Pondicherry: Health workers distributing medicines to members of a household in a rural village. The work is part of research into mass drug administration methods to combat lymphatic filariasis. Photo: WHO/TDR/Crump
New and improved policies and control strategies
TDR is helping to develop a number of strategies that involve the community in disease control. During the biennium, studies on home management of malaria in several countries indicated the benefits of pre-packaging of antimalarials for children, ensuring that more of them receive the correct dose of treatment, and receive it promptly. The successful approach of community-directed treatment (ComDT), first developed for onchocerciasis and now for lymphatic filariasis, is also being evaluated as a strategy for integrated delivery of a range of other health interventions. Another community practice for lymphatic filariasis is simple footcare, which TDR studies have helped show to be an effective intervention that improves quality of life for patients.

TDR studies are also helping towards elimination of some diseases. Information to guide strategies for elimination of lymphatic filariasis is being collected in large studies in India and Africa. The long-term impact of the strategy for onchocerciasis – of mass treatment with ivermectin – on transmission of the disease has now been evaluated. Other strategies TDR is working on include those for rapid assessment, for example, RAPLOA is a strategy for rapidly assessing and diagnosing *Loa loa* in communities. Strategy development is covered by area D of the TDR strategy.

There were no activities in this area for African trypanosomiasis during the biennium. However, the development of sustainable community-based strategies for tsetse control was identified as a priority area in 2001, and activities will begin as soon as funds become available.

MALARIA

TDR has been developing methods for home management of malaria, including ways to treat and prevent the disease, for a number of years. While methods have been developed and implementation strategies tested on a small (up to 'district') scale, it remains to work out implementation strategies for scaling up those that are effective to cover provinces and, gradually, the whole territory, and so achieve a large-scale impact on the disease.

Four projects on home management of malaria, in Burkina Faso, Ghana, Uganda and Nigeria, were completed during the biennium. The studies are aimed at providing children with appropriate treatment within 24 hours of onset of symptoms as close as possible to the home, since appropriate treatment of children in the early stages of malaria can prevent progression to severe disease and save lives. Interventions in Uganda, Ghana and Nigeria,
New and improved policies and control strategies

Each for 2-3 communities of around 10 000 population, consisted of: prepackaged chloroquine and cotrimoxazole (separately in unit doses), networks of community-based agents trained to treat children with these drugs, and information, education and communication (IEC) focusing on the whole community.

In Burkina Faso,\(^1\) where the study involved a larger population of about 450 000 people, of whom 67 500 were children under five, the study provided evidence that prepackaged antimalarials can reduce progression to severe disease. In this trial, only prepackaged antimalarials were used (not cotrimoxazole, which is for acute respiratory infection). The study involved teaching mothers how to recognize presumptive malaria episodes while ensuring availability of low-cost antimalarial drugs in unit-dose packages at village level. Local health staff were retrained, and sensitization meetings held in each of 375 villages. Prepackaged drugs were made available through village volunteers, who sold the packs at a price agreed with the local health management team and calculated to cover the purchase cost of the drugs and a 10% incentive for the volunteer. A four-fold increase in percentage of children treated correctly and a 53% reduction in the proportion of sick children that progressed to severe malaria (see box 1) were achieved at low cost.

In Ghana, community members were trained to administer prepackaged chloroquine to children with fever, and prepackaged chloroquine plus cotrimoxazole to children with fever plus fast breathing (symptoms suggesting acute respiratory infection) as confirmed by a community health worker. Other activities included management of supplies to ensure ample drugs were always available, supervision for quality assurance, and monitoring and evaluation. The prepacks were used intensely (75% of drugs used were prepacked), promptly (75% of children receiving treatment sooner than 24hrs), and correctly (94% compliance to prescribed regimen).

<table>
<thead>
<tr>
<th>Box 1</th>
<th>Children treated with prepacks</th>
<th>Children not treated with prepacks</th>
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<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Number (%) progressing to SEVERE MALARIA</td>
</tr>
<tr>
<td></td>
<td>1806</td>
<td>93 (5.1)</td>
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Sirima SB et al. Early treatment of childhood fevers with pre-packaged antimalarial drugs in the home reduces severe malaria morbidity in Burkina Faso. Tropical Medicine and International Health, 2003, 8(2), 133-139.
visits and effective IEC materials were shown to be critical for effective use and compliance.

In Nigeria, the aim was to provide a baseline understanding of seeking of healthcare for childhood illnesses on which to build a programme for promoting prepackaged drugs for early and appropriate treatment of childhood fevers at community level. The study was carried out in three rural communities of approximately 10,000 population each. The most prevalent recent illnesses were 'hot body' (43.9%), malaria – known as iba (17.7%), and cough (7.4%). The most common form of first-line treatment was drugs from a patent medicine vendor or drug hawker (49.6%). Only 3.6 per cent did nothing. Most who sought care (77.5%) were satisfied with their first line of action, and did not seek further treatment. The average cost of an illness episode was less than US$2.0.

Analysis found that high temperature and loss of appetite were the symptoms associated with perception of malaria and hence with chloroquine use, while cough and difficult breathing were associated with antibiotic use. The ability of the child’s care-givers, both parental and professional, to make these distinctions in medication use will provide the foundation for health education in promoting appropriate early treatment of childhood fevers in the three study sites.

The study also tested different distribution systems of the drugs, and the market share that prepackaged drugs may achieve. Results showed that it is possible to gain a significant market share for prepackaged drugs using locally available distribution channels. The value lies in using a variety of channels, to maximize the strengths of each. Effective use of prepackaged drugs was inversely related to cost.

The challenge now is to develop appropriate mechanisms for sustainable and effective implementation of the home treatment strategy over time and on a much larger scale.

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New and improved policies and control strategies

As discussed below for onchocerciasis, community directed treatment (ComDT) is being evaluated to determine if community directed distributors (CDDs) can take on responsibilities in addition to distributing ivermectin for onchocerciasis. This is particularly important in areas where schistosomiasis and geo-helminths are co-endemic with either onchocerciasis or filariasis.

Until now, even though the recommended drug for schistosomiasis, praziquantel, is safe for distribution at community level by paramedics and school teachers, no attempt was made to distribute the drug through the ComDT approach. One limitation was the need to use weight for determining the appropriate individual dose, and another concerned the safety of co-administration of praziquantel and ivermectin. However, for school-age children, height can be used to determine the treatment dosage, while treatment for onchocerciasis and schistosomiasis can be integrated safely as long as the respective drugs are given on separate days.

The feasibility of integrating ComDT with ivermectin for onchocerciasis, with praziquantel (PZQ) for schistosomiasis and mebendazole (MBD) for intestinal helminths, in school-age children was studied in Uganda, where these infections are co-endemic. The three interventions were: school-based treatment for schistosomiasis, where PZQ and MBD were administered by school teachers; routine ComDT, where CDDs administered ivermectin to the total populations of selected communities; and integrated ComDT, where CDDs administered ivermectin and MBD on one day and PZQ the next day to all community members in selected villages.

Treatment coverage, adverse reactions to treatment, and reasons for non-treatment, were assessed by questionnaire. Treatment coverage with PZQ and MBD was higher under the integrated ComDT approach (85% of respondents) than the school-based approach (79% of respondents); and treatment coverage with ivermectin was higher under integrated ComDT (81.3%) than routine ComDT (77.2%). Adverse reactions, reported more frequently under the school-based approach (33%) than under integrated ComDT (18%), were mild and included headache, nausea/vomiting and abdominal pain, and were resolved without further medication. Reasons for non-treatment included being unaware the drugs were available, and insufficient supply of drugs.

This research shows that schistosomiasis treatment can be delivered through ComDT and can be integrated with onchocerciasis and geo-helminth control. Because it is delivered at community level, ComDT may ensure better treatment coverage of school-age children than a school-based programme. Integration of schistosomiasis, onchocerciasis and geo-helminth control did not negatively affect coverage with ivermectin treatment.
CHAGAS DISEASE

In 2002, activities for research to generate new methods and strategies for use in control of Chagas disease were transferred from Geneva to the Pan American Health Organization (WHO/PAHO). The Steering Committee for Operational Research on Chagas Disease was held in Arequipa, Peru, 3-6 September 2002, when 63 new research proposals, 16 progress reports, and 5 final reports were reviewed from which 16 new proposals and 6 renewals were funded.

Research supported by TDR through PAHO includes a variety of studies on vectors. Methods for control of sylvatic (living in the wild as opposed to domestic environment) vectors in Andean countries and Central America are being developed, as well as improved strategy for controlling vectors living outside the domestic environment, which includes evaluating social communication strategies in vector surveillance and economic analyses.

Other research includes evaluation of tools for detecting vectors in low transmission areas, evaluation of insecticides for effectiveness, and evaluation of the emergence of resistance in vectors. There are studies on the influence of climate change on vector populations, and on the vector’s environment immediately around the home as a link between the wild and domestic cycles of infection. Ongoing are studies on the population genetics of vectors and on mobility of the vectors Triatoma dimidiata and Rhodnius prolixus.

Looking towards new indicators for control programmes, there is support for evaluating clinical markers that predict progression of the disease from the indeterminate phase to the cardiac or digestive forms, and for identifying factors related to the parasite, host and environment that are responsible for clinical variations of the disease. Non-conventional diagnostic tests are being evaluated, and other studies are looking at congenital transmission including the prevalence, incidence and parasite strains involved. Determinants for effective implementation of T. cruzi-safe blood programmes are being identified.
Information to guide strategies for elimination of lymphatic filariasis is being collected in large longitudinal transmission studies in India and Africa. The longest study, in rural south India, which began in 1993 and covers a population of 34,000 people of whom about 65% receive treatment, has shown more than 85% reduction in transmission of Bancroftian filariasis after mass treatment with single-dose ivermectin or diethylcarbamazine (DEC). However, after six annual rounds of treatment, transmission is not yet interrupted. So far the data suggest DEC and ivermectin are equally effective in drastically reducing all parameters (infection rate of resting mosquitos, infectivity rate, transmission intensity index). Four rounds of therapy with the two drugs combined indicate that combination therapy may be even more effective, though again complete interruption of transmission has not been achieved, suggesting that more rounds of mass drug administration are necessary to achieve elimination. Thus the study continues; there are three more annual treatment rounds to go. Similar studies have been started for combinations of DEC or ivermectin with albendazole.

In another study, and as part of a mass drug administration for elimination of filariasis, the efficacy of DEC against geohelminths was compared with DEC + albendazole (ALB). Combination therapy (DEC + ALB) produced a cure rate of 74.3% and an egg reduction rate of 97.3% for geohelminths, while with the single therapy (DEC alone) these rates were 30.4% and 79.0% respectively. The odds of cure with combination therapy for hookworms and roundworms was significantly higher than the odds of cure with DEC alone, though both therapies were equally effective against whipworms.

Analysis of the results using the LYMPHASIM model shows that the probability of elimination of lymphatic filariasis depends in a non-linear fashion on treatment coverage, number of treatment rounds, and endemicity level. If, for example, an area has a microfilaraemia prevalence of 10%, and 80% of the population is covered at each round, 4-5 rounds will be sufficient to achieve elimination, but if treatment coverage is 60%, then at least nine rounds will be needed.

Figure 1: Required treatment coverage and duration to achieve lymphatic filariasis elimination in India (LYMFA SIM model predictions)

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The LYMPHASIM model has been under development for some years. Recently, data concerning the effect of age and immune factors on prevalence and intensity of infection, based on a meta-analysis of published data from 213 communities in different parts of the world, were integrated into the model. The pattern of infection was remarkably similar in most sites, showing prevalence reaching a plateau. The main difference between Africa and Asia was the age at which this plateau was reached – in Africa at about 40 years, and in Asia at 15-20 years. These data have been incorporated into the LYMPHASIM model.

A user-friendly Windows version of LYMPHASIM is now developed and available for filariasis control managers.

The strategy of community directed treatment (ComDT) has been under development by TDR for a number of years. Because the treatment for onchocerciasis and lymphatic filariasis is simple, consisting of single-dose tablets taken just once a year, it is feasible to involve communities in delivery of the medication. One lymphatic filariasis programme that has adopted the ComDT approach is the national elimination programme in Ghana. During implementation of ComDT in the first five districts, a study indicated that upscaling of ComDT through the district health system was feasible in rural areas and small towns, but difficult in large towns due to lack of a closely knit community structure, and to intense migration.

An issue in lymphatic filariasis is the community’s role in care of the patient. Footcare consists of using soap and water (and occasionally topical ointments containing antibiotics) to treat and prevent acute attacks of adenolymphangitis (ADL, or filarial fever). For one year, 140 filariasis patients in India were supervised and instructed in footcare, after which they were advised to continue the simple measures without supervision. One year later, the patients were interviewed and examined. Most had been able to maintain the treatment and the severity of ADL episodes was considerably less than before (95.2% of patients had either no ADL or ADL of reduced severity); they abstained less from work and for a much shorter period. Thus their quality of life had improved. Footcare is therefore seen as an effective method for preventing ADL attacks, which can be sustained by patients themselves.

Baseline data from a study in Mali on community-based management of lymphoedema (swellings) and ADL indicated that community members considered prevention to be a collective activity of the community, and care of the patient to be the reserve of the family. The community’s role was considered to be mobilizing the community, providing information, selecting distributors of mass treatment, and selecting family members to care for the patient on recommendation from the head of household. The head of household was seen to play a key role in decisions about action and financial resources, while other family members are responsible for feeding and taking care of the patient, administering treatment, etc.

Following on from earlier studies that indicated a 50km grid sampling strategy (RAGFIL) was useful for rapidly assessing the distribution of lymphatic filariasis, the method was elaborated into a mapping strategy which took

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New and improved policies and control strategies

into account considerations of the WHO lymphatic filariasis elimination programme of the so-called implementation unit, i.e. level of the health system where lymphatic filariasis treatment is provided to all eligible persons in a unit. In the strategy proposed, the spatial sampling and analysis of the RAGFIL method are combined with sampling by the implementation unit. This combined strategy was successfully tested at scale in Benin, Burkina Faso, Ghana and Togo. Results revealed that prevalence of infection with *Wuchereria bancrofti* in the adult population of some communities exceeded 70%. The prevalence map produced should be useful for prioritizing areas for filariasis control, identifying potential overlap with ivermectin distribution activities undertaken by onchocerciasis control programmes, and enabling inter-country planning. Results indicated the disease to be more widespread in arid areas of Burkina Faso than previously thought and that the infection had been relatively stable for 30 years. So the campaign to eliminate lymphatic filariasis as a public health problem will require significantly more resources than previously anticipated.
**ONCHOCERCIASIS**

The ComDT approach, first developed for onchocerciasis, is becoming more and more popular and interest in it is growing at community level. A multicountry study on additional health care responsibilities of community directed distributors (CDDs) has been launched. Eighty-five per cent of CDDs of ivermectin for onchocerciasis control were seen to be involved in other health and development activities, especially expanded programme of immunization (EPI) activities, but this was seen to not have a negative effect on their work as CDDs – ivermectin treatment coverage was not affected. Communities, CDDs and health workers strongly supported further involvement of CDDs in other health care activities. Many CDDs had been selected for the other activities after becoming a CDD, and often received financial incentives for the other activity, which led to greater motivation. Nearly all CDDs wanted to continue working as a CDD “to help my community”, some for self-fulfilment and recognition, although few received or expected any financial reward.

Thus additional health and development activities for CDDs were found to not pose a threat to ComDT, but to provide opportunities to strengthen sustainability.

Ivermectin treatment for onchocerciasis has been in operational use for over a decade. To evaluate the long-term impact of mass treatment on onchocerciasis transmission, an in-depth analysis of data from 15 river basins in the Onchocerciasis Control Programme (OCP) area, and one basin in Cameroon, was carried out. The data were discussed at a joint OCP/TDR meeting held at Erasmus University Rotterdam, the Netherlands, October 2001. In the areas under review, ivermectin treatment has been extremely successful in eliminating onchocerciasis as a public health problem, but elimination of transmission has proved more difficult. These results were reported at an international meeting on eradicability of onchocerciasis, which concluded, on the basis of this result, that global eradication will not be possible with ivermectin alone.

When ivermectin is used as treatment for onchocerciasis or lymphatic filariasis, there is risk of severe adverse reactions to the drug in communities where loiasis is highly endemic. RAPLOA is a rapid assessment procedure for Loa loa developed by TDR. It is based on use of a simple questionnaire on the history of eye worm to predict whether or not loiasis is present at high levels in a community, and facilitates planning of ivermectin distribution by predicting in which communities ivermectin treatment for onchocerciasis can be safely implemented.
The method was substantiated in a TDR multi-country study in 103 villages, and the results analysed at a workshop in September 2001. A prevalence of 40% or more of eye worm in a community, confirmed by showing a photograph of a worm in the lower part of an eye, was identified as the threshold above which there is a risk of adverse reactions to ivermectin treatment during ComDT. The RAPLOA procedure in these villages was 100% sensitive and more than 90% specific. This simple method is effective because eye worm is a very well known infection in endemic communities. Guidelines on how to implement RAPLOA, and how to interpret the results, were published in 2002.

Whereas RAPLOA is a strategy for rapidly assessing and diagnosing communities, for area-wide rapid mapping and diagnosis it has been proposed that RAPLOA be combined with an environmental risk model (ERM) developed by the Liverpool School of Tropical Medicine, which predicts prevalence using remote sensing data on environmental risk factors. The combined ERM and RAPLOA strategy was designed at a workshop in June 2002; validation of the separate and combined methods is ongoing. The rapid mapping method consists of: drawing a preliminary operational contour map using the ERM; conducting RAPLOA surveys in spatial samples of villages selected using the preliminary contour map; and refining the local operational contour map using results of the RAPLOA surveys. Thus the ERM is re-calibrated using data from the RAPLOA study, allowing estimation of 'confidence' of prediction. The addition of RAPLOA data significantly improves local ERM predictions. Currently the method is being validated in the Congo and the Democratic Republic of the Congo.

Figure 2  Correlation between history of eyeworm and prevalence of Loa loa

Correlation between history of eyeworm and prevalence of Loa loa

