Intervention for the Control of Soil-Transmitted Helminthiasis in the Community

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ABSTRACT

The global strategy for the control of soil-transmitted helminthiasis, based on regular anthelminthic treatment, health education and improved sanitation standards, is reviewed. The reasons for the development of a control strategy based on population intervention rather than on individual treatment are explained. The evidence and experience from control programmes that created the basis for (i) the definition of the intervention package, (ii) the identification of the groups at risk, (iii) the standardization of the community diagnosis and (iv) the selection of the appropriate intervention for each category in the community are discussed. How to best deliver the appropriate intervention, the impact of the control measures on morbidity and on indicators such as school attendance, cognitive development and productivity are presented. The factors influencing the cost–benefits of helminth control are also considered. The recent progress on the control of soil-transmitted helminth infections is illustrated. Research needs are analysed in relation to the most recent perceptions from private–public partnerships involved in helminth control. The way forward for the control of soil-transmitted helminth infections is described as a multi-disease approach that goes beyond deworming and fosters a pro-poor strategy that supports the aims of the Millennium Development Goals.

1. POPULATION-BASED INTERVENTIONS TO CONTROL SOIL-TRANSMITTED HELMINTHIASIS

Ascaris lumbricoides, Ancylostoma duodenale, Necator americanus and Trichuris trichiura constitute the major soil-transmitted helminth (STH) infections. Disease due to these infections is now recognized as a serious public health problem wherever suitable environmental
conditions co-exist with inadequate sanitation and poor hygiene. In such conditions, STH infections are normally highly prevalent with 2 billion people infected worldwide and several million suffering from the chronic debilitating morbidity (Crompton, 1999, 2000; de Silva et al., 2003).

The World Health Organization (WHO) promotes the combined control of soil-transmitted helminthiasis and schistosomiasis where both these infections are endemic (WHO, 2002a). Schistosomiasis and soil-transmitted helminthiasis present some similarities in terms of geographical distribution, epidemiology, groups at high risk and control interventions. Although this article focuses on the control of soil-transmitted helminthiasis, it should be noted that where the two infections are often co-endemic, combined control greatly increases impact and cost-effectiveness, and is strongly recommended where appropriate.

The WHO has identified the population-based approach as the main strategy for the control of mortality and morbidity due to STH infections, for the following reasons:

- The clinical appearance of STH infection often lacks specific symptoms and may not be recognized by the infected person, even when causing significant health damage. When control measures are limited to curative services, only a small fraction of the infected population receives appropriate treatment.
- Individual diagnosis is relatively expensive requiring the availability of microscopes, laboratory material and trained personnel. The cost of establishing and maintaining an efficient STH diagnosis facility at peripheral level is much more expensive than the cost of treatment, now available for a few US cents per dose (WHO, 2002a).
- Identifying risk is usually based on parasitological data that classify communities according to the risk of developing morbidity. To overcome the paucity of epidemiological information, environmental information can be used to predict the large-scale distribution of infection (Brooker et al., 2002a). Epidemiological assessments can be undertaken in a limited number of communities in order to collect reliable data for risk identification and then select and monitor the appropriate intervention (Brooker et al., 2002b; Montresor et al., 2002).
Drugs used in population-based interventions for the control of STH have a secure safety record. The drugs are given orally and, because they are usually poorly absorbed, they reach and kill the parasites in the digestive tract causing negligible side effects. Two WHO Informal Consultations have recommended treatment with anthelminthics of pregnant women after the first trimester (WHO, 1996) and of children over 1 year of age (WHO, 2002b) to improve the health and development of these two high-risk groups in endemic countries.

Delivering population-based interventions for the control of STH requires minimal infrastructure. Owing to the safety profile of WHO-recommended anthelminthics, non-medically trained personnel can safely and effectively distribute the drugs after instruction (WHO, 2002a; Urbani and Albonico, 2003). Distribution by school-teachers is particularly well accepted by the community (Nwaorgu et al., 1998; Partnership For Child Development, 2001).

The morbidity caused by STH is directly related to the number of worms (intensity of infection) and the duration of infection. Infections of moderate to heavy intensity are mainly responsible for the morbidity due to STH. Regular treatment reduces the number of worms in each individual and keeps the worm burden permanently low throughout the year. Regular treatment, despite re-infection, is able to control morbidity in high-transmission areas (Savioli et al., 2002) because, even if prevalence of infection remains high, moderate to heavy infections (responsible for morbidity) decline over time (Figure 1).

The use of anthelminthic treatment is no longer limited to the clinical domain; it has become the intervention for large-scale prevention and reduction of morbidity in endemic communities.

2. INTERVENTION PACKAGE

Three interventions are recommended by WHO to control morbidity due to STH infections: (i) regular drug treatment of high risk groups, aimed at reduction of the worm burden over time; (ii) health education to increase population health awareness; (iii) sanitation
supported by personal hygiene aimed at reducing soil contamination with infected human faeces and the likelihood of re-infection (WHO, 2002a).

An appropriate combination of these three measures should be applied according to different epidemiological situations and to the availability of resources.

### 2.1. Regular Anthelminthic Treatment

Regular drug treatment represents the main measure in areas where infections are intensely transmitted, where resources for disease control are limited, and where funding for sanitation is insufficient.

Drug treatment can be administered in the community using different strategies:

- **Universal treatment.** Treatment is offered to the entire community, irrespective of age, sex, infection status and any other social characteristics.

![Figure 1](image-url)  
*Figure 1* Effects of periodical treatment with mebendazole on total prevalence and prevalence of moderate–heavy *T. trichiura* infections. (Montresor *et al.*, unpublished data from the control programme in Zanzibar, United Republic of Tanzania.)
• *Targeted treatment.* Treatment is targeted at population groups, which may be defined by age, sex or other social characteristics, irrespective of the infection status.

• *Selective treatment.* Individual-level application of anthelminthic drug administration, where selection is based on diagnosis to detect the most heavily infected people who will be most at risk of serious morbidity and mortality.

The selection of the distribution strategy and the frequency of treatment is based on analysis of available epidemiological data.

Recommended drugs *(WHO, 2004a)* for use in public health interventions to control STH infection are:

- Albendazole (400 mg) tablets given in single dose, reduced to 200 mg for children between 12 and 24 months.
- Levamisole (40 mg) tablets given in single dose by weight (2.5 mg/kg). Levamisole at a dose of 80 mg has been successfully used in primary school-age children *(Albonico et al., 2003)*.
- Mebendazole (500 mg) tablets given in single dose.
- Pyrantel pamoate (250 mg) tablets given in single dose by weight (10 mg/kg). A combined preparation of pyrantel–oxantel has been proved more effective than pyrantel alone in treating *T. trichiura* infection *(Albonico et al., 2002)*.

These drugs are have undergone extensive safety testing and have been given to millions of individuals with only minimal adverse events *(Horton, 2000; Urbani and Albonico, 2003)*. Anthelminthics can now be safely used in children as young as 12 months *(Montresor et al., 2003; WHO, 2002b)*. Drugs that do not need dosage according to weight, such as albendazole, mebendazole and levamisole (in school-age children) are considered easier to use for population-based interventions *(de Silva et al., 1997)*. All these drugs produce excellent egg reduction rates for *A. lumbricoides* (>95%) and for hookworms (>80%), but are less effective against *T. trichiura* *(WHO, 1999; Bennet and Guyatt, 2000)*. The efficacy of single-dose anthelminthics is summarized in Table 1.

The patents of the anthelminthic drugs recommended by WHO have expired and therefore the drugs can be produced at very low
### Table 1  Recommended drugs for the treatment of soil-transmitted nematode infections in public health

<table>
<thead>
<tr>
<th>Substance</th>
<th>Therapeutic activity</th>
<th>Dosage</th>
<th>Use in pregnancy and in children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albendazole (tablet 200 and 400 mg, suspension 100 mg/5 ml)</td>
<td><em>A. lumbricoides</em></td>
<td>+ + + 400 mg single dose</td>
<td>Not recommended in the first trimester of pregnancy. In children between 12 and 24 months use 200 mg</td>
</tr>
<tr>
<td></td>
<td><em>T. trichiura</em></td>
<td>+ 400 mg single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hookworm infections</td>
<td>+ + + 400 mg single dose</td>
<td></td>
</tr>
<tr>
<td>Levamisole (tablet 40 mg, syrup 40 mg/5 ml)</td>
<td><em>A. lumbricoides</em></td>
<td>+ + + 2.5 mg/kg single dose (80 mg single dose in school-age children)</td>
<td>No evidence of teratogenicity</td>
</tr>
<tr>
<td></td>
<td><em>T. trichiura</em></td>
<td>+ 2.5 mg/kg single dose (80 mg single dose in school-age children)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hookworms</td>
<td>+ + 2.5 mg/kg single dose (80 mg single dose in school-age children)</td>
<td>For heavy necatoriasis repeat after 7 days</td>
</tr>
<tr>
<td>Mebendazole (tablet 100 and 500 mg, suspension 100 mg/5 ml)</td>
<td><em>A. lumbricoides</em></td>
<td>+ + + 500 mg single dose</td>
<td>Not recommended in the first trimester of pregnancy and in children under 1 year</td>
</tr>
<tr>
<td></td>
<td><em>T. trichiura</em></td>
<td>+ + 500 mg single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hookworms</td>
<td>+ + 500 mg single dose</td>
<td></td>
</tr>
<tr>
<td>Pyrantel (tablet 250 mg, suspension 50 mg/ml)</td>
<td><em>A. lumbricoides</em></td>
<td>+ + + 10 mg/kg single dose</td>
<td>Not recommended in the first trimester of pregnancy</td>
</tr>
<tr>
<td></td>
<td><em>T. trichiura</em></td>
<td>— 10 mg/kg single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hookworms</td>
<td>+ + 10 mg/kg single dose For heavy necatoriasis repeat for 3 days</td>
<td></td>
</tr>
</tbody>
</table>
price by generic manufacturers. The price in the international market for mebendazole (500 mg), produced under Good Manufacturing Practice conditions is approximately US$ 0.02 per tablet (Management Science for Health, 2004). The price is further reduced in case of local production, but in this case special attention should be given to assuring the good quality of the product. WHO, with a network of quality control laboratories, may facilitate the quality control exercise (Montresor et al., 2002).

2.2. Health Education

Health education aims to increase health and hygiene awareness and to change health behaviour in the population. Health awareness is usually increased when communication strategies of proven efficacy are adopted (Kinzie, 2005). Marketing techniques and tools imported from the private sector are increasingly being advocated for their potential value in crafting and disseminating health messages (Bull et al., 2001), but this technology should be appropriately transferred to reconcile differences between commercial marketing and public health (Walsh et al., 1993). Education materials (posters, leaflets, radio and video messages) have been traditionally used to transmit and disseminate health messages. The expansion of commercial advertising in developing countries, however, calls for upgraded skills in designing such tools in order to compete for attention (Bull et al., 2001; Whitelaw and Watson, 2005).

The adoption of safe behaviour is more difficult to obtain since it is not simply a direct consequence of the health awareness. Especially for diseases related to poverty such as STH infections, the suggested solution might not be available or too expensive to adopt. Although deprived communities understand the importance of the safe disposal of faecal matter and of wearing shoes, poverty often hinders the construction of latrines and the purchase of shoes.

For STH infections, the aims are: (i) to reduce the faecal contamination of the soil, by recommending the use of latrines, (ii) to develop self-protection from re-infection, through personal/family hygiene measures such as washing hands and proper food
preparation, and (iii) to avoid spraying night soil on vegetables in communities where this habit is common.

Frequently, in STH endemic areas, latrines are not available or not in sufficient number for the population needs (Cairncross, 2003), therefore the knowledge and motivation for behavioural change must be sustained with the availability of proper facilities for excreta disposal.

Providing information on the disease and the possible adoption of preventive measures frequently results in increase of knowledge but not necessarily in behavioural change (O’Cathain et al., 2002). Informed choice in the context of health care, competence (of patients to understand the problem) and the possibility of making a decision (availability of an alternative choice) are also necessary (Reeves, 2002).

Promotion of latrine maintenance and use, washing of hands and proper food handling have benefits that go beyond the control of STH infections. From this perspective, it is reasonable to include health education in all STH control programmes when the health education message can be provided in a simple and inexpensive way. Health education messages can be delivered by teachers in schools thereby fostering changes in health behaviour in children, which in turn involve their parents and guardians. On the other hand, intensive and sophisticated campaigns can represent the main cost for an STH control programme and impair significantly the cost-effectiveness of the control effort (Mascie-Taylor et al., 1999). The effectiveness of health education campaigns in increasing health awareness and changing defecation habits varies according to different reports (Guanghan et al., 2000; Lansdown et al., 2002).

2.3. Sanitation

Sanitation is composed of two elements, which are complementary: “hardware” such as toilets, latrines and sewage treatments, and “software” such as personal hygiene and legislation. Sanitation in the context of economic development is the only definitive intervention that eliminates STH infections. STH infections are never a public
health problem where hygiene and sanitation standards are appropriate. Improvement of the sanitation standard always has a repercussion on infection and reinfection levels. Studies from the West Indies showed that prevalence of STH infections were significantly lower in areas with improved sanitary conditions as was reinfection. Crowding and the type of excreta-disposal facility were the only significant predictors of reinfection (Henry, 1988). Similar results were obtained in urban slums of Bangladesh (Henry et al., 1993) and in the plantation sector of Sri Lanka (Sorensen et al., 1994).

Sanitation, however, does not become effective until it covers a high percentage of the population (Esrey et al., 1991). In Zimbabwe, despite the marked increase in the number of latrines, no relationship was found between hookworm reinfection intensities and the availability of latrines on individual farms (Bradley et al., 1993). The effect of improved sanitation on helminth transmission is slow to develop and may take decades to achieve a measurable impact. Often, the high costs involved, prevent the provision of sanitation to the communities most in need (Asaolu and Ofoezie, 2003).

In addition, latrine coverage is not a solution, unless the latrine is used and maintained. Studies in Senegal (Sow et al., 2004) demonstrated that, despite high latrine coverage, the majority of the children in a village, interviewed with a questionnaire, claimed to defecate elsewhere. Experience in Mozambique demonstrated that in areas with low latrine coverage, even in houses where a well-maintained latrine existed, the soil in the house-yard was contaminated (Muller et al., 1989).

On the other hand, an alternative model, which offers a market-based approach considers the rural poor as customers and not beneficiaries, and may accelerate access to sanitation, enhance sustainability and deliver services more efficiently. An international NGO recently launched a project to stimulate the acquisition and use of sanitation in rural areas of Viet Nam. A range of options that were appealing and affordable to potential customers was developed, the community’s willingness to pay was assessed and the perception of benefits of sanitation was promoted through media channels and tailored messages. Within a year coverage of sanitation access has increased by 100% compared with the pre-project access rate. This
success indicated that the population’s willingness to pay for sanitation is often underestimated, provided that quality product and services are offered with effective information (Mukherjee, 2005).

3. GROUPS AT RISK

3.1. Preschool Children

Children between 1 and 5 years of age are particularly vulnerable to disease caused by STH infections (Carrera et al., 1984; Oberhelman et al., 1998; Crompton and Nesheim, 2002). Though they are less likely to harbour heavy infections, such young children, whose worm burdens are housed in smaller bodies, are at higher risk of anaemia and wasting malnutrition (Awasthi and Pande, 2001).

The negative effect of STH infection on iron status and nutrition in non-immune children with light infections may be linked to an inflammatory-triggered cytokine response in “naive” children, and a consequent suppression of protein metabolism, appetite and erythropoiesis, and not only to iron and micronutrient loss (Stoltzfus et al., 2004).

3.2. School-Age Children

Children of primary school age (6–14 years) should be a major target for regular treatment, because they are the group that usually has the heaviest worm burdens for *A. lumbricoides* and *T. trichiura*, and are steadily acquiring hookworm infections. In addition, they are in a period of intense physical and intellectual growth and benefit most from deworming in terms of growth and school performance (Bundy et al., 1992; Crompton and Nesheim, 2002). Schoolchildren are the most accessible group to reach in countries where school enrolment rates are good (Partnership For Child Development, 1999) and even non-enrolled siblings could be effectively outreached by promoting advocacy through the schools (Montresor et al., 2001).
3.3. **Women of Childbearing Age**

Women between 15 and 49 years of age are susceptible to iron deficiency anaemia because of iron loss during menstruation and because of increased nutritional needs during pregnancy (Torlesse and Hodges, 2001; Nurdia et al., 2001). The problem is aggravated if they have diets low in bioavailable iron and if they suffer from hookworm infection. Hookworms feed on blood and iron deficiency is often the consequence of this activity. Hookworm infection invariably reaches peak intensity in this age group (Bundy et al., 1995a). Antenatal anthelminthic treatment in hookworm endemic areas is recommended for the control of maternal anaemia (WHO, 1996). The benefits of deworming after the first trimester far outweigh the health risks and result in improvements in maternal iron status, birth weight and perinatal survival (Christian et al., 2004).

4. **FREQUENCY OF TREATMENT**

Frequency of regular treatment should vary according to the intensity of transmission and rates of re-infection. These factors must be considered in relation to the resources available and the cost involved in drug purchase and distribution. When there are budgetary constraints it is more efficient to treat a greater proportion of the population less frequently than to treat a smaller proportion of the population more often (Evans and Guyatt, 1995). For *A. lumbricoides* infections, the most cost-effective option is to treat infrequently (every 2 years) when effectiveness is assessed in terms of reduced mean worm burden and reduction in disease prevalence, both in low- and high-transmission areas. In contrast, when prevalence reduction is used as the measure of effectiveness (prevalence recovers more rapidly than intensity), the most cost-effective option is to treat every 4 months in high-transmission areas and every year in low-transmission areas (Guyatt et al., 1993).

- Treatment frequency of twice or three times a year is effective in reducing morbidity in areas of intense transmission (prevalence
470% and more than 10% of infections of moderate or heavy intensity) such as in Zanzibar (Albonico et al., 1999b), Nepal (Khanal and Walgate, 2002) and Myanmar (Thein-Hlaing, 1989).

- In areas with a lower intensity of transmission (prevalence between 40% and 60% and less than 10% of infections of moderate and heavy intensity), for example in Oman (Idris et al., 2001), India (Chhotray and Ranjit, 1990) and Brazil (Machado et al., 1996), once-yearly intervention was found to be sufficient to reduce morbidity.

Based on these experiences and on logistic limitations, endemic communities are classified into three categories according to the levels of cumulative STH prevalence and intensity estimated in the population (Table 2). An indication of the epidemiological situation of the community can be estimated from the data collected in school-age children (Guyatt et al., 1999) and guidelines on how to conduct school surveys have been proposed by WHO (Montresor et al., 2002).

Each STH infection can be classified as being of light, moderate or heavy intensity according to the thresholds established by a WHO Expert Committee (WHO, 2002a) based on the number of STH eggs per gram of faeces (Table 2). Helminths in different areas of the world have different levels of egg output (Hall and Holland, 2000), so the thresholds proposed by WHO are not rigid and should be adjusted for the local situation. The appropriate population-based treatment strategies recommended for each category is illustrated in Table 3 (WHO, 2002a).

5. TARGETS

The World Health Assembly in 2001 endorsed a strategy for the prevention and control of schistosomiasis and soil-transmitted helminthiasis in high-transmission areas (WHO, 2001). In the short term, morbidity will be reduced by:

- access to drugs (praziquantel and broad-spectrum anthelmintics) and good case management in all health services;
Table 2  Community classification for soil-transmitted helminth infections

<table>
<thead>
<tr>
<th>Community category</th>
<th>Results of school survey</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prevalence of any soil-transmitted helminthiasis</td>
</tr>
<tr>
<td>I High prevalence or high intensity</td>
<td>$\geq 70%$</td>
</tr>
<tr>
<td>II Moderate prevalence and low intensity</td>
<td>$\geq 50%$ but $&lt; 70%$</td>
</tr>
<tr>
<td>III Low prevalence and low intensity</td>
<td>$&lt; 50%$</td>
</tr>
</tbody>
</table>

Note: Each community can be classified according to prevalence and (if available) intensity of infection. Intensity of infections are classified as below:

- *Ascaris lumbricoides*: Light 1–4999 epg; Moderate 5000–49999 epg; Heavy $> 50000$ epg
- *Trichuris trichiura*: Light 1–999 epg; Moderate 1000–9999 epg; Heavy $> 10000$ epg
- Hookworms: Light 1–1999 epg; Moderate 2000–3999 epg; Heavy $> 4000$ epg


Table 3  Recommended treatment strategies for soil-transmitted helminth infections

<table>
<thead>
<tr>
<th>Community category</th>
<th>Intervention in schools (enrolled and non-enrolled children)</th>
<th>Community-based intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Targeted treatment of school-age children, 2–3 times/year</td>
<td>Systematic treatment of preschool children and women of childbearing age in mother and child health programmes</td>
</tr>
<tr>
<td>II</td>
<td>Targeted treatment of school-age children, once per year</td>
<td>Systematic treatment of preschool children and women of childbearing age in mother and child health programmes</td>
</tr>
<tr>
<td>III</td>
<td>Selective treatment</td>
<td>Selective treatment</td>
</tr>
</tbody>
</table>

Note: These treatment strategies always need to be accompanied by efforts to improve water supply, sanitation, information, education and communication.


- regular treatment of at least 75% of school-age children by 2010;
- targeting other high-risk groups (young children, women of childbearing age and occupational groups) through existing public health programmes and channels.
For long-term sustainability, environmental health will be required including:

- improving access to safe water and sanitation;
- improved hygiene behaviour through health education.

Field experience has shown that 75% coverage is an attainable target even in areas where school enrolment rates are low (Montresor et al., 2001) and that a significant reduction in morbidity can be achieved in situations of intense transmission (Albonico et al., 1999a). Cambodia is the first country to have reached this target ahead of schedule and other countries such as Brazil, Equador, Nepal, Tanzania, Uganda and Viet Nam are on track to succeed.

6. DELIVERING THE INTERVENTION

Implementation of any helminth control programme at country level requires strong links with existing interventions that already target women and children. Deworming can readily be added to ongoing public health programmes.

6.1. Helminth Control through Schools

Helminth control in schools is reckoned to be a most cost-effective public health intervention in low-income countries (World Bank, 1993). Schools represent an ideal setting to reach children. Trained teachers can distribute and administer the drug and give health education messages to the pupils (Montresor et al., 2002). Schools can be used to reach non-enrolled school-age children with a simple child-to-child approach (Montresor et al., 2001). Deworming of school-age children requires minimal financial input (Partnership For Child Development, 1999) and gives notable nutritional and cognitive benefits. In addition, enrolment figures and school attendance normally increase after such interventions (Miguel and Kremer, 2001).

School feeding programmes help to break the interrelated cycles of hunger, illiteracy, poverty and disease, and serve as a platform for deworming and other interventions (World Food Programme, 2004).
Thirty countries worldwide now report active deworming combined with school feeding programmes. Almost 2 million children were reached in 2002, nearly 3 million in 2003, and over 7 million in 2004 (WHO, 2003a). STH control programmes rely strongly on volunteer personnel who are not remunerated but need basic training for distributing the drug. The safety profile of drugs distributed without the supervision of medical personnel must be explained. In case of any adverse events the child should be referred to the nearest health centre. Close collaboration between the Ministry of Education and Ministry of Health at all levels is mandatory for the success of deworming and other control measures such as health education through the school system.

6.2. Helminth Control through Community-Based Intervention

Recent experience demonstrates that many preschool children can be reached by adding deworming to vitamin A distribution or immunization campaigns. Worms and vitamin A deficiency thrive in impoverished communities where the two problems often co-exist. The advantage of adding deworming to vitamin A supplementation is the coverage opportunity: over 167 million children are reached yearly by vitamin A supplementation programmes worldwide and more than 50 countries report more than 70% coverage (UNICEF, 2005). Deworming has been found to increase the vitamin A supplementation coverage and worm-free children have a better vitamin A status than infected children (Curtale et al., 1995). Delivering deworming by using the vitamin A distribution infrastructure reduces costs and takes advantage of the access to remote communities that is already in place.

Nepal is successfully pioneering this approach. Deworming is now offered to children under 5 by using existing resources and the success of vitamin A distribution campaigns is being reinforced (Khanal and Walgate, 2002). Deworming is also being delivered during the National Child Health Days, a way of reaching children with a package of health measures including immunization and vitamin A
supplementation. A similar intervention is proving to be successful in Angola, Republic of Korea, Tanzania and Uganda (WHO, 2004b, 2005a). In Cambodia, the Ministry of Health uses monthly outreach services to deliver a minimum package of activities through health centres including immunization, antenatal care, health education, family planning, tuberculosis, leprosy care, vitamin A supplements and deworming (WHO, 2004b, 2005a).

Mother and Child Health (MCH) services offer opportunities to provide regular deworming for childbearing women and children over the age of 1 year (Savioli et al., 2003). The inclusion of routine deworming now reaches 75% of pregnant women in Sri Lanka (N.R. de Silva, personal communication). STH control measures can also be added to other public health initiatives including Integrated Management of Childhood Illness (IMCI), School Health Programmes, Roll Back Malaria, Micronutrient Initiatives and Reproductive Health—Making Pregnancy Safer.

7. IMPACT ON MORBIDITY

7.1. Preschool Children

Children under 5 experience the detrimental consequences of acute and chronic STH infections. Recent data from East Africa indicate that hookworms are an important cause of anaemia in preschool children (Brooker et al., 1999) and that regular distribution of anthelmintics has a positive effect on motor and language development in this age group (Stoltzfus et al., 2001). After 12 months of quarterly mebendazole treatment in Zanzibari children, mild wasting malnutrition was reduced by 62% in children <30 months, moderate anaemia (Hb <9 g/dl) was reduced by 59% in children <24 months, and appetite was improved by 48% in all 460 children (Stoltzfus et al., 2004). In India, Awasthi et al. (2000) found that when children aged between 1.5 and 3.5 years received vitamin A and albendazole every 6 months they gained 3.5 kg in 2 years, compared with 2.5 kg gained by children given vitamin A only. In Nepal, twice-yearly
distribution of vitamin A and albendazole to 2 million children under 5 reduced anaemia by 77% in 1 year (Mathema et al., 2004).

7.2. School-Age Children

Deworming school-age children has a considerable benefit on their nutritional status (Stoltzfus et al., 1996; Curtale et al., 1995), physical fitness, appetite, growth (Stephenson et al., 1993) and intellectual development (Partnership For Child Development, 2002). Although re-infection is inevitable where sanitation is lacking (Albonico et al., 1995), treatment three times a year with a single dose of 500 mg mebendazole prevented 1208 cases of moderate–severe anaemia and 276 cases of severe anaemia in the schoolchildren study population ($n = 30,000$) in Zanzibar (Stoltzfus et al., 1998).

Studies in low-income countries of Africa (Kvalsvig et al., 1991) and the Caribbean (Nokes et al., 1992) have shown that children with intense STH infections perform poorly in learning ability tests, cognitive function and educational achievement. Differences in test performance equivalent to a 6-month delay in development can be attributed to moderate/heavy $T.\ trichiura$ infections (Nokes and Bundy, 1994). Deworming schoolchildren assists their ability to learn. Tests have shown that a child’s short-term memory, long-term memory, executive function, language, problem solving and attention respond positively to deworming (Watkins and Pollit, 1997). Interestingly, girls display greater improvements than boys. For the most heavily infected children, their educational performance shows an improvement after treatment. For the less heavily infected, deworming may allow them to catch up with uninfected peers over the longer term (Nokes et al., 1992).

Deworming is usually followed by a significant reduction in school absenteeism. For example, Jamaican children enduring intense infections with $T.\ trichiura$ miss twice as many school days as their infection-free peers (Nokes and Bundy, 1993). A randomized trial in Kenya indicated that school-based targeted treatment with deworming drugs reduced school absenteeism in treated schools by 25% (Miguel and Kremer, 2001.)
7.3. Pregnant Women

Despite understandable concerns about the risk to the unborn child of offering deworming drugs to pregnant women, significant benefits follow for mother and infant when hookworm infections are reduced. A study in Sierra Leone demonstrated that a single dose of albendazole given to pregnant women after the first trimester helped to prevent the decrease in haemoglobin concentrations that continued to occur in the untreated group (Torlesse and Hodges, 2001). An analysis of over 7000 pregnancies in Sri Lanka reported that mebendazole therapy during pregnancy is associated with a significant improvement in birth weights, fewer stillbirths and perinatal deaths, and that there was no increase of birth defect rates compared to the untreated women (de Silva et al., 1999).

A controlled study in rural Nepal, where the prevalences of hookworm and Ascaris infection were roughly 70% and 50%, respectively, demonstrated that deworming greatly improves the health of pregnant women and the birth weight and survival of their infants. After albendazole treatment in the second trimester there was a significant decrease in the prevalence of severe anaemia in pregnant women, the birth weight of babies from mothers given two doses of albendazole rose on average by 59 g, and the infant mortality rate at 6 months had fallen by 41% (Christian et al., 2004). This work confirms that deworming should be considered as part of routine antenatal care in areas where hookworm infections are endemic. The Essential Care Practice Guide for Pregnancy and Childbirth (WHO, 2003b), which provides support to the Integrated Management of Pregnancy and Childbirth (IMPAC), recommends anthelminthic treatment for all pregnant women in the second and third trimester attending clinics if they did not receive such treatment in the last 6 months, and also treatment for all postpartum women.

Women in the first trimester of pregnancy are precautionally excluded from any treatment (including anthelminthic). In developing countries, this principle presents some problem of application because some women in the first trimester of pregnancy may not be aware of their pregnancies. Also the performance of pregnancy testing in all women of childbearing age before administering
anthelminthic treatment is not usually affordable. Adolescent girls who may be in early pregnancy while still at school and when the school is in a deworming scheme are a concern. Results from studies that have evaluated inadvertent deworming during the first trimester, however, have indicated that the risk of extra birth defects is negligible and that benefits in treating hookworm-induced iron deficiency anaemia both for the mother and the newborn far outweigh the risk of taking anthelminthic tablets in early pregnancy (de Silva et al., 1999; Torlesse and Hodges, 2001; Diav-Citrin et al., 2003; Christian et al., 2004).

7.4. Adults

Adult populations are also vulnerable to high-intensity hookworm infections. Studies conducted in rural China, Brazil and elsewhere reveal that the elderly often suffer from high intensity of hookworm infection and clinical hookworm disease with impairment of work productivity (Gandhi et al., 2001; Bethony et al., 2002). The relationship between STH infections and labour productivity has been studied in various settings, such as tea-picking communities in Asia (Gardner et al., 1977; Gilgen et al., 2001), road workers in Africa (Brooks et al., 1979; Wolgemuth et al., 1982) and rural communities in Latin America (Viteri and Torun, 1974). Iron deficiency anaemia, the hallmark of hookworm infection, is the major cause of weakness and fatigue in adults in endemic countries (Crompton and Nesheim, 2002). Not only do the infections significantly reduce the ability to sustain even moderate levels of labour, they also reduce the pace and time spent at work. STH control would increase country productivity and aid economic development (Guyatt, 2000).

8. COST OF THE INTERVENTION

The cost–benefits of the control measures for morbidity due to STH infection is influenced by the ecological and environmental situation, by the availability of local anthelminthic drug production, and by the
presence of infrastructures and facilities that can be used to reach the high-risk groups.

8.1. Regular Chemotherapy

Calculations indicate that a bundle of diseases, including schistosomiasis, soil-transmitted helminthiasis, onchocerciasis, lymphatic filariasis, trachoma and vitamin A deficiency, can be controlled at costs for drug and nutrients ranging from about US$ 1 to 2.50 per patient (Molyneux and Nantulya, 2004). Fenwick et al. (2005) estimated that a package of interventions could be provided at a cost of US$ 0.40 per person per year. The infrastructure for the delivery of such a package of health care to millions of poor people already exists in many endemic areas through primary health care provision, public and private schools, faith-based organizations and social institutions. In deprived communities, where sanitation is practically non-existent and the prevalence and intensity of infection are high, a suitable infrastructure (such as the school system or a national immunization day) should be used to distribute at least regular treatment to the groups at risk. The cost of adding this intervention is normally marginal.

Over 1.3 million preschool children were dewormed during the 2002 vitamin A distribution campaign in Nepal. The yearly cost of the vitamin A intervention is estimated at US$ 1.7 million (Fiedler, 2000). An additional expenditure of US$ 80,000 (about 4% of the cost of the vitamin A distribution) covered the cost of adding biannual deworming to the vitamin A campaign (Mathema et al., 2004).

Since 1998, the World Food Programme (WFP) has incorporated deworming in the School Feeding Programme (SFP) in Nepal and, in light of the nutritional consequences, decided to include deworming (including schistosomiasis control) in all the countries where SFPs are conducted (Bordignon and Shakya, 2003). Thirty countries now conduct combined deworming and school feeding programmes. The average cost per child per year is 70 US cents: 4 cents for mebendazole, 25 cents for praziquantel, 30 cents for training, monitoring and educational materials; and the remaining 11 cents for delivering both drugs (WHO, 2003a).
In Ghana with over 80,000 school-age children treated and Tanzania with over 100,000 school-age children treated, the estimated costs for school-based delivery of albendazole was US$ 0.04 and US$ 0.03, respectively (Partnership for Child Development, 1999).

In Cambodian schools, deworming is promoted by means of a school kit, which contains deworming tablets, health education posters and pamphlets for teachers, games and attractive pictures giving simple messages on how to prevent infection. The coverage of primary school-age children was 84% in 2003, and the biannual deworming campaign from 2004 onward is estimated to cost US$ 0.04 per child treated (Sinoun et al., 2005).

The advantage of regular deworming lies in its simplicity (one tablet per child), cheap delivery (by teachers through schools), and safety record (the benefits of treatment far outweigh the risk of minor side effects). Many organizations, including NGOs, could include an STH control package in their routine activities and, even with limited budgets, relieve the burden of STH in the population covered.

8.2. Health Education

The contribution of health education towards the control of STH infections and morbidity varies according to different reports. A randomized trial in 25 schools in Viet Nam did not find that intensive health education had any effect on the intensity of re-infection 6 months after treatment (Partnership For Child Development, unpublished results). Other authors observed increased levels of knowledge and improved health behaviour in the population (Lansdown et al., 2002), and measured a decrease in re-infection rates (Guanghan et al., 2000). Cost analysis of work in Bangladesh indicates that regular mass treatment with albendazole is the most cost-effective control strategy and strategies involving health education were the least cost-effective (Mascie-Taylor et al., 1999).

The importance of health education, however, should not be measured merely by cost-effectiveness alone. Health education, in community health, has the same role as the medical information and counselling given by the physician to the patient in clinical medicine.
The effects of establishing a good relationship between the health system and the community is not always directly measurable with regard to the success of the control measures. The effect of health education in community health includes improvement in loyalty and trust between the educators and the community. When such a relationship is established, the community is no longer a simple recipient of the medical intervention but becomes one of the partners in the health process.

8.3. Sanitation

The investment needed to provide access to adequate sanitation is beyond the resources of low-income countries. In addition, although improved water and sanitation contribute to reduce incidence of infection (Esrey et al., 1991), morbidity due to infection may persist (Asaolu et al., 2002). The coverage of properly built, used and maintained sanitation has to be higher than 90% to have any effects on worm transmission and critically depends on the general socioeconomic status of the community (Asaolu and Ofoezie, 2003).

A recent experience from STH control in Viet Nam, based on regular deworming, latrine construction and health education, has shown that the cost per child for each latrine has been estimated at US$ 7.9 (an amount equal to receiving over 200 doses of regular deworming). The building of new latrines was considered important as a good example for the schoolchildren and a way for providing essential sanitation at least in school. This intervention, however, increased the latrine coverage in each community of less than 1%. To have a significative impact (e.g. 20%) in the latrine coverage, an investment of US$ 50,000 is considered necessary in each community, and a total of over US$ 9 million for an entire province (Montresor, personal communication).

The magnitude of the problem of providing sewerage is a big challenge in large urban centres in developing countries. In Lagos, Nigeria, according to population projections, there may be an additional 1240 tons of human stool being deposited daily in the areas where the poor people live. The installation costs of modern sewerage
similar to the type found in developed countries for the poor population of Lagos could amount to a billion US dollars or more. Progress has been made in developing a variety of latrines for rural communities, but these may not be appropriate for slums and squatter settlements with a shortage of land for dwellings and at sea level (Crompton and Savioli, 1993).

The resources needed to improve hygienic standards can be huge, but the collaboration of different initiatives dealing with hygiene and prevention of diseases related to poor hygiene will help create the synergy needed to reduce both disease and poverty. A reliable evaluation of the advantage of investments in sanitation must include the consequences for other health services and for economic development. An efficient sanitation infrastructure removes the underlying cause of most poverty-related communicable diseases and so supports the economic development of a country.

9. NEW TECHNOLOGY FOR SUSTAINING DEWORMING

Regular chemotherapy with single-dose anthelminthic drugs will be the mainstay for control of morbidity due to helminth infection in endemic countries for several years. No new drugs have been recently developed, tested and registered and it is essential to make the best use of existing products. This is particularly important in the light of increasing drug resistance of nematodes of livestock to veterinary versions of anthelminthic products also used in human (Geerts and Gryseels, 2001). Recent evidence suggests reduced efficacy of benzimidazoles against hookworm infections in humans after 15 rounds of treatment (Albonico et al., 2003). Reduced efficacy after drug exposure and treatment failures are signs that drug resistance may emerge. Assessment and monitoring of efficacy of anthelminthic drugs in areas where they are commonly used should be performed in a standard way so as to warn of possible treatment failures and stimulate further investigations. In addition to the available measurement of reduction in faecal egg count following treatment, tests such as the Egg Hatch Assay have been developed to monitor benzimidazole efficacy against human hookworms (Albonico et al.,
The development of molecular probes with PCR techniques offers a more sensitive technique for drug efficacy monitoring (Roos et al., 1995). Research studies to identify sensitive and resistant genes in worm populations are still at an early stage in humans (Albonico et al., 2004).

The creation of a global network for monitoring anthelminthic drug efficacy and resistance, coordinating research efforts, and translating operational research outcome into health policy is a much-needed response to this emerging threat. Such a network will depend on action by different partners and dedicated funding. A successful example is the concerted action on the use of praziquantel for the treatment of schistosomiasis in Africa, which is funded by the European Union and involves a forum of scientists and public health planners (Hagan et al., 2004).

Combined treatment with two drugs with different modes of action or their alternate use are among the strategies used to safeguard efficacy and to delay the possible emergence of drug resistance. Combined treatment with mebendazole and levamisole has been proved safe and more effective than either drug alone (Albonico et al., 2003). A pyrantel–oxantel combination is more effective than benzimidazole drugs in curing *T. trichiura* infections (Albonico et al., 2002). Ivermectin and albendazole are effectively and safely given in combination in some countries as mass treatment to eliminate lymphatic filariasis and have ancillary benefits in controlling other helminthiases including strongyloidiasis (Belizario et al., 2003). Co-administration of praziquantel and albendazole is recommended where schistosomiasis and intestinal helminthiasis are endemic (Olds et al., 1999).

In addition to chemotherapy, a new hookworm vaccine against *N. americanus* infection is being developed and tested by the Human Hookworm Vaccine Initiative (Hotez et al., 2003). It is proposed that chemotherapy would be given first to treat existing cases and then a vaccine would be administered to prevent or to delay further re-infection. It is unlikely that a hookworm vaccine will interrupt transmission due to the heterogenicity in hookworm transmission and the need for a vaccine to provide protection for at least two-thirds of an individual’s lifetime (Anderson, 1982). The vaccine would decrease
the number of L3 larvae invading the gastrointestinal tract, prevent their development into adult worms (larvicidal effect), and it would also reduce the sexual development of female worms (antifecundity effect). The major benefit will be directly reducing individuals’ worm burden. A first generation product known as Na-ASP-2 hookworm vaccine against *N. americanus* has been developed and comprises a larval hookworm recombinant protein engineered and purified from yeast. Proof-of-concept for the efficacy of the Na-ASP-2 vaccine to reduce hookworm burden and intestinal blood loss will be evaluated in a Phase 2b clinical trial in Minas Gerais State, Brazil. An uncertainty is how much such a vaccine costs to manufacture. Finding an innovative financing mechanism and a cost-efficient delivery mechanism represent the major challenges for the successful deployment of hookworm vaccines (Bundy *et al.*, 1995b; Brooker *et al.*, 2005).

10. SCALING UP DEWORMING FOR SCHOOL-AGE CHILDREN

Following the 2001 WHA resolution, WHO was requested to set up a system to monitor each endemic country’s progress towards the 2010 target. A global databank has been established at WHO (http://www.who.int/wormcontrol) to track the number of people who are treated each year for soil-transmitted helminthiasis and schistosomiasis, and epidemiological data describing the distribution of infections are regularly collected and displayed using the geographical information system technology. Country profiles, including information on coverage data, plans of action, anthelminthic drugs on the Essential Drug List and their cost, are collected through questionnaires and extensive liaison with other partners, regional colleagues and national programme managers. Global progress in coverage in school-age children from 1999 to 2004 is reported from 73 out of 104 endemic countries. Although data is awaited from 26 countries in the Pan American Health Organization and from India and China, there is a steady increase of coverage over time. Thirty of the 73 countries are known to be expanding control activities (Figure 2, which is Plate 8.2 in the separate colour plate section) (WHO, 2005b).
The Schistosomiasis Control Initiative (SCI) is assisting Uganda, Burkina Faso, Mali, Niger, Tanzania (including Zanzibar) and Zambia to scale up schistosomiasis and helminthiasis control to a national level. SCI has promoted integration of other deworming programmes at the country level, the synergistic deworming in collaboration with the Programme to Eliminate Lymphatic Filariasis (PELF) being an example. SCI, with funds from the Bill and Melinda Gates Foundation, has facilitated registration of drug products in each country, promoted local production by national pharmaceutical companies and strengthened procurement agencies at country level according to local needs (Fenwick, in press). In addition to these countries Cambodia, Nepal, Ecuador, Brazil, and Viet Nam, are also examples of good progress in helminth control.

WHO and other partners are building regional and country capacity to strengthen implementation of control programmes. WHO has provided evidence as to how deworming helps to meet some Millennium Development Goals and progress towards achieving them should be further documented (Lancet, 2004). In order to meet the target of reaching about 650 million children by 2010, deworming should become part of a multi-disease control approach, by maximizing links with chemotherapy-based control of lymphatic filariasis, onchocerciasis, trachoma and other diseases of poverty, thereby building a pro-poor strategy for sustainable development (Lancet, 2004; Molyneux and Nantulya, 2004; Molyneux et al., 2005).

11. QUESTIONS NEEDING ANSWERS

Partners for Parasites Control recently gathered to discuss the best way forward in helminth control; the following research needs and priorities emerged (WHO, 2005b).

- Advocacy for sustaining the effort to control helminthiasis requires the latest and best information. The compelling evidence for detrimental effects of helminth infections and the benefits from deworming should be sustained with further knowledge and
updated data. The disease burden should be regularly revised and expressed in terms of the most reliable DALYs available.

- There is emerging evidence that concurrent worm infections may have synergistic effects on the severity of malaria, on progression of HIV/AIDS, and on the development and effects of anaemia (Fincham et al., 2003; Spiegel et al., 2003). These interactions and potentially important consequences merit more extensive investigation.

- Impressive benefits of deworming on education, poverty reduction and contribution towards the Millennium Development Goals have been put forward, though they need further quantification and wider dissemination.

- Further research on the possible use of “packaging” deworming with other programmes is needed to sustain science-based synergy and integration with lymphatic filariasis and onchoceriasis elimination programmes, vitamin A distribution campaigns, Child Health Days, malaria, expanded programme of immunization.

- There is inconsistency between WHO recommendations and drug producers’ prescribing information about the use of anthelminthic drugs during pregnancy. The WHO recommendations are based on toxicological evidence presented to experts in two Informal Consultations (WHO, 1996, 2002b). The full-scale toxicological review and the extensive process required by regulatory bodies should be undertaken by the pharmaceutical industry. A pressing issue to be addressed is the need to set up a reliable system for pharmacovigilance in community deworming campaigns.

- Sensitive molecular tools to monitor anthelminthic drug efficacy need to be developed. Waiting for drug resistance to occur before seeking funds for research on drug efficacy monitoring might be too late a response to this potential problem.

- The possibility of development of new anthelminthic drugs and the efficacy and safety of available drugs administered in combination should be evaluated.

- Availability of efficient vaccines would make a difference in helminth control. Trials for the development of vaccines against schistosomiasis and hookworms should be supported, and collaboration between research and control should be encouraged.
REFERENCES


and low-cost method. *Tropical Medicine and International Health* 6, 535–537.


Plate 8.2  Global coverage of deworming treatment for soil-transmitted helminths, school-age children 1999–2004. Data from 73 endemic countries. (WHO, 2005.)

Plate 9.2  DALYs lost due to onchocerciasis. Results for 1990.