically reduced (by 80–85%). Thus, praziquantel remains a powerful tool for disease control, and there is no immediate reason to reduce or abandon its use in the field.

3.8 Strategies for avoiding or delaying the development of drug resistance

Although anthelminthic drug resistance in human nematodes and schistosomes has yet to be demonstrated, the fact of resistance in species that affect livestock suggests that measures should be taken to delay or avoid the development of the problem in human infections. Possible approaches to this include effective management of periodic drug treatment, evaluation of drug combinations, new drug products, and development of vaccines.

Effective management of periodic drug treatment is the most realistic measure and has already been recommended by WHO for implementation in helminth control programmes. The current strategy of targeted drug treatment for control of schistosomiasis and soil-transmitted helminthiasis has evolved as a balance between the need for regular treatment and the cost of intervention. Whether the protocols involved are likely to lead to drug resistance is unknown; measures for the identification and monitoring of drug resistance are therefore essential, and steps are being taken for their implementation.

Targeted treatment of the groups at greatest risk (school-age and preschool children and women of childbearing age) has the effect of leaving a small proportion of the nematode population free from exposure to the drugs concerned. Selection pressure for the expression of drug resistance is consequently reduced. Moreover, repeating treatment at intervals greater than the nematode generation time acts against selection for drug resistance; it is thus fortunate that the 10–15 treatments per year that are needed in veterinary control programmes

will never be used for human intestinal nematode infections. The use of combinations of anthelminthic drugs in control programmes is also expected to reduce or delay selection for resistance. Drug combinations that have been tested include the following:

— mebendazole (500 mg) + levamisole (2.5 mg/kg body weight)
— pyrantel (10 mg/kg) + oxantel (10 mg/kg)
— albendazole (400 mg) + ivermectin (200 µg/kg).

There is a continuing need for new and more effective anthelminthic compounds, but their development is hampered by the lack of interest among drug manufacturers in investing in the limited market of anthelminthics for human use. One reason for this lack of interest is that the demand for these drugs comes largely from developing countries and, although efforts are being made by WHO and other international agencies to encourage the development of new and inexpensive drugs, the impetus for research is likely to come from the more lucrative veterinary market. Several developing countries have active pharmaceutical companies that should be encouraged to engage in the development and production of anthelminthic drugs.

The development of effective vaccines against soil-transmitted helminths and schistosomes in both humans and animals may eventually contribute to control of these parasites, but extensive research is still needed in this area.

3.9 Concurrent administration of anthelminthic drugs

Resource constraints and efficiency concerns have stimulated interest in the simultaneous administration of two or more anthelminthic drugs in large-scale deworming programmes. However, this approach can be used only after reliable information has been accumulated on the safety and side-effects of a single intake of multiple drugs.

A double-blind, placebo-controlled study with albendazole and praziquantel has recently been carried out in 1500 school-age children in China, Kenya, and the Philippines. The helminths concerned were *S. japonicum*, *S. haematobium*, *S. mansoni*, and the common soil-transmitted helminth species. Neither drug was observed to influence the effectiveness of the other, nor was there any significant difference in the incidence of side-effects with albendazole and with the placebo. Children treated with praziquantel experienced more side-effects (abdominal pain, headache, nausea), especially if they were suffering with schistosomiasis, indicating an effect of the dying parasites. Quantitative improvements in the growth and health of the children were noted after combined treatment. Importantly, haemoglobin levels increased when praziquantel was included in the treatment for schistosomiasis (24).

A compelling conclusion from this study is that, in regions where schistosomiasis has public health implications, an annual dose of praziquantel is likely to provide significant health benefits to school-age children. More than one dose of albendazole is probably necessary if morbidity due to soil-transmitted helminth infections is to be reduced.

Little information is available about the use of praziquantel concurrently with levamisole, mebendazole, or pyrantel. The effects of giving praziquantel simultaneously with any of the WHO-recommended broad-spectrum anthelminthics to pregnant women or preschool children are also unknown.

3.10 Administration of anthelminthic drugs by non-medical personnel

Although a range of side-effects may be associated with anthelminthic drugs, with appropriate precautions (such as not giving praziquantel on an empty stomach) they are generally reported to be mild, transient, and self-limiting. Because of this, anthelminthic drugs may be distributed by non-medical personnel, for example by schoolteachers in school-based programmes.

Reports of severe reactions are extremely rare, but still suggest the need for effective reporting systems to be established in community treatment campaigns. Data on side-effects should be collected at the central level and made available without delay to the international scientific community. Published data provide no evidence so far that side-effects following drug treatment require immediate treatment and clinical care from expert personnel. To avoid the reporting of problems that are not attributable to anthelminthic drugs, children who are sick on the day of treatment should be treated after recovery.

Care-givers should be fully informed about the drug to be given before it is administered and should be free to withdraw children from the programme at any time without fear of prejudice.

The use of teachers – and sometimes parents – to administer anthelminthic drugs has been highly successful in several countries. However, there should always be a link to health services in case of emergency.

3.11 Administration of praziquantel according to height (dose pole)

The lack of a sufficient number of weighing scales during the Onchocerciasis Control Programme in West Africa made accurate dosing difficult and led to the development of a "tablet pole" or "dose pole" to facilitate administration of the appropriate ivermectin dose on the basis of an individual's height. Extensive use of these poles in the Onchocerciasis Control Programme has established their practicality. In

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addition, they are cheap and robust and can easily be made locally. Original experience with a praziquantel dose pole in Ghana, Malawi, and the United Republic of Tanzania showed that around 75% of children treated would have received a praziquantel dose in the same range had they been accurately weighed (25).

The praziquantel dose pole was further developed on the basis of data specifically collected for the purpose during a school-based survey. Height was measured to the nearest 10 mm and weight to the nearest 0.1 kg. The pole was developed to deliver a dose of 40–60 mg/kg, in order to minimize under-dosage, and was designed to identify five height intervals corresponding to 1 ½, 2, 2 ½, 3, and 4 tablets of praziquantel; details are given in Annex 3. Use of the pole was validated in a number of existing data sets, totalling more than 24 000 records (26). This validation confirmed that 98.6% of school-age children would have received a praziquantel dosage between 30 and 60 mg/kg body weight, and that 84.7% would have been given between 40 and 60 mg/kg. Corresponding figures for whole populations (including young children and adults) were 95.5% and 68.2%. The dose pole is now to be tested further in a number of field situations.

The dose pole is thus considered to be a reliable and practical method for determining the dose of praziquantel needed to treat schistosomiasis; with further development and evaluation, a pole can be produced that can be used throughout sub-Saharan Africa.

3.12 Rapid epidemiological assessment of schistosomiasis

An important feature of schistosomiasis is its focal distribution, which means that the public health importance of the disease varies across a region or even across a country. Appropriate targeting of treatment is therefore essential to optimize the cost-effectiveness of control activities. A simple tool – the school questionnaire – has been developed for the rapid assessment of *Schistosoma haematobium* and has been extensively validated in a variety of ecological, epidemiological, and sociocultural settings across sub-Saharan Africa. The method has more recently been extended to cover *S. mansoni*, but validity testing in several studies seems to indicate that it underestimates the number of cases.

3.12.1 *Questionnaires for rapid screening of Schistosoma haematobium*

The usefulness of asking people in endemic areas about their history of haematuria – an indirect diagnostic method for *S. haematobium* infection – has been extensively investigated. A standardized questionnaire (see Annex 4) was used in different endemic areas with many varied ecological and sociocultural characteristics; it proved to be

accurate, well accepted, and cost-effective. This tool is now ready for use for the rapid identification of communities in need of treatment for urinary schistosomiasis, and WHO has developed a manual for managers of control programmes to facilitate its use (27).

3.12.2 *Questionnaires for community diagnosis of intestinal schistosomiasis*

There is no obvious and simple sign or symptom of intestinal schistosomiasis that is sufficiently sensitive and specific to be used for rapid screening: the most consistent observation is of an association between the infection and a recent history of "blood in stool". The diagnostic performance of questionnaires for intestinal schistosomiasis is inferior to that for urinary schistosomiasis, and rapid identification of communities at high risk for the intestinal infection remains difficult, except in the case of *S. mekongi* (for which the presence of rocks in rivers has proved to be useful as a rapid detection method). Programme managers should note, however, that other methods and tools are available for surveys to assess the extent of schistosomiasis in the community and for monitoring the impact of control measures; details are published elsewhere (28, 29).

3.13 Cost of delivering and sustaining deworming programmes

Delivery systems for deworming have often been dependent on vertical programmes, in which mobile teams visited schools or communities to carry out treatment. Estimated costs for this approach to treating soil-transmitted helminthiasis are US$ 0.51 per treatment in Montserrat, US$ 0.32 in Nigeria, and US$ 0.21 in the United Republic of Tanzania. Added to concerns about "sustainability", these high costs have prompted workers to suggest integrated approaches to treatment that capitalize on existing infrastructure. Using the education system is a particularly attractive option. since anthelminthic treatment can be targeted to school-age children. who carry the heaviest burdens of infection. Delivery of treatment is achieved at low cost by "piggy-backing" on existing programmes and systems within the education sector, so that drugs reach the schools through established channels. Routine delivery of treatment targeted in this way could cost as little as US$ 0.03 per child (30), which may be up to 10 times cheaper than the estimated costs for vertical delivery. Thus, at current drug prices, the total cost (i.e. of drug plus delivery) of a single treatment with albendazole or mebendazole may be as low as US$ 0.05–0.10, and of a combined treatment with praziquantel US$ 0.25–0.30 per child.

Operational research in Ghana and the United Republic of Tanzania has generated a simple cost menu to illustrate the cash expenditure and resources needed to undertake delivery of treatment with albendazole or

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mebendazole plus praziquantel in a school-based programme. The cost menu is set up so that all resources are expressed in common units of "per child" or "per school" (see Table 4); this permits easy extrapolation to different settings and provides crude figures for minimum financial investment required.

Table 4
Cost menu for targeted deworming of schoolchildren with albendazole or mebendazole plus praziquantel[a]

Item	Base unit	Base unit cost (C)	Quantity per child or school (Q)	Unit cost per child or school ($C \cdot Q$)
Per child				
Drug:				
albendazole	per tablet	0.02	1.1[b]	0.022
mebendazole	per tablet	0.02	1.1[b]	0.022
praziquantel	per tablet	0.07	2.5[b]	0.175
insurance, freight, clearance	per tablet	0.007	3.6	0.025
Per school				
Equipment:				
dose poles	–	–	–	3.5
Health education:				
adaptation and duplication of materials	–	–	–	10
Training:				
stationery	–	–	–	3.5
trainers' per diem allowances	per person	25	0.1	2.5
trainees' allowances	per person	2.5	3.0	7.5
Drug distribution:				
officers' training allowances	–	–	–	0.25
instruction forms	per form	0.05	4.0	0.2
treatment forms	per form	0.05	10.0	0.5
school officer collection allowance	–	–	–	5.0
senior officer collection allowance	–	–	–	0.2

[a] Adapted from Guyatt (personal communication).
[b] Including approximately 10% wastage.

The menu ignores the cost of using existing personnel to administer the drugs. Trials in the United Republic of Tanzania suggest that 18 person-days would be required for drug administration in the 350 schools. In planning programmes to reduce morbidity due to schistosomiasis and soil-transmitted helminthiasis in school-age children, the additional costs of initial needs assessments must also be taken into consideration. Examples of such costs in the United Republic of Tanzania – to examine 250 children in each of four ecologically different areas – are shown in Table 5.

Table 5
Example of a budget for needs assessment: baseline data collection[a]

Item	Cost (US$)
Questionnaire	2000
Four-wheel-drive vehicle	(available)
Vehicle maintenance	400
Fuel	500
Training of laboratory technicians	–
Allowances for the data collection team	960
Laboratory material and microscopes	1500
Drugs administered during the survey	620
Data entry and analysis	–

[a] Adapted from reference 31.

Unit costs of deworming vary with the density of schools in a country and the average number of children in each school. Using the cost menu for Ghana (80 000 children in 577 schools) and for the United Republic of Tanzania (100 000 children in 350 schools), the unit deworming cost – including initial needs assessment, training, and purchase of equipment and materials – can be as low as US$ 88–136 per school, or US$ 0.48–0.65 per child, during the first year in an area where children need one annual treatment for schistosomiasis and two for soil-transmitted helminthiasis. Routine delivery of this treatment schedule during subsequent years would cost US$ 51–92 per school or US$ 0.32–0.37 per child.

Where only one yearly round of treatment with albendazole or mebendazole has to be delivered, the cost would be US$ 41–50 per school or US$ 0.17–0.29 per child during the first year, and US$ 10–15 per school or US$ 0.05–0.08 per child for routine delivery during subsequent years.

The operational costs of deworming in a given field situation can thus vary from US$ 0.05 to US$ 0.65 per child per year.

Monitoring is an important part of the managerial process and should be carried out with the minimum of expense to avoid diverting much-needed resources from intervention activities. At the planning stage, it is recommended that approximately 5% of the programme budget be reserved for monitoring activities (including non-financial inputs such as personnel time and subsistence, and fuel).

As regards the extra cost of covering non-enrolled school-age children through a school-based intervention, two different approaches have been documented. The "sibling approach", used in Zanzibar, was able to deliver treatment to these children for essentially the cost of the drugs alone (32). In the more elaborate approach used in Egypt, which was based on community mobilization, the delivery cost was reckoned to be US$ 0.16–0.21 per extra treatment (33).

The question remains of whether parents would be willing to meet, or contribute to, the costs of deworming in schools. In many countries, it is likely that they would not, although there is little reliable evidence to support this impression. However, where fees are charged for children's education, it might be possible to suggest cost-sharing.

3.14 Helminth infections and immunocompetence

Based on the fact that any helminth infection produces a reaction in the immune system of an immunocompetent host, the proposition has recently been advanced that helminths may affect lymphocytes in a manner that facilitates establishment of the human immunodeficiency virus. It has also been postulated that host–helminth interactions may result in reduced immunocompetence in young children at the time of immunization against potentially life-threatening infections.

3.15 Vaccine development for schistosomiasis and hookworm

Candidate vaccines for schistosomes and hookworms have been identified, and preclinical testing of these formulations is in progress. Those who would benefit most from vaccination are at-risk adults who do not participate in school-based anthelminthic treatment programmes and who therefore need repeated drug treatment in order to lower worm burden. Clearly, such research is to be encouraged, but it is unlikely that vaccines against these parasites will become available during the next decade.

3.16 Success of schistosomiasis control in Latin America, Asia, and the Middle East

Enormous progress has been made in reducing the public health importance of schistosomiasis in many countries, although the number of infected people globally has not changed in 50 years. Reductions in the amount of schistosomiasis in Latin America, Asia, and most countries of the Caribbean and the Middle East are balanced by increases in the at-risk populations, mainly in sub-Saharan Africa. Population movements and increases, water resource development, and competing health priorities have all contributed to the rise in schistosomiasis in sub-Saharan Africa.

Successful control programmes have been carried out in many countries over the past 20 years. In April 2000, WHO held an Informal Consultation in London to document these successes and to determine further specific needs and targets (34). A few countries and a number of islands have managed to eliminate schistosomiasis altogether. The last locally contracted case in Japan, for example, was detected in 1977, and Tunisia achieved interruption of transmission in 1984. Prevalence of the

disease in the Islamic Republic of Iran, Mauritius, and Puerto Rico is now so low that transmission may well have been interrupted. Morocco and Venezuela are in the final stages of eliminating schistosomiasis, and transmission to humans in the Caribbean islands – except the Dominican Republic – is almost non-existent.

Significant reductions in morbidity have been achieved in Brazil, China, Egypt, the Philippines, and several countries of the Middle East, all of which are moving towards elimination. Some areas within these countries are no longer endemic. In Cambodia, even in conditions of considerable civil unrest and with a poor health infrastructure, current control measures have been able to reduce the morbidity associated with *S. mekongi* infection over the past 5 years. The significant reductions in morbidity, prevalence, and intensity of infection achieved in all these countries demonstrate that schistosomiasis control is a realistic goal. Nevertheless, active surveillance programmes are essential to guard against re-emergence of the disease, and active screening and treatment programmes are needed to sustain morbidity control. In particular, there is concern that these successes might persuade health care planners to prematurely divert resources to other health problems, with a consequent re-emergence of morbidity. In Asian countries, moreover, there is the additional problem of animal reservoirs, which maintain the infection in the environment.

As morbidity diminishes, more sensitive diagnostic techniques are needed to detect infections in people living in areas with continuing transmission. While immunodiagnostic techniques showed promise in the laboratory, they have rarely been used in control programmes: only in China and Venezuela have immunological tests been used for primary screening. In Puerto Rico, immunodiagnosis was used to evaluate the endemic situation throughout the island. Further discussion and research are essential to establish both whether available sensitive diagnostic methods are suitable for widespread use in low-transmission areas and whether new techniques need to be developed. There is also a pressing need for standardization of clinical case definition and diagnostic criteria.

4. Recommended control objectives and strategies

4.1 Opportunities for a combined approach for schistosomiasis and soil-transmitted helminthiasis in highly endemic situations

The occurrence of both schistosomiasis and soil-transmitted helminthiasis is intimately related to the conditions of poverty: both diseases are entrenched where there is poor hygiene, and a lack of safe water and of adequate sanitation.

For both schistosomiasis and soil-transmitted helminthiasis, WHO recommends that the first objective should be a strategy for morbidity control. The objective should be to reduce the consequences of these infections – early morbidity associated with infection, as well as late-stage chronic and irreversible sequelae – to a level that no longer constitutes a public health burden.

Effective, safe, and inexpensive single-dose drugs are available to treat both types of infection. It is now clear that the objective of morbidity control can be met cost-effectively by ensuring access to essential anthelminthic drugs in all health care facilities and by regularly treating population groups that are at risk of developing morbidity. The safety and current low cost of anthelminthic drugs mean that treatment without prior diagnosis is an effective option in areas of high prevalence or high transmission; even for selective treatment, the cost of diagnosis may be disproportionately high.

These considerations, together with concerns about emerging drug resistance, have prompted WHO to promote a more targeted control approach in highly endemic areas, in preference to the community-wide (universal or selective) approach once advocated for the control of schistosomiasis. A carefully planned and targeted approach is expected to yield benefits, in terms of morbidity control, comparable to those achieved by a community-wide approach but at much lower cost. A targeted approach can be more easily carried out within existing structures and be harmoniously integrated into the public health agenda of most developing countries. It is seen as attractive by national health authorities and donor agencies in endemic countries (*35*).

The high-risk groups for the two infections largely overlap: for soil-transmitted helminthiasis they include preschool and school-age children, women of childbearing age, and people in certain occupations (e.g. tea-pickers and miners); for schistosomiasis the groups are school-age children and adolescents, but also those whose occupations involve contact with infested water (e.g. fishermen, farmers, irrigation workers, and women in their domestic tasks). These groups can be reached through the same channels – the existing health and education systems – with extended community-based coverage where populations are severely affected and under-served.

Since both infections result from poor hygienic conditions, and deworming alone is unlikely to have a lasting impact on transmission, more permanent control can be achieved only by improvements in water supplies and sanitation, coupled with appropriate health education. Improvements in sanitation and access to clean water, appropriate health education, and environmental measures (notably, snail control

where there is schistosomiasis) should therefore be promoted in all cases. The investments required for these measures are offset by the benefits in terms of improved health, productivity, and socioeconomic stability. Opportunities for reducing the risk of transmission of these infections should also be sought outside the health sector. For example, water development projects, usually backed by resources unavailable to the health sector, provide an opportunity to tackle schistosomiasis. For the health sector to benefit from these resources will require appropriate legislation and intersectoral collaboration.

Even without these additional measures, however, drug treatment of the infections brings immediate benefit and has a long-lasting effect on morbidity, preventing irreversible sequelae in adulthood.

4.2 Differential strategies for schistosomiasis control in areas of high and low endemicity

A marked discrepancy is now apparent in the status of schistosomiasis control between sub-Saharan Africa and most of the affected countries of Latin America, Asia, and the Middle East. During the 1980s, a number of African countries implemented donor-funded control programmes; in the absence of national financing capacity, it later proved impossible to sustain these programmes once the external funds were withdrawn. Many national health authorities in sub-Saharan Africa may now feel that the resources required for control are out of proportion to the perceived public health importance of schistosomiasis. A deteriorating socioeconomic situation, progressive loss of diagnostic capacity in peripheral health care facilities, the appearance or re-emergence of more visible health problems, and the focal nature of the disease may all have contributed to the downgrading of schistosomiasis on the public health agenda. The net result of this, in much of sub-Saharan Africa, is the persistence of high morbidity in places where praziquantel is not readily available.

Schistosomiasis control is not an "all-or-nothing" phenomenon: simple control measures can relieve the unnecessary – and often underestimated – disease burden in areas of high prevalence, and can be implemented in all circumstances.

Once areas of high prevalence have been identified, the strategy in such areas should be one of morbidity control, as outlined in section 4.1. Integration of control efforts into existing structures and interventions, together with decentralization of decision-making and delivery, is crucial to ensuring commitment and sustainability. Health authorities need to recognize schistosomiasis control as an integral part of primary health care.

More substantial, and costly, measures may be adopted by individual countries wanting to extend their efforts beyond morbidity control, provided that the technical and financial resources required can be sustained over sufficiently long periods.

A number of countries in which prevalence of schistosomiasis was once high have succeeded in sustaining community-wide treatment approaches for considerable periods and have achieved low prevalences of infection with massive reductions in morbidity. Most have managed to consolidate their achievements with an improved standard of living. Several countries have also made progress in reducing schistosomiasis through environmental management and snail control (34). All should be encouraged to continue their control efforts and to set a goal of eliminating the disease at regional and national levels.

4.3 A minimal package of activities for schistosomiasis and soil-transmitted helminthiasis in high-burden areas

Any morbidity control programme must include permanent provision at all levels of the health care system for the adequate management of people with symptomatic disease who seek care. Typically, this will require schistosomiasis and soil-transmitted helminthiasis to be included in diagnostic procedures, in cost recovery and drug supply systems, and in the regular health information systems.

Since a considerable part of the burden of schistosomiasis and soil-transmitted helminthiasis involves subtle morbidity that particularly affects children, it is recommended that children be provided with regular treatment. This approach provides the opportunity to prevent nutritional deficiencies, illness, and sequelae in later life. Coverage of young individuals is the core element of morbidity control, with benefits that will extend to the whole community as the children become adults. In countries with moderate to high rates of enrolment in schools, excellent coverage of school-age children has been achieved in school-based interventions. Children of preschool age can be reached through broad public health programmes such as the Integrated Management of Childhood Illnesses (36), baby clinics, and day nurseries, and through social and religious networks. Once morbidity has been reduced during adolescence, retreatment on a less frequent basis can be introduced to maintain this benefit into adulthood.

World Health Assembly resolution WHA54.19 (see Annex 1) requires that, by the year 2010, regular treatment at appropriate intervals be offered to 75–100% of all school-age children living where schistosomiasis, ascariasis, hookworm disease, and trichuriasis have public health consequences. That is, by 2010, whenever a round of anthelminthic

treatment is due, it must be offered to at least 75% of children aged 6–15 years in each community to be treated, regardless of whether they are enrolled in school. Experience of parasite control programmes has shown that 75% coverage is an attainable target, delivering significant reductions in morbidity and preventing irreversible sequelae in adulthood.

Although school-age children are seen as the primary target group for regular treatment, other groups in the community are also at risk for morbidity, as specified in section 4.1. Extensive migration from rural to urban areas, and population movements resulting from civil strife, have led to the establishment of large slum areas around towns and cities in many developing countries. These areas are characterized by overcrowding and very poor standards of hygiene; as a consequence, transmission of schistosomes and soil-transmitted helminths is often intense in these marginalized communities but is seldom addressed by control programmes.

It is important that the needs of the community are evaluated when control interventions are planned. Well-functioning health services can provide early treatment of symptomatic cases of infection, and health facilities can meet the needs of particular communities by systematically treating individuals at risk. Where communities lack access to adequate health or educational facilities, other channels should be explored for the delivery of regular treatment, such as professional groups or associations or existing public health programmes (vaccination outreach services, community-directed drug delivery programmes, etc.).

4.4 Containment of disease in water resources development

In the specific case of schistosomiasis, certain development initiatives – particularly water resources development for agriculture or energy production – are likely to favour emergence or spread of the disease. Preventive action is needed on two fronts:

— a proper health impact assessment (HIA), with procedures ensured by ministries of health through policy adjustment and capacity building;

— compliance with HIA recommendations, consisting largely of environmental engineering and management measures.

From the economic perspective. the concept of infrastructural and engineering measures is often rejected outright because of the perception that major capital investment would be involved. Experience shows, however, that a timely HIA allows design changes in hydraulic structures and a reconsideration of settlement location. at little additional cost. Similarly, decision-making criteria and procedures for improved water

management in irrigation schemes and reservoirs that take due account of the need to reduce the risk of transmission can be implemented at little or no extra cost. The measures that do require capital investment usually have dual goals, such as reduction of health risks combined with improved agricultural yields. At the level of the rural community, agricultural extension programmes and agricultural training and support programmes provide appropriate mechanisms for relaying messages on agricultural practices that reduce the risk of schistosomiasis transmission.

To slow reinfection and to sustain lasting reductions in transmission, regular treatment has to be supported by adequate access to sanitation and clean water, plus appropriate health education. Snail control measures are essential if control of schistosomiasis transmission is to be achieved. As poor hygienic conditions are the underlying cause of most parasitic diseases, and of poverty-related infectious diseases in general, collaboration with any service dealing with hygiene and hygiene-related diseases and their prevention will create the synergy needed to reduce both poverty and disease.

5. Operational approaches to the control of morbidity due to schistosomiasis and soil-transmitted helminthiasis

5.1 WHO-recommended anthelminthic drugs

Drugs recommended by WHO for reducing morbidity due to soil-transmitted helminthiasis are albendazole, levamisole, mebendazole, and pyrantel (*14*). For reducing morbidity due to schistosomiasis, WHO recommends praziquantel (effective against all schistosome species) and oxamniquine (effective only against *S. mansoni*) as a second choice. Metrifonate (effective against *S. haematobium*) has been withdrawn by its original producer but can still be found on the generic market in some countries. Since oxamniquine is at least as safe as praziquantel and equally effective against *S. mansoni*, it is recommended that this drug remain on the market.

Details on how these drugs should be used can be found in the *WHO model formulary* (*37*). Ivermectin, which has an important role in onchocerciasis control, is now known to be highly effective against *A. lumbricoides* and to have some activity against *T. trichiura*; it is now the drug of choice for strongyloidiasis. Information about these drugs is summarized in Table 6.

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Table 6
Drugs currently used for the treatment of schistosomiasis and soil-transmitted helminthiasis

Drug and formulation	Therapeutic activity[a]	Dosage
Albendazole (tablets 200 and 400 mg, suspension 100 mg/5 ml)	Ascariasis +++	400 mg, single dose
	Trichuriasis ++	400 mg, single dose
	Hookworm infection +++	400 mg, single dose
	Strongyloidiasis ++	400 mg daily for 3 days
Ivermectin (tablets 6 mg)	Ascariasis +++	200 µg/kg, single dose
	Trichuriasis +	200 µg/kg, single dose
	Hookworm –	–
	Strongyloidiasis +++	200 µg/kg, single dose
Levamisole (tablet 40 mg, syrup 40 mg/5 ml)	Ascariasis +++	2.5 mg/kg, single dose
	Trichuriasis +	2.5 mg/kg, single dose
	Hookworm infection ++	2.5 mg/kg, single dose (for heavy infection repeat after 7 days)
	Strongyloidiasis –	–
Mebendazole (tablets 100 mg and 500 mg, suspension 100 mg/5 ml)	Ascariasis +++	500 mg, single dose
	Trichuriasis ++	100 mg twice daily for 3 days, or 500 mg, single dose (less effective)
	Hookworm infection ++	100 mg twice daily for 3 days, or 500 mg, single dose (less effective)
	Strongyloidiasis +	100 mg twice daily for 28 days[b]
Oxamniquine (capsules 250 mg, syrup 250 mg/ml)	Schistosomiasis +++ (S. mansoni)	*Adults:* 15–60 mg/kg,[c] single (up to 20 mg/kg) or divided doses *Children:* 20–60 mg/kg,[c] single (up to 20 mg/kg) or divided doses
Praziquantel (tablets 600 mg, tablets 200 mg in China, syrup 600 mg/5 ml in Egypt)	Schistosomiasis +++ (all species)	40–60 mg/kg, in single or divided dose[d]
Pyrantel (tablets 250 mg, suspension 50 mg/5 ml)	Ascariasis +++	10 mg/kg, single dose
	Trichuriasis –	–
	Hookworm infection ++	For heavy hookworm infection, 10 mg/kg, repeated for 4 days
	Strongyloidiasis	–

[a] +++ ≥ 80% cure rate (CR) or ≥ 80% egg reduction rate (ERR)
 ++ 50–80% CR or 50–80% ERR
 + 10–50% CR or 10–50% ERR
 – not considered to be effective
[b] From literature reports – not WHO recommendations.
[c] As an alternative, dose could be calculated according to height (see Annex 3)
[d] According to geographical locations.

5.2 Drug procurement and quality assurance

The most appropriate way to ensure the sustainable supply and distribution of drugs is to rely on a well-functioning national system of procurement, distribution, and delivery that includes mechanisms for quality assurance. It is part of WHO's mission, as outlined in World Health Assembly resolution WHA28.66 (*38*), to assist Member States with advice on the selection and procurement, at reasonable cost, of essential drugs of established quality corresponding to their national health needs.

By resolution of the Executive Board (*39*), WHO has also been mandated to assist Member States, on request, with drug procurement. In emergency circumstances, WHO can support the procurement of drugs, including anthelminthics, at no cost to the health ministry of the Member State concerned. Under normal conditions, WHO makes a charge of 3% of drugs costs for the service of procurement.

5.3 Needs assessment: rapid epidemiological evaluation and choice of appropriate interventions

In planning the control of schistosomiasis and soil-transmitted helminthiasis, collection of baseline information is essential:

— for selecting the appropriate control measures to be used in the control programme;
— to provide data for monitoring the impact of the programme at a later stage.

Generally. soil-transmitted helminthiasis is widely distributed, both geographically and demographically in the population, and a parasitological stool survey in a sample of schools is usually sufficient to evaluate its distribution in a particular area. Schistosomiasis, however, tends to be much more focally transmitted. Visible blood in the urine is a symptom of urinary schistosomiasis that is easily recognized by children. Urinary schistosomiasis can therefore be rapidly and accurately assessed by using a simple questionnaire distributed to all schools in a defined administrative or geographical area. Using this method, it is possible to rank schools in order of the level of transmission of the infection (*40*). For intestinal schistosomiasis, additional stool surveys may need to be undertaken, based on available knowledge of the distribution of infection.

The factors that should be considered when control strategies are planned in a particular country include the felt needs of the community; the types of infection present. and their distribution and abundance (health centre records and other sources of data on positive cases should be checked); the extent and severity of morbidity; the availability and accessibility of primary health care; the nature of the environment and

ecological features; the potential for intersectoral collaboration; and the levels of managerial and technical support.

Where a control programme is to address both urinary and intestinal schistosomiasis, as well as soil-transmitted helminthiasis, records of passive cases diagnosed at health facilities should be sought as an indication of the need for active intervention. If there are no available records, it is important to strengthen the health services so that such cases can be diagnosed and treated.

The following paragraphs provide an example of data collection, evaluation, and use under conditions likely to prevail in sub-Saharan Africa:

In a particular coverage area (district, region, or even country):

- Conduct the questionnaire survey in *all* schools in the zones where urinary schistosomiasis is likely to be present, and evaluate the results.
- Divide the area into ecological zones where the occurrence of soil-transmitted helminthiasis is likely to be different. Conduct a stool survey in a random sample of schools to assess the prevalence and intensity of soil-transmitted helminthiasis (and intestinal schisto-somiasis). A sample of 200–250 children in each ecologically homogeneous zone (e.g. one class of 50 children in each of five randomly selected schools) is considered to be adequate for the evaluation of the prevalence and intensity of the different helminth infections and to determine appropriate control measures (*31*).
- In zones likely to be endemic for intestinal schistosomiasis, extra school stool surveys may have to be conducted to complete the assessment of the prevalence and intensity of intestinal schistoso-miasis, which is usually more focally distributed than soil-transmitted helminthiasis.

For each individual examined, the intensity of infection can be quantified (see Table 7). In the case of soil-transmitted helminthiasis, the prevalence of infection – or heavy infection – with at least one of the three commonly transmitted soil-transmitted helminths is more relevant than the prevalence of infection with each individual helminth.

The results of this initial survey can be used to classify the endemic level in the community (*community diagnosis* – see Table 8). On the basis of this classification, the optimal frequency of treatment of school age children can be determined, as well as the urgency for other control measures (see Table 9).

Since praziquantel is now available at low cost, the Expert Committee recommended that targeted treatment for schistosomiasis be given in all

Table 7
Classes of intensity for schistosome and soil-transmitted helminth infections

By stool examination:

Organism	Light-intensity infections	Moderate-intensity infections	Heavy-intensity infections
A. lumbricoides	1–4999 epg[a]	5000–49 999 epg	≥ 50 000 epg
T. trichiura	1–999 epg	1000–9999 epg	≥ 10 000 epg
Hookworms	1–1999 epg	2000–3999 epg	≥ 4000 epg
S. mansoni	1–99 epg	100–399 epg	≥ 400 epg

By questionnaire or urine filtration:

Organism	Light-intensity infections	Heavy-intensity infections
S. haematobium	< 50 eggs/10 ml	Visible haematuria, or ≥ 50 eggs/10 ml

[a] epg: eggs per gram (of faeces)

endemic areas; the treatment interval should be determined by the pre-control prevalence rate – the indicator of intensity of transmission.

With the substantial reductions in the cost of anthelminthic drugs generally, new options for treatment and retreatment strategies should be considered, with greater emphasis on targeted, rather than selective, treatment. Selective treatment remains an option for urinary schistosomiasis (S. haematobium); indirect morbidity markers, such as reagent strips for haematuria, can be used for this purpose. However, this option is cost-effective only in areas of low endemicity.

Once the appropriate control measures have been selected for each operational unit, needs can be determined. These will be both operational and financial, and must include training (health personnel, teachers), drug distribution, and health education. The cost menu provided in Table 4 (page 21) can be useful to determine the required budget.

5.4 Monitoring and evaluation

5.4.1 Monitoring

Use of process and parasitological indicators facilitates the monitoring of ongoing control activities.

Process indicators

Process indicators reflect the performance of the control programme and include such items as consumption of drugs and regular treatment coverage. Careful definition of a limited number of key indicators,

Table 8
**Community diagnosis (through schools) for schistosome and
soil-transmitted helminth infections**

Soil-transmitted helminth infections

Community category	Result of school survey:	
	prevalence of any infection	moderate to heavy infections (%)
I High prevalence *or* high intensity	≥70%	≥10%
II Moderate prevalence and low intensity	≥50% but <70%	<10%
III Low prevalence and low intensity	<50%	<10%

Schistosome infections

Community category	Prevalence in school survey:
I High prevalence	≥30% visible haematuria (*S. haematobium*, by questionnaire) or ≥50% infected (*S. mansoni. S. haematobium*, by parasitological methods)
II Moderate prevalence	<30% visible haematuria (*S. haematobium*, by questionnaire) or ≥10% but <50% infected (*S. mansoni, S. haematobium*, by parasitological methods)
III Low prevalence	<10% infected (*S. mansoni, S. haematobium*, by parasitological methods)

focusing on the issues stressed in World Health Assembly resolution WHA54.19 (see Annex 1), allows activities to be closely monitored and overall coverage to be calculated.

Parasitological indicators

It is possible that no significant reduction in the prevalence of soil-transmitted helminthiasis will be detected; in practice, a reduction in the number of heavily infected cases is much more relevant. The underlying principle of this evaluation method is that, among all infected individuals, most of the morbidity is accounted for by the 10–15% who are the most heavily infected. The reduction in egg counts among those with infections of moderate to heavy intensity will ensure that morbidity declines in the long term. Indicators should be assessed in representative sentinel areas at intervals of one to several years according to the treatment schedule. After some years of sustained intervention, parasitological monitoring may provide guidance for a change of strategy. For schistosomiasis, a number of sentinel sites representative of each treatment strategy should be chosen, in which the proportion of heavy infection and the incidence of infection should be determined at appropriate intervals.

Table 9
Recommended treatment strategies for schistosome and soil-transmitted helminth infections[a]

Soil-transmitted helminth infections

Community category	Intervention in schools (enrolled and non-enrolled children)	Health services and community-based intervention
I High prevalence *or* high intensity	Targeted treatment of school-age children, 2–3 times a year	Systematic treatment of preschool children and women of childbearing age in mother and child health programmes
II Moderate prevalence and low intensity	Targeted treatment of school-age children, once a year	Systematic treatment of preschool children and women of childbearing age in mother and child health programmes
III Low prevalence and low intensity	Selective treatment	Selective treatment

Schistosome infections

Community category	Intervention in schools (enrolled and non-enrolled children)	Health services and community-based intervention
I High prevalence	Targeted treatment of school-age children, once a year	Access to PZQ[b] for passive case treatment[c]; community-directed treatment for high-risk groups recommended
II Moderate prevalence	Targeted treatment of school-age children, once every 2 years	Access to PZQ[b] for passive case treatment[c]
III Low prevalence	Targeted treatment of school-age children twice during primary schooling (once on entry, again on leaving)	Access to PZQ[b] for passive case treatment[c]

[a] Treatment strategies should always be accompanied by efforts to improve water supply and sanitation.
[b] PZQ = praziquantel.
[c] Can be done on presumptive grounds, according to diagnostic algorithms adapted to the endemic situation.

5.4.2 *Evaluation*

Defining morbidity indicators to evaluate the long-term impact of control is not a simple matter. Sufficient time must be allowed for a reliable change in these indicators to be detected. A distinction should be made between early (visible haematuria, anaemia) and late morbidity (portal hypertension, hepatic fibrosis, bladder cancer). Documenting both morbidity before the start of control activities and the rationale for initiating those activities may help in identifying the most appropriate morbidity indicators for long-term follow-up.

5.5 Drug administration to children in schools and extension of coverage to non-enrolled school-age children

Existing school-based programmes for reducing morbidity due to soil-transmitted helminthiasis and schistosomiasis have used a targeted treatment strategy. Experience from these programmes indicates that deworming, especially for soil-transmitted helminthiasis, may have to be carried out two or three times a year, depending on the epidemiological situation. Deworming treatment may be administered in schools by teachers, assisted and supervised by health personnel; teachers should also provide health education to children. Ideally, deworming should be part of a wider public health package delivered via a school health programme.

From the planning stage, any programme that aims to treat school-children for soil-transmitted helminthiasis and schistosomiasis should involve the education sector as a full and equal partner, especially if the education system is to be used to deliver anthelminthics to schools and teachers are to administer them. Teachers may not necessarily be willing to treat children who are not their pupils (preschool and non-enrolled children, for example) and schools may therefore need active support from the personnel of local health facilities.

Age and sex inequalities in enrolment ratios and the late enrolment of children of short stature should be taken into account in school-based programmes. Non-enrolled school-age children should be included: the latest estimates from the United Nations Children's Fund (UNICEF) indicate that 40% of school-age children in the least-developed countries are not enrolled in schools. Similarly, preschool children should be offered treatment, since they are often infected with helminths and it is in this age group that growth faltering begins.

Organizing "deworming days" at schools and inviting non-enrolled school-age children to attend for treatment seems to be a promising strategy in areas where the education infrastructure will support this. The appropriate means of disseminating information and persuading people to participate in deworming days will depend on the area concerned. Where most non-enrolled children share households with enrolled children, the enrolled children can spread the information (32). Where this is not the case, information will need to be disseminated on a community basis (33). It is important that any person who seeks treatment should be accommodated.

Because control programmes have been largely school-based, targeted treatment has concentrated on children enrolled in schools; coverage of non-enrolled school-age children and of preschool children has been much lower. In the Seychelles, however, deworming campaigns based in

primary schools have included preschool children from day-care centres. In many countries where soil-transmitted helminthiasis is a problem there are no preschool facilities, and it is important for preschool children to be invited to attend school-based deworming treatment sessions. Similar problems apply to the coverage of women of childbearing age. In the Seychelles, pregnant women were treated in antenatal and mother and child health clinics, but non-pregnant women were not covered. Here again, it may be possible to extend deworming to non-pregnant women and adolescent girls by inviting them to attend school treatment days.

5.6 Case management at the peripheral health care level

The availability of anthelminthic drugs at health facilities is a prerequisite of any activity to control morbidity (see section 5.5). Clinical diagnosis in peripheral health services may not be easy when symptoms are nonspecific, and should ideally be based on parasitological examination. For urinary schistosomiasis, reagent strips may be used to detect haematuria or urine can be visually examined if a microscope is not available. Diagnosis can also be made on presumptive grounds if a patient complains of haematuria. In areas where intestinal schistosomiasis is a common infection, diarrhoea (especially bloody diarrhoea), abdominal pain, or hepatomegaly may be a basis for presumptive diagnosis and subsequent treatment. Severe cases with gross symptoms should be referred to the secondary or tertiary level of care.

5.7 Community-directed treatment

Where there are insufficient health facilities and trained health workers to cover all communities, the community-directed approach is an effective means of delivering public health interventions. The African Programme for Onchocerciasis Control adopted such an approach as its principal strategy for the distribution of ivermectin, and achieved good coverage and compliance.

If community-directed treatment is to be successful and sustainable, affected communities need to be involved in its planning, implementation, monitoring, and evaluation. They should be asked to participate in social mobilization and be involved in decisions on the mode of drug distribution, the period of treatment, and the choice of community-based drug distributors. They can also assist in collecting drug supplies from a central distribution point and overseeing the distribution process, provide appropriate incentives to the chosen drug distributors, and participate in evaluation of the intervention.

The Global Programme for the Elimination of Lymphatic Filariasis has as its principal strategy the simultaneous administration of two drugs once a year for 4–6 years; this regimen is thought to be sufficiently effective to reduce microfilaraemia to levels below those capable of sustaining transmission of infection. The two possible drug regimens are albendazole/ivermectin and albendazole/diethylcarbamazine. Since both regimens include albendazole, they can also have a major positive impact on soil-transmitted helminthiasis.

These opportunities must now be rationalized by coordinating national activities for the elimination of onchocerciasis and/or lymphatic filariasis with control programmes for schistosomiasis and soil-transmitted helminthiasis. For soil-transmitted helminthiasis, treatment once a year may not be sufficient to control morbidity in children and women: the delivery once a year of albendazole (with or without ivermectin) may need to be supplemented by treatment with one of the anthelminthics included in WHO's Model List of Essential Drugs (14). These treatments may be further integrated with delivery of praziquantel for the control of schistosomiasis. In areas where schistosomiasis and cysticercosis are co-endemic, community-based interventions need to be carried out with caution, as praziquantel at a dose of 40 mg/kg body weight may increase peri-cystercal inflammation.

5.8 Opportunities to integrate control of schistosomiasis and soil-transmitted helminthiasis in other public health interventions

Every opportunity should be taken to integrate measures for controlling morbidity due to soil-transmitted helminthiasis and schistosomiasis into existing public health programmes. Indeed. helminth control activities may actually enhance the value of programmes aimed at the delivery of food and micronutrient supplements: iron supplementation, for instance, will be more effective if allied to deworming at regular intervals. Examples of programmes designed to improve the health of schoolchildren may be found in WHO's Information Series on School Health (41). Antenatal and mother and child health programmes also offer important opportunities for helping to reduce anaemia through deworming.

5.9 Environmental sanitation, control of health hazards, and health education

5.9.1 Environmental sanitation

Since the early 1960s, when the impact of a large dam (the Akosombo Dam/Lake Volta in Ghana) on schistosomiasis was documented for the first time, there have been numerous studies and reports on the adverse impacts of water resources development on health. The consequences for

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schistosomiasis of the Aswan Dam in Egypt and the Diama Dam and Manantali Dam in the Senegal River basin stand out particularly. Irrigation schemes too, while boosting agricultural production and food security, have had an impact on health by creating snail habitats – compounded in some cases by a failure to provide adequate sanitation and access to safe water for local communities. In fact, there are few irrigation schemes that have successfully incorporated health safeguards: the Blue Nile Health project in the Sudan and the rehabilitated Mushandike Irrigation scheme in Zimbabwe are rare examples.

By 2000, some 45 000 large dams had been built worldwide, of which 90% were completed in the second half of the 20th century. In China alone 22 000 large dams are operational, and 80% of the world's large dams are located in China, India, Japan, Spain, and USA. Globally, the rate of large dam construction has slowed, with 160–320 being completed each year compared with more than 1000 a year between 1970 and 1975, but there is a distinct shift towards construction in developing countries (42). Currently, there are about 1100 large dams in Africa. These figures take no account of the tens of thousands of small dams built for agricultural irrigation and to supply drinking-water and water for livestock; the cumulative effect of these on schistosomiasis transmission may be greater than that of one large dam retaining a similar volume of water. It is expected that dam building will increase in Africa south of the Sahara – the area with the greatest risks for the spread and intensification of schistosomiasis.

WHO, often in conjunction with other agencies such as the Food and Agriculture Organization of the United Nations and the United Nations Environment Programme, has long advocated early consideration of health in the planning and design of water resources development and of environmental management for vector and snail control. In its submission to the World Commission on Dams (43), WHO defined three principles that are fundamental in dealing with the association between water resources development and human health:

- **Equity.** The benefits of water resources development are not disputed, but the uneven distribution of benefits (including health benefits), and of health risks to vulnerable groups, needs to be addressed in the planning, construction, and operation of such projects.
- **Economics.** Negative health impacts of water resources development represent a hidden cost to the health sector whose resources are, as a rule, already over-stretched.
- **Sustainability.** The economic returns from investments in water resources development will suffer substantially from the ill-health of local communities, with no sustainability at all in extreme cases where dramatic health impacts force people to move away.

Two areas in which ministries of health, in an intersectoral context, could strengthen their performance are health impact assessment and environmental management to reduce the risk of transmission. In this connection, schistosomiasis prevention can play a pathfinder role because engineers and water resources professionals have a relatively high level of awareness and understanding of the disease.

5.9.2 *Health impact assessment*

Health impact assessment (HIA) should be carried out in close association with, but distinct from, environmental assessment, because it considers changes in both environmental and social determinants of health. Its recommendations should first address mitigating actions to be taken by the instigator of a water resources project and the opportunities for promoting health within the context of the project. Any residual health issues should be dealt with by strengthening of health services.

If HIA is to become an integral part of water resources development, three elements require attention:

- **Policy adjustment.** The development policies of sectors other than health should take account of health considerations and the need for an early HIA in project planning; all sectors should adopt a policy of intersectoral coordination and action.
- **Skills development.** Programme managers in the various ministries need to acquire the skill necessary to participate in intersectoral dialogue on development planning and to negotiate responsibilities and resource allocations for health safeguards.
- **Strengthening ministries of health.** Ministries of health need to strengthen, or establish, a unit that can take responsibility for the health sector's role in HIA (formulating terms of reference, appraising HIA reports), negotiating with other sectors, and providing health information in a form that other sectors can use. This can be, but does not have to be, an environmental health unit.

5.9.3 *Best practice*

Good environmental management practice with regard to reducing the risk of schistosomiasis transmission depends on measures dealing with dam design, reservoirs, irrigation design and water management, and human settlements. The following measures, adapted from the list in WHO's submission to the World Commission on Dams (*43*), are suggested for consideration:

- **Dam design**
  Diameters of take-offs sufficiently large to allow a rapid draw-down of reservoir water level to leave snails stranded to dehydrate.

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Construction of dams on one river basin to allow for optimal management of reservoir levels.

- **Reservoirs**
  Shoreline management to eliminate shallow areas suitable for aquatic vegetation/snail breeding.
  Construction of jetties and piers to reduce water contact for fishing communities.
  Regular clearance of aquatic weeds in shoreline transmission foci.

- **Irrigation design**
  Lining of canals to speed up water flow and dislodge snails.
  Installation of self-draining hydraulic structures.
  Sufficiently steep canal gradients to avoid standing water when the system is dry.
  Exclusion of high-risk structures such as duck-bill weirs and night-storage dams.
  Incorporation of effective drainage system.
  Replacement of irrigation and drainage canals by underground pipes.
  Selection of a low-health-risk irrigation system – sprinkler, drip, or central pivot irrigation.

- **Irrigation water management**
  Clearance of aquatic weeds from drainage canals.
  Maintenance of minimum water speeds in canals to prevent snail lodging.
  Where possible, regular flushing of stretches of canals with transmission foci to dislodge snails.
  Rotational irrigation and drying of different sectors of an irrigation scheme.
  Focal application of molluscicides in very specific situations.

- **Human settlements**
  Siting settlements away from potential transmission foci.
  Provision of access to safe drinking-water and adequate sanitation in settlements.
  It is also important to ensure that health centres are fully equipped and functional before a dam is constructed and that health personnel can detect, and deal with, emerging health problems.

5.9.4 *Health education*

For all communities, health education is recommended as a first step towards creating an enabling environment in which other strategies can thrive. It is expected to improve people's knowledge of the causes, prevention, and treatment of endemic diseases, to encourage community

participation in control programmes, to modify beliefs, customs, and disease-causing habits and taboos, and to promote sanitary behaviours and use of proposed control measures. Health education can be incorporated into the primary health care system and linked to deworming programmes in schools. Tools such as the mass media (radio, television, newspapers), posters, and public enlightenment campaigns (using cinema, theatre, primary health care personnel, and school-based educators) have all been used at times to prepare communities for helminth disease control. However, there is less information about the effects of these different health education tools on disease control than there is about the effects of sanitation.

6. Operational approaches to elimination of schistosomiasis in areas where sustained control has led to low endemicity

Sustained control efforts may reduce endemicity to a level at which disease is no longer a public health issue. New control objectives then need to be formulated with a view to elimination, and new approaches – defined according to local circumstances – should be adopted.

Where the aim is *elimination* of disease, case-detection may be a problem if the commonly used clinical and parasitological diagnostic procedures are not sufficiently sensitive. Approaches must then be modified to incorporate more sensitive diagnostic techniques. Currently available antibody and antigen assays could be used for the diagnosis of schistosomiasis in low-transmission areas (in China, for example), but new antigen assays suitable for field use are needed. Regardless of available technology, it is essential that programme managers maintain enthusiasm for case-finding and treatment.

As endemicity falls, sustainable control of transmission should become the major consideration, based on hygiene and sanitation improvements and snail control. These measures will not only help to prevent a resurgence of schistosomiasis, but will also build on health improvement already achieved.

Globally, it is possible to identify three different conditions in areas where concerted efforts to control schistosomiasis have resulted in low endemicity:

— transmission still present
— low transmission but a significant risk of re-emergence as a consequence of population movements and/or environmental change
— little or no risk of re-emergence.

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However, no two situations are identical and each merits individual consideration. In particular, it is essential that control efforts do not overlook the possibility of zoonotic reservoirs of infection.

In low-transmission areas, resources may be more cost-effectively used if central authorities delegate the implementation of schistosomiasis control to regional authorities. This will require greater reliance on established health and education resources: training and transfer of expertise from central to peripheral levels will be essential. Integration of control activities with services that deal with hygiene and hygiene-related diseases will result in greater benefits to health overall. Moreover, integration of schistosomiasis control with activities for the control of other diseases, particularly if new and more sensitive diagnostic tests can be made available, is likely to increase the motivation of the personnel concerned. Motivation and skills retention can also be enhanced, and other local priority health issues supported, by "cross-training" of laboratory staff, i.e. training staff in the control of several diseases.

Where surveillance and a capacity for rapid reaction are major issues, it is important that control activities are implemented through existing structures, such as the health service, and complemented by surveys in high-risk populations. Operational decisions need to be based on sound geographical knowledge of high-risk areas, and planning and management therefore need to be flexible. A combined approach with other diseases is also useful here for determining comprehensive local control and surveillance measures. There should be no let-up in surveillance until the risk of resurgence has diminished substantially; snail survey data are essential to indicate the potential for a resurgence in schistosomiasis. Operational research may be needed to allow control and surveillance activities to be adapted to local circumstances and to changing situations.

Schistosomiasis is not currently a target for global eradication or elimination, nor has WHO established a standardized certification process, which would involve the establishment of an international commission and the definition of standard criteria by which a country or area would be certified as no longer endemic for the disease. Indeed, the fact that asymptomatic cases are common and that there are animal reservoirs of some schistosome species would make the definition of criteria for elimination particularly complex. Moreover, interruption of transmission may be achieved in different ways – elimination of the parasite by drug treatment, control of the snail intermediate host, and interruption of contact with infected water. The risk of reintroduction of the disease into an area from which it has been eliminated, for example through water resource development or population movements, adds a further complication.

Documenting the fact that no new, locally contracted infections have been observed over an appropriate period is one means by which an individual country can demonstrate the elimination of schistosomiasis from its territory. The length of the observation period depends greatly on the risk of re-emergence or reintroduction of the infection in particular circumstances. Similarly, the degree of certainty that no new cases have been detected depends on the reliability of the surveillance system – the sensitivity of the diagnostic method used and the operational performance of the reporting system. If a country is concerned that elimination of schistosomiasis should be certified, a request should be made to WHO to convene an international commission to make an appropriate assessment.

In countries where morbidity has been significantly reduced but transmission continues, it is critical both to maintain active surveillance and to avoid the premature diversion of resources to other health priorities. With success in reducing endemicity comes the need to change treatment cut-offs and strategies. Where there has been repeated drug treatment over many years, active monitoring for the emergence of drug resistance is essential.

7. Recommendations

Policy issues

The Expert Committee recommends that:

1. Member States should ensure access to essential drugs for the treatment of schistosomiasis and soil-transmitted helminthiasis in all health systems in all endemic areas.

2. Member States should ensure that a minimum of 75% of all school-age children living in areas of high endemicity for schistosomiasis and/or soil-transmitted helminthiasis are offered periodic drug treatment. Other groups at high risk of morbidity should also be offered regular drug treatment.

3. Member States should integrate operational control programmes for schistosomiasis and/or soil-transmitted helminthiasis into existing primary health care systems and continue active surveillance and treatment in all endemic areas. Health education, safe water supplies, sanitation, and – for schistosomiasis – snail control should remain important elements in prevention and control. In the longer term, environmental sanitation and infrastructural strengthening should aim for interruption of transmission.

4. Member States should work to reduce the risks of schistosomiasis and other public health problems associated with development and management of water resources (dams, irrigation, reclamation projects). Policy frameworks and other capacities for intersectoral dialogue and action should be developed. Health impact assessment methods should be institutionalized as part of the planning process. Best practice in environmental management, hygiene education, and appropriate and targeted sanitation should be promoted in affected communities.

Technical issues

The Expert Committee recommends that:

5. WHO should consider convening an Informal Consultation as a matter of urgency to evaluate the risk–benefit of treating pregnant and lactating women with praziquantel for schistosomiasis and to make recommendations regarding such treatment. In addition, the Consultation should evaluate the risk–benefit of treating children under the age of 2 years with albendazole or mebendazole for soil-transmitted helminthiasis, and should make recommendations regarding such treatment.[1]

6. A mechanism should be established for monitoring the quality of anthelminthic drugs.

7. Methods should be developed for the detection, monitoring, and prevention of drug resistance in schistosomes and soil-transmitted helminths.

8. WHO should urge the pharmaceutical industry to develop and market new drugs for the treatment of schistosomiasis and soil-transmitted helminthiasis.

9. In response to concerns about an apparent underestimation, WHO should recalculate DALYs lost due to schistosomiasis, taking into account mortality, severe morbidity specific to schistosomiasis (hepatic fibrosis, urinary obstruction), and "subtle" morbidity (anaemia, growth stunting) in which schistosomiasis is a significant contributory factor.

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[1] Since the meeting of the Expert Committee and the preparation of this report, WHO has convened the recommended Informal Consultation. The reader is referred to *Report of the WHO Informal Consultation on the Use of Praziquantel during Pregnancy/Lactation and Albendazole/Mebendazole in Children under 24 Months* (document WHO/CDS/CPE/PVC/2002.4), which is in preparation.

Topics for research

10. The Expert Committee recommends research in the following areas:

- Development of effective and efficient strategies for health-system-based control and drug delivery. For example, improved passive case-detection or systematic outpatient treatment, and assessment of its long-term impact on morbidity.
- Development of tests for rapid assessment of the prevalence of intestinal schistosomiasis in areas of high endemicity.
- Development of more sensitive and specific diagnostic tools for use · in areas of low schistosomiasis endemicity.
- The efficacy and safety of increased doses of single drugs against *Trichuris trichiura*, and the use of drug combinations that increase efficacy while sustaining compliance. Also, the possibilities of increasing the single dose of praziquantel to 60 mg/kg or more while avoiding side-effects and maintaining compliance.
- The usefulness of prevalence of schistosomiasis and soil-transmitted helminthiasis as an indirect indicator of poverty and poverty-related diseases.
- The impact of soil-transmitted helminth and schistosome infections on anaemia, cognitive development, educational achievements of schoolchildren, and worker productivity.
- Development of effective and practicable measures of (micro-)focal transmission control – including mapping, use of molluscicides, environmental management, and ecotoxicology.
- Improved methods of collecting data as a basis for local decisions on how to target and implement deworming programmes.
- Prospective randomized trials of the impact of repeated deworming on susceptibility to viral and bacterial infections and on the effectiveness of vaccines in routine child immunization programmes.
- Development of vaccines against hookworm and other nematodes and the schistosomes, as well as animal vaccines to control transmission of *Schistosoma japonicum*.

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Annex 1

World Health Assembly resolution WHA54.19 Schistosomiasis and soil-transmitted helminth infections

The Fifty-fourth World Health Assembly,

Recalling resolutions EB5.R5, WHA3.26, EB55.R22, WHA28.53 and WHA29.58 on schistosomiasis;

Noting the report on the control of schistosomiasis and soil-transmitted helminth infections;

Recognizing that where control measures have been implemented in a sustainable way, as demonstrated in several countries, mortality, morbidity and transmission have decreased dramatically, leading to elimination in a number of countries;

Expressing concern that 2000 million people are infected by schistosomes and soil-transmitted helminths worldwide, of whom 300 million have associated severe morbidity, and that schistosomiasis and soil-transmitted helminth infections are invariably more prevalent in the poorest sections of the populations residing in the least-developed countries;

Further recognizing that sanitation and safe water are essential, and that repeated chemotherapy with safe, single-dose, affordable drugs at regular intervals ensures that levels of infection are kept below those associated with morbidity, and improves health and development, especially of children,

1. ENDORSES as the best means of reducing mortality and morbidity and improving health and development in infected communities, the regular treatment of high-risk groups, particularly school-age children, and ensured access to single-dose drugs against schistosomiasis and soil-transmitted helminth infections in primary health care services, complemented by the simultaneous implementation of plans for basic sanitation and adequate safe water supplies.

2. URGES Member States:
   (1) to sustain successful control activities in low-transmission areas in order to eliminate schistosomiasis and soil-transmitted helminth infections as a public health problem, and to give high priority to implementing of intensifying control of schistosomiasis and soil-transmitted helminth infections in areas of high transmission while monitoring drug quality and efficacy;

(2) to ensure access to essential drugs against schistosomiasis and soil-transmitted helminth infections in all health services in endemic areas for the treatment of clinical cases and groups at high risk of morbidity such as women and children, with the goal of attaining a minimum target of regular administration of chemotherapy to at least 75% and up to 100% of all school-age children at risk of morbidity by 2010;

(3) to promote access to safe water, sanitation and health education through intersectoral collaboration;

(4) to ensure that any development activity likely to favour the emergence or spread of parasitic diseases is accompanied by preventive measures to limit their impact;

(5) to mobilize resources in order to sustain activities for control of schistosomiasis and soil-transmitted helminth infections;

3. ENCOURAGES organizations of the United Nations system, bilateral agencies, and nongovernmental organizations:

(1) to intensify support for control of helminth infections, and to take advantage of the synergy that can be created with existing initiatives for the prevention, control and elimination of other communicable diseases;

(2) to intensify support to sanitation and safe water programmes as well as taking into account the health aspects of agricultural development programmes and programmes to develop water resources with respect to the possible re-emergence of diseases;

4. REQUESTS the Director-General:

(1) to combat schistosomiasis and soil-transmitted helminth infections by advocating new partnerships with organizations of the United Nations system, bilateral agencies, nongovernmental organization and the private sector, and by continuing to provide international direction and coordination;

(2) to continue to seek the resources required to support advocacy, coordination, programmes and research activities;

(3) to continue to promote the strengthening of health systems and services as an important component of successful disease control programmes;

(4) to keep the Executive Board and Health Assembly informed of the progress made in controlling or eliminating schistosomiasis and soil-transmitted helminth infections in high- and low-transmission countries, respectively.

Annex 2

Glossary of key terms and abbreviations

This glossary provides brief definitions of terms and abbreviations used in the report; they may have different meanings in other contexts.

community
A group of people living in a particular area or ecological zone.

cure rate
The number (usually expressed as a percentage) of previously positive subjects found to be egg-negative on examination of a stool or urine sample using a standard procedure at a set time after deworming.

DALY
The "disability-adjusted life year" (DALY) concept is based on the definition, by patients in their particular socioeconomic context, of "disability weights" (0 = healthy; 1 = death) for different conditions, and weighting of further years further lived with a disability to calculate years lost due to the disability.

A major challenge facing public health planners is to place problems in an order of priority for action. The introduction of the DALY is considered to be a useful approach for estimating disease burdens in a quantitative and comparative manner. The Expert Committee wished to draw attention to the fact that some infections, such as schistosome and soil-transmitted helminth infections, frequently occur concurrently in the same person. Moreover, the severity of a helminth infection may be complicated by poor nutrition and other adverse factors. DALYs do not take this into account. Estimates of DALYs must be kept under regular review and should be expected to change as information on morbidity and interaction of diseases improves.

deworming
Use of anthelminthic drugs in an individual or in a public health programme.

drug resistance
A genetically transmitted loss of susceptibility to a drug in a worm population that was previously sensitive to the appropriate therapeutic dose.

ecological zone
A zone reflecting homogeneity in the distribution of a worm species or its intermediate host. This depends on a number of variables such as topography, soil type, altitude (temperature), rainfall, and frost.

ED$_{50}$
The drug dose (effective dose) that reduces the worm count by 50% in treated patients compared with non-treated controls.

effectiveness
A measure of the effect of a drug against a worm infection under operational conditions.

efficacy
A measure of the effect of a drug against a worm infection in isolation under ideal conditions.

egg reduction rate (ERR)
The percentage fall in egg counts after deworming based on examination of a stool or urine sample using a standard procedure at a set time after the treatment.

elimination
A reduction to zero of the number of new cases of a specific infection in a defined geographical area, as a result of deliberate efforts. Continued intervention or surveillance measures are required.

environmental management
The planning, organization, performance, and monitoring of activities for the modification and/or manipulation of environmental factors or their interaction with human beings with a view to preventing or minimizing vector or intermediate host propagation and reducing contact between humans and the infective agent.

environmental sanitation
Interventions to reduce environmental health risks, including the safe disposal and hygienic management of human and animal excreta, refuse, and wastewater; the control of vectors, intermediate hosts, and reservoirs of disease; the provision of safe drinking-water; food safety; the provision of housing that is adequate in terms of location, quality of shelter, and indoor living conditions; the provision of facilities for personal and domestic hygiene; and the provision of safe and healthy working conditions.

eradication
A permanent reduction to zero of the world-wide prevalence of infection caused by a specific agent, as a result of deliberate efforts. Continued measures are no longer required.

HIA
Health impact assessment.

incidence
The number of new cases of infection appearing in a population in a given period of time.

intensity
The number of worms (measured directly or indirectly) per infected person (worm burden).

morbidity
Clinical consequences of infections or diseases that affect an individual's well-being.

morbidity control
Avoidance of illness caused by worm infections. It is achieved by periodically deworming individuals and groups, known to be at risk of morbidity.

prevalence
The number (usually expressed as a percentage) of individuals in a population estimated to be infected with a particular species of worm at a given time.

PZQ
Praziquantel

risk group
Those identified to be at risk of morbidity and mortality as a result of infection with schistosomes and soil-transmitted helminths. Such groups include preschool children, school-age children, pregnant women, and workers in particular occupations (e.g. miners and tea-pickers for hookworms; for schistosomiasis, individuals whose work involves contact with fresh water).

sanitation
The provision of access to adequate facilities for the safe disposal of human excreta, usually combined with access to safe drinking-water.

school-age children
Children aged between 6 and 15 years who may or may not be enrolled in school.

sentinel information system
Information system based on a limited number of *sentinel sites* periodically reporting on a defined list of topics. A *sentinel network* keeps a watchful eye on a sample of the population by supplying regular and standardized reports.

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treatment strategies

- *selective*

  Individual-level deworming with selection for treatment based on a diagnosis of infection or an assessment of the intensity of infection, or based on presumptive grounds. This strategy can be used in whole populations, or in defined risk groups.

- *targeted*

  Group-level deworming where the (risk) group to be treated (without prior diagnosis) may be defined by age, sex, or other social characteristics, irrespective of infection status.

- *universal*

  Population-level deworming in which the community is treated irrespective of age, sex, infection status, or other social characteristics.

Annex 3

Pole for dosing praziquantel in sub-Saharan Africa

The tablet pole with the height thresholds shown in the diagram below has been tested on 25 688 individuals in 10 sub-Saharan African countries.[1] In more than 98% of cases, a dose of between 30 and 60 mg/kg was indicated by this method, which is within the dose range that is both effective and safe.

70 inches —	— 178 cm
63 inches —	— 160 cm
59 inches —	— 150 cm
54 inches —	— 138 cm
49 inches —	— 125 cm
43 inches —	— 110 cm

The pole has be propped vertically against a wall, and each individual classified, according to his or her height, in one of the 5 intervals corresponding to a number of PZQ tablets. For example, the person in the above diagram needs 2 tablets of praziquantel

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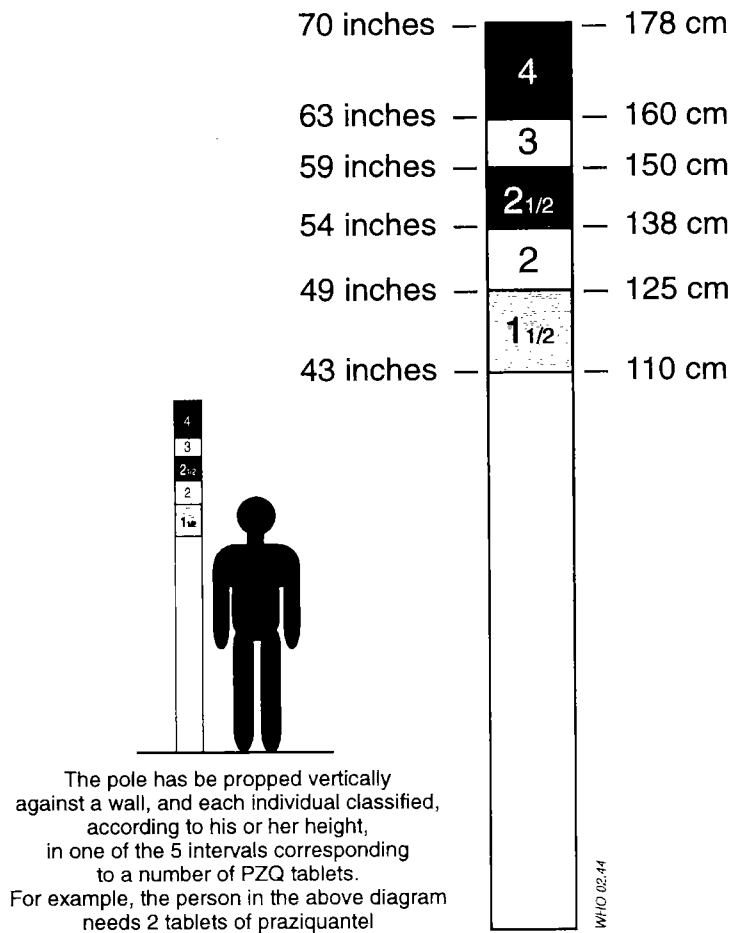
[1] Montresor A et al. Development and validation of a "tablet pole" for the administration of praziquantel in sub-Saharan Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2001, 95:542–544.

Annex 4

Example of a rapid assessment questionnaire for urinary schistosomiasis[a]

Put a mark: √ for "yes", ○ or "no", and — if the child does not remember or cannot answer. Answer the following questions. Each column if for one child only. If there are not enough boxes on one page, use the back of the page. Return the questionnaire to the head teacher. Thank you.

Name of school _____   Class _____ (use only for Classes I, III, and V)

Pupils	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
Age																																			
Sex																																			

Question 1   Which of the following symptoms did you experience during the past month? Put a mark √ or ○ or – in the boxes in front of corresponding symptoms.

Coughing																																			
Itching																																			
Headache																																			
Fever																																			
Abdominal pain																																			
Blood in urine																																			
Blood in stool																																			
Diarrhoea																																			

Question 2   Which of the following diseases did you experience during the past month? Put a mark √ or ○ or – in the boxes in front of corresponding symptoms.

Malaria																																			
Diarrhoea																																			
Eye diseases																																			
Schistosomiasis																																			
Respiratory infection																																			
Worms																																			
Abdominal problems																																			

[a] As used in primary schools of Kilosa District, United Republic of Tanzania.