



# TDRnews

UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR)



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## K E Y N O T E A R T I C L E

# A massive effort against diseases of poverty: What role will research play?

By *David Heymann, David Nabarro (World Health Organization)*



WHO/TDR/Gramp

A WHO-led massive effort against diseases of poverty (announced in October 2000) is a process that is primarily about prosperity and strengthened health delivery systems, not about diseases. It is about people and how to improve their health, about health systems and how they respond to poor people. It is about getting well-tested and effective control interventions to the people who need them, whether by reducing their costs, improving their distribution, increasing their efficacy, or slowing down the development of antimicrobial resistance. Such a massive effort would involve a whole range of partners from public, private and not-for-profit sectors, bringing focus to the disconnection in what we actually do and what we would like to do in terms of controlling the diseases of poverty.

Bednets: how can this cost-effective solution for reducing child mortality in Africa best be delivered to those in greatest need?

> (next page)

A massive effort against the diseases of poverty is necessary to meet the call by heads of state for a reduction of serious illness amongst the poor. In this article, David Heymann, Executive Director of the Communicable Diseases Cluster at WHO, and David Nabarro, Executive Director in the Director-General's Office at WHO, highlight the necessary contribution of research to a massive effort in developing new disease control tools and improving strategies to make existing tools (drugs, vaccines, diagnostics) more accessible to those in need.

## A massive effort...

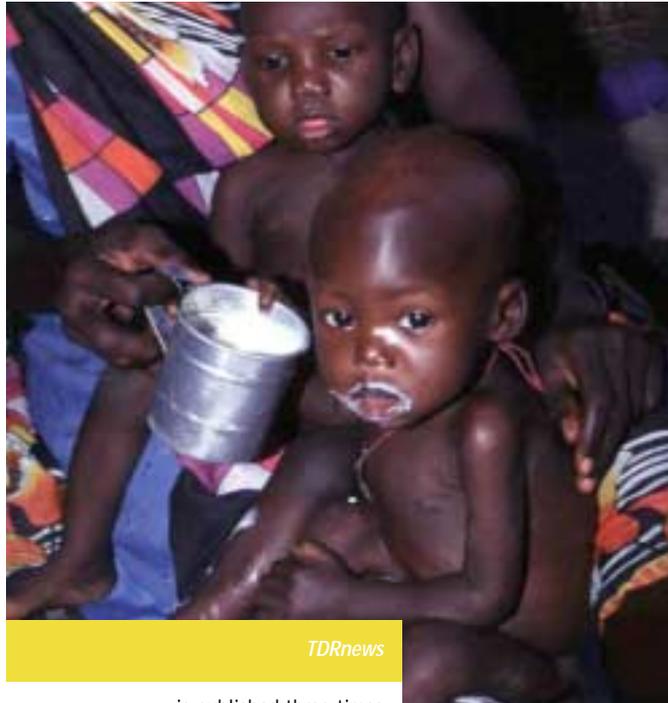
(continued) > A massive effort would eventually make available a sustained high level of resources that would make possible both increased access to existing drugs, vaccines and diagnostic tests, and research to better use these existing goods and develop the new ones necessary.

What is the place of research in this effort? Disease control today depends on cost-effective strategies to best use the many drugs, vaccines and diagnostic tests that, when used properly, are capable of reducing mortality. But, today these strategies don't reach all who need them, and maybe we can develop better strategies. So the massive effort will, in part, be about developing better strategies to make existing drugs, vaccines and diagnostic tests more accessible to those in need (e.g. the use of bednets in Africa would need to be scaled up 20 times using strategies that ensure better access and increase demand). Operational research is therefore required in a massive effort.

With evidence in the form of data from well-designed operational research and its analysis and synthesis, we can demonstrate that existing interventions get drugs, vaccines and diagnostic tests to where they are needed in a way such that they can be maximally used.

At the same time, research in a massive effort is also required to develop new tools – new drugs and vaccines, and easier-to-use diagnostic tests. Adaptations of existing products, such as better fixed-dose combinations of drugs for tuberculosis and malaria, simplified for field use, are also required.

TDR, with its broadened disease mandate and new emphasis on operational research, is well placed to ensure the research necessary for a massive effort. As increased funds for a massive effort become available, the balance between funds used to make existing vaccines, drugs and diagnostic tests available, and funds for operational and more basic research and development, will be a great challenge. TDR has successfully maintained the correct balance between research and implementation in the past, and will surely rise to the task of doing the same as a massive effort continues to evolve. ■



WHO/TDR/Crump

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## Dear Reader,

*If you wonder why TDRnews has a new look, its because, in 2000, TDR completed its first quarter century of existence. As we enter 2001, many things are changing – and rapidly. TDR is changing too, embarking on a new strategic direction with regard to many of its activities. As part of the programme's new working practices, we will be greatly expanding our communications activities. In particular, we will be using all our communications tools to encourage a 2-way information flow. Consequently, from now on, each issue of the new look TDRnews will have a 'feedback' section, which will carry a letter or correspondence from our readers. This could be feedback on something that has appeared in the newsletter, or be observations and comment from readers on any aspect of TDR's target diseases or the programme's work. Please send us your comments and views (in writing or by e-mail) to:*

**Communications Unit, TDR, World Health Organization, 1211 Geneva 27, Switzerland**

or to

**tdr@who.int**

*We look forward to hearing from you, and encourage and welcome the participation of all our readers in the effort to ensure a 2-way flow of information. Ed.*

*TDR reserves the right to edit any correspondence published in the newsletter. Please note that we can neither guarantee publication nor are we able to return any materials submitted.*

# TDR increases its efforts in social, economic and behavioural research

The new Steering Committee on Strategic Social, Economic and Behavioural Research (SEB) issued its first call for grant applications in October 2000. Over the next 2-3 years, SEB will focus on supporting research that increases understanding of:

- how large-scale social and economic forces affect inequality of access to treatment, prevention and information related to infectious diseases;
- the implications of globalization on the persistence, emergence and resurgence of these diseases.

Studies of this nature will require innovative research methods, involving multi-level analyses that allow for investigation of the effects of large-scale forces on local level processes and outcomes. An important aspect of the Committee's work will be to support capacity building to conduct such analyses.

## *Social science research in TDR: past, present and future*

From the beginning, TDR has placed considerable emphasis on the social and economic aspects of tropical infectious diseases and their control. From 1979-94, TDR supported social science research through its Steering Committee on Social and Economic Research (SER), and since 1994, applied social science research has been supported by the Intervention Development and

Implementation Research team (formerly the Applied Field Research team).

In June 1999, TDR's Joint Coordinating Board (JCB) approved the creation of a new Steering Committee on Strategic Social, Economic and Behavioural Research (SEB).

As mentioned in *TDRnews* No. 63, SEB is located within the Basic and Strategic Research team (STR) to reflect its focus on basic social, economic and behavioural research issues of trans-disease and global importance.

A Scientific Working Group (SWG) of experts from a range of social, economic and policy sciences met in Geneva in June 2000 to set the overall direction for SEB.

In September, the SEB Steering Committee met for the first time, and developed a vision for the next five years and a detailed workplan for the coming two years.

The focus of SEB reflects WHO's growing interest in the complex relationship between poverty and health. On a worldwide scale, infectious and parasitic diseases disproportionately affect populations living in poverty. Social, political and economic inequalities are central to the persistence and spread of these diseases, and the performance of health systems in protecting vulnerable populations from the impact of these diseases often falls far short of potential. Over the next several years, the SEB Steering Committee will examine these issues within the context of globalization, the changing role of the state, and the emerging role of non-state actors (the private sector, NGOs and civil society). ■

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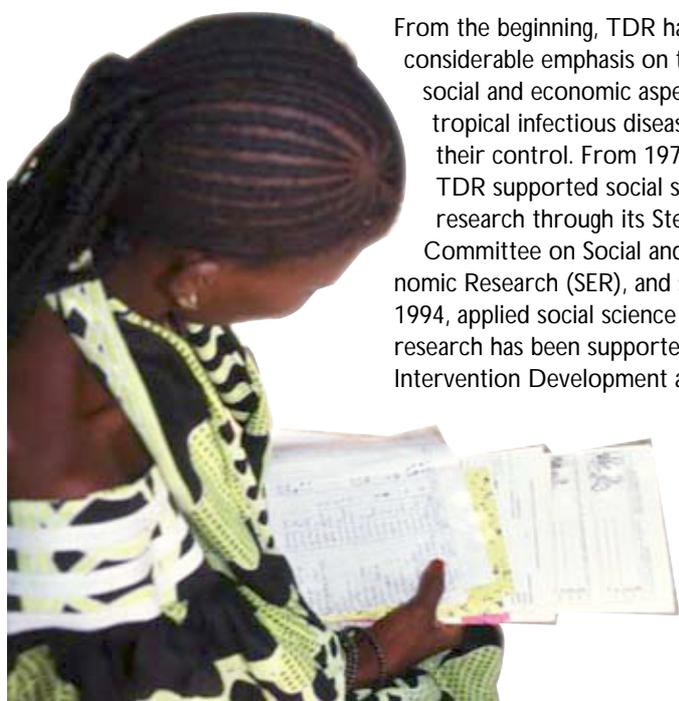
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The SEB workplan and current call for grant applications can be retrieved at the TDR website:

[www.who.int/tdr/grants/workplans/seb.htm](http://www.who.int/tdr/grants/workplans/seb.htm)

[www.who.int/tdr/grants/grants/seb.htm](http://www.who.int/tdr/grants/grants/seb.htm)

or requested, by regular mail, from the SEB secretariat.



# Web of Science: Bridging the digital divide

Major awards for electronic communication in science have been approved for four centres in Africa (which are all TDR partners in research) and five centres in central Asia and eastern Europe.

This is the first phase of a public/private initiative – the Health Internetwork project – which aims to boost access by researchers and health workers to reliable information via the Internet and to improve global public health by facilitating the flow of information worldwide.

Partners in the initiative include the World Health Organization (WHO) and other UN organizations, the Open Society Institute (OSI), which is part of the Soros Foundation network, leading information providers ISI(r) and Silver Platter, and other public and private partners, possibly including the leading scientific publisher, Elsevier.

In the first phase of the study, the nine centres are to be provided with a 'connectivity package' consisting of hardware, wide band connectivity, full access to several databases and more than 100 medical journals (online, full text). For their part, the centres will help work out how to introduce locally-produced information to the Internet, stressing priority public health programmes and local translation and adaptation of content as necessary. They will also help work out how to expand the project to the rest of their country and region, and how to evaluate its impact. The pilot trial will test whether online delivery of high-quality information and international connectivity addresses the information and communication needs of developing country researchers.

The four TDR partners selected in Africa for the pilot phase are:

- Noguchi Memorial Medical Research Institute, Accra, Ghana
- Malaria Research and Training Centre, University of Mali, Bamako, Mali
- Makerere University Medical School, Kampala, Uganda
- National Institute for Medical Research, Dar es Salaam, United Republic of Tanzania.

Research, and the sharing of knowledge through research, is fundamental to improving public health. Through the Health Internetwork pro-

*Public and private partners team up to facilitate the flow of health information via the Internet*

ject, researchers and scientists will begin to "read the same journals, search the same databases, join in the same discussion groups, compete for the

same grants; it will bring them into the international community of researchers and eventually improve the dissemination of their own results" (Dr Gro Harlem Brundtland, WHO Director-General).

The project aims to facilitate research in countries that have first-hand experience of diseases and health issues that affect the poor. As to the



roles of the different founding partners, the private partners will focus on organizing comprehensive training for research staff, while the WHO and UN will discuss provision of high-speed connectivity to the Internet with service providers in the eight initial countries. NGOs and foundations will provide resources and logistics support.

After the one-year pilot phase, the intention is to extend the facility to a large number of needy countries. It is anticipated that, by the end of 2003, some 13 000 new health information access points in some 40 countries will be equipped with Internet technology, thus enabling communication and networking among public health information users, and improving monitoring of health situations. ■

Internet cafe in Burkina Faso.

SEE ALSO  
WHO press release

[www.who.int/  
inf-pr-2000/en/  
pr2000-76.html](http://www.who.int/inf-pr-2000/en/pr2000-76.html)

WHO/TDR/Morel

## Public/private partnership for research training: a new kind of TDR trainee

**Mahamadou Thera** was on his way home after spending 11 months in Belgium with a pharmaceutical company, learning design and management of product development. He stopped off in TDR for a few weeks to learn how TDR promotes good clinical practices, and then returned to Mali, his home, to directly implement what he had learned during these months. He hopes to use his knowledge and experience to manage malaria vaccine trials that could begin as soon as mid-2001



Mahamadou is the first of a new kind of TDR researcher who is supported by a public/private partnership in capacity strengthening. Awards under this scheme are for periods of 12 months, and are explicitly for young nationals of malaria endemic countries who have relevant control/research experience – they are advanced trainees. In Mahamadou's case, TDR's private partner is the pharmaceutical company SmithKline Beecham Biologicals (SB Bio, now GlaxoSmithKline), which is active in the field of malaria vaccines. Mahamadou believes that a malaria vaccine is, in the long run, our best bet for control of

malaria. "What is 10-20 years to develop a vaccine compared to the hundreds of years we've been suffering from malaria?" he says.

During his 11 months with SB Bio, Mahamadou has learned how to design clinical trial protocols, and conduct and monitor studies ensuring respect of good clinical practice (GCP). "It was a new kind of collaboration for the company" says

Mahamadou, "they had not participated in such a partnership before, but they adapted very quickly." Back home, he works in a parasitology laboratory – a WHO collaborating centre – headed by Professor Doumbo. Already a small team of five medical and pharmaceutical doctors exists in the vaccine unit at the laboratory. "There have been many clinical trials in malaria so far," says

Mahamadou, "but not all of them according to GCP standards." So, in the proposed trials of malaria candidate vaccines, Mahamadou and the rest of the team will try to bring some kind of clinical monitoring facility into practice.

Mahamadou was born in a beautiful mountainous area of Mali, a highly malarious region. Returning home from his studies abroad (in Belgium and Romania), he was horrified to experience his first malaria transmission season as a young doctor, in the paediatric ward of a hospital in North Mali.

"There were so many cases of severe malaria, of convulsions and coma, that I ran to the hospital director: 'Our home is exploding. All our children are dying.' " He waited for

the children to come and then treated them with quinine, a highly-efficient drug but one which can only be used in a hospital, as directed. After a couple of years spent treating people, he realized that there was something which was much more important than simply curing them in hospital, and that was community action. So he shifted from working in clinics to working in public health. In 1993, Mahamadou participated in a malaria survey in his home town and helped establish a malaria control programme, with which he worked for three years. Later he joined Professor Doumbo's laboratory. Having worked in a malaria control programme, our TDR researcher knows how complex and time-consuming control is. He also knows the value of open-minded discussion between researchers and control programmes – as a malaria control programme coordinator, Mahamadou had regular exchange with researchers. "Researchers have to learn what the needs are, and to involve control programmes in the planning of their research activities." He suggests that perhaps there could be units of research within malaria control programmes, staffed with epidemiologists, who would have one foot in the control camp and one in the research camp. ■

# First vaccine trial against visceral leishmaniasis

The results of the first trial of a vaccine against visceral leishmaniasis in humans have been published in *The Lancet* by Khalil et al. (356 [9241] 4 November 2000). In a study performed by scientists of the Institute of Endemic Diseases, University of Khartoum, Sudan, supported by TDR and assisted by Médecins sans Frontières (MSF)-Holland, a vaccine composed of autoclaved *Leishmania major* promastigotes (Fesharki, et al. at Razi Vaccine and Serum Institute, Iran) mixed with a low dose of BCG (as adjuvant) was compared with BCG alone.

The trial was carried out in the Sudan, where visceral leishmaniasis is a major cause of morbidity and mortality and where, in the study areas, there was a prevalence of 80-130 per 1000. Although drug treatment for visceral leishmaniasis does exist, it is not always available where needed. As well, it is expensive, comprising daily injections for one month, and is associated with side-effects. Drug resistance is also becoming common. In Sudan, as in other endemic countries, the development of a safe, effective and cheap vaccine would seem to offer the only real solution for controlling visceral leishmaniasis, vector control being prohibitively expensive in the vast endemic areas, although there have been encouraging results from pyrethroid impregnated bednet trials. The presence of extensive cross-reactivity between different species of *Leishmania* was the rationale behind this trial of a vaccine made from *L. major*, that had proved almost 40% effective in one area of Iran endemic for *L. tropica* (see *TDRnews* No.57). The double-blind study was carefully designed and monitored. There was no evidence that two injections of *Leishmania* + BCG offered significant protective immunity against visceral leishmaniasis compared with BCG alone. However, the *Leishmania* + BCG vaccine did induce significantly higher rates of leishmanin skin test (LST) conversion (30% vs. 7% by BCG alone) at 42 days, which was associated with lower incidence of disease. Similar results, i.e. lower incidence of disease in LST converted than non-converted individuals, have been obtained by others, including Mayrink's group in Brazil (Antunes et al., *Int J.*

*Results suggest that*

*vaccine may be associated with a lower incidence of disease*

*Epidemiol*, 1986, 15: 572-80) and Momeni and colleagues in Iran (*Vaccine*, 1999, 17: 466-72), both using whole killed *Leishmania*. In the Sudan study

with two injections, responders had a 43% lower incidence rate as compared to LST non-responders (7.2% vs.12.7%,  $p < .003$ ).

There is a need to identify a suitable adjuvant to improve immunogenicity of killed *Leishmania* vaccines. Recent preliminary studies in Sudan, by the same team and using a new preparation of *Leishmania* + BCG with the addition of alum, are highly encouraging since various doses induced a strong LST conversion in all (although small numbers of 5-8) volunteers. Further studies are being planned. ■

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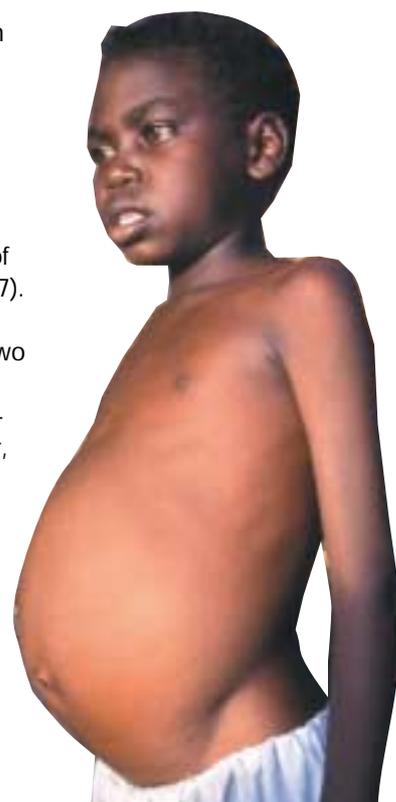
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A young Sudanese boy with visceral leishmaniasis; new vaccine trials are encouraging.

WHO/TDR/Crump

## Expert Committee on Control of Chagas disease meets



WHO/TDR/Chimp

*Advances in interruption of transmission highlighted as a major achievement in the Americas*

The Second Meeting of the Expert Committee on the control of Chagas disease was held in Brasilia, Brazil, from 20-28 November 2000. Prof J. R. Coura, Director of the Oswaldo Cruz Institute, Rio de Janeiro, was elected chairman; Dr M. Lorca, from the School of Medicine, University of Chile, was elected vice-chairman; and Dr F. Guhl from the University of Los Andes, Bogota, Colombia, was the rapporteur. A thorough review of the different aspects of Chagas disease, its con-

trol and (eventual) elimination, was undertaken by the Committee. The advances in the interruption of transmission were underlined as a major public health achievement in the Americas. The Committee also defined research priority areas with direct and immediate bearing on completing the interruption of transmission of Chagas disease and developing new drugs to prevent chronic lesions. A report of the meeting is under preparation and will be formally submitted to the 108<sup>th</sup> Meeting of the WHO Executive Board in May 2001. It will be published in the WHO Technical Report Series, as mandated by the WHO Constitution. ■

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Chemotechnica factory, Buenos Aires: A lit and smoking MUSAL fumigant canister (produced at the factory for supply to the Argentinian government). When lit inside houses, the canister produces insecticidal fumes to kill the insect vectors of Chagas disease.

## Counting current anti-TB drug candidates

*Low number of drug candidates leads to call for more discovery research for new anti-TB drugs*

Pharmaceutical companies and academic research laboratories that work on antibiotics often test molecules for activity against mycobacteria, the causative agents of tuberculosis, but – for economic or other reasons – very few companies currently consider developing active molecules further as specific anti-TB drugs. How many of the molecules reported to have anti-TB activity are actually realistic anti-TB drug candidates? To attempt to answer this question, a meeting was jointly convened by TDR and the Global Alliance for TB Drug Development in December 2000, in Geneva. The starting point for the meeting was a list of about 35 compounds or classes of compound with known activity

against mycobacteria (usually *M. tuberculosis*) growing in vitro, in some cases confirmed by in vivo experiments. This list had been compiled from publicly available sources by Dr Toshiko Imamura, working in TDR with funding from the Rockefeller Foundation. At the meeting, the participants (about 25 people, drawn from academia, industry and the public sector) updated and added to this list, and discussed each candidate on the revised list in detail with respect to its likelihood of finally giving rise to a safe, effective and inexpensive anti-TB drug. The candidates were classed as presently being in the research and discovery, preclinical or clinical phases of development, and candidates in different phases were discussed in separate breakout groups. The last session of the meeting drew together these discussions and summarized the

meeting's conclusions, which will be published in report form later this year: the number of realistic candidates for new anti-TB drugs, among compounds or classes of compound currently known to have anti-TB activity, is small – not more than one in clinical development, two or three in preclinical development, and a handful in the discovery phase. The lead times needed for development of an anti-TB drug are long (at least 10 years), and the dropout rates of compounds in development, especially going from discovery into preclinical and clinical tests, are potentially high. These factors underline the importance of more discovery research – for example, based on the recently sequenced *M. tuberculosis* genome – to bring new anti-TB drug candidates into the development pipeline. ■

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# The Institute for Medical Research, Kuala Lumpur: 100 years of contributing to the health of the nation

*The oldest research institute in Malaysia celebrates its 100th birthday with a look back over its achievements*

The Institute for Medical Research, Kuala Lumpur (IMR) – the oldest research institution in Malaysia – celebrated its 100th birthday in 2000. It was

established in 1900 by the British as the Pathological Institute, and its mission was to undertake research in tropical diseases in order to improve the living standards of the local population. From its beginning, the role and scope of the Institute's work was wide and varied, encompassing research, diagnostic, investigative and consultative services, and training. Throughout its 100 years, the Institute has contributed significantly in the field of health research and the overall health services of the country and, for this, IMR can justly be proud of its achievements.

The IMR has a long and illustrious history of conducting innovative biomedical research which has led to a better understanding of tropical diseases in the region. Three of the most notable achievements made in its early years of existence include:

- research into parasitology, including the diagnosis, treatment and control of malaria
- research into the cause and treatment of beri-beri
- research into the vector biology, ecology and treatment of scrub typhus.

In the last two decades, research efforts at the IMR have led to several more new findings. A new species of schistosome was found in riverine areas of Pahang between 1980-83. The IMR achieved a significant breakthrough in filariasis research by establishing an in vitro culture system for the infective stage larvae of *Brugia malayi* and *B. pahangi* for the first time, and this has enabled the in vitro testing of potential filaricides in the fight against filariasis worldwide. Studies on nutritional status in rural areas have helped shape the nutrition programmes and laid the foundation for many of the national nutrition policies today. Studies of diarrhoeal diseases, acute respiratory tract infections and immuniza-

tion in children have assisted programme managers to fine-tune disease control programmes in children.

Improved control methods for common diseases like dengue and malaria were developed as a result of research carried out on the effectiveness of insecticides and resistance to them in disease vectors. In 1990, IMR researchers discovered the first insecticidal anaerobic killing bacteria in the country, *Clostridium bifermentans malaysia*, and this discovery has been duly recognized by way of a 50-cent stamp commemorating the centennial of the IMR.

Although commercialization of research findings is a recent activity, the IMR is proud to note that, to date, three of its research findings have been commercialized:

- MOSBAC®, an aqueous suspension formulation containing the spore-crystal complex of IMR-BT-1, a Malaysian isolate of *Bacillus thuringiensis*, for the biological control of mosquito larvae
- R-EST®, a test kit for the rapid detection of insecticide resistance
- Nutri-Cal, a nutrient analysis and food composition data management software.

Since independence, Malaysia has evolved from an essentially agro-based society to an industrializing one, resulting in changing lifestyles and demographic patterns. In line with these changes, the IMR has, in recent years, embarked on new directions in its research, while retaining its traditional strengths in tropical medicine. In 1990, the IMR was reorganized into five departments: namely tropical medicine, clinical pathology, community medicine, support services and administration, to meet the challenges of health research more effectively. New areas of research undertaken included cancers and cardiovascular diseases as well as environmental health. In addition, biotechnology was introduced as a new research tool to further enhance and improve our research capabilities.

## NOTABLE ACHIEVEMENTS OF THE LAST TWO DECADES INCLUDE:

- New species of schistosome found
- In vitro culture system for the infective stage larvae of *Brugia malayi* and *B. pahangi* established



Main building of the Institute for Medical Research.

Linkages with other research institutes and agencies are crucial to IMR's development. Two of IMR's oldest linkage partners are the South-east Asian Ministers of Education Organisation (SEAMEO) (since 1969) and the World Health Organization (WHO) (since 1978), and the IMR is thankful to these organizations for their tremendous contributions to its research and training programmes. The more recent linkages include the Japan International Cooperation Agency (JICA) and the Inter-Islamic Network for Tropical Medicine, and we look forward to more such linkages in the future so as to further enhance networking among researchers.

Besides its research function, the IMR has been very active in providing training and consultan-

cies in various fields of tropical medicine and public health. Specialized diagnostic testing remains a key function of the IMR, particularly in the areas of HLA tissue typing and cross-matching, endocrinology, biochemistry, virology and bacteriology.

Today, the IMR, which continues to be the research arm of the Ministry of Health, is undergoing yet another phase of change to make it more relevant to meet the challenges of the new millennium. It is currently being reorganized to enable it to focus on important areas such as infectious diseases, cancer research, cardiovascular diseases and nutrition, environmental health research, herbal medicine and allergic disorders. In the years ahead, the IMR aspires towards a culture of excellence in order to be able to contribute even more significantly to the improvement of health of the human population. ■

#### UPDATE

## An artesunate + sulphadoxine/ pyrimethamine combination blister pack for malaria treatment being developed

*TDR, MSF and IDA are working together to develop a blister package of artesunate and sulphadoxine/pyrimethamine for malaria treatment*

Malaria parasites are becoming increasingly resistant to first-line medications, and drugs that are effective, safe

and long-lasting are urgently needed. Combination therapy is being advocated to delay the development of resistance and play a significant role in "rolling back malaria". A blister package containing one dose of sulphadoxine/pyrimethamine and three doses

of artesunate is being developed to meet the need for high-quality, affordable, effective and safe treatments for malaria. The product will be produced entirely under GMP (good manufacturing practice) guidelines. The final price of the product will be signifi-

cantly lower than generally anticipated for drug combinations. The approach followed is to consider this medication as a "public good", and to address the proprietary right issues upfront. In this respect, investments are being made for the process to > (overleaf)

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(continued) > produce both raw material and formulated product belonging to the public sector. As a result, the cost of development will not be included in the final price of the drugs, and the process can be sub-licensed to third parties as needed. The choice of development partner was made through a tendered process, and the International Dispensary Association (IDA, a non-profit making pharmaceutical

organization) was selected. TDR will oversee development of the drug package. Médecins sans Frontières (MSF) is funding most of the development work with money received from the Nobel peace prize awarded in 1999. TDR is also contributing funds. To ensure that drug dosing is optimal, easy to administer in the field, and based on sound scientific data, a study was conducted

with the US Centers for Disease Control (CDC). In this study, mostly African anthropometric data rather than US population-based data were used (the current CDC/WHO National Center for Health Statistics standard is based on a healthy US population). Weight-for-age data from 137 000 persons from disease-endemic areas, primarily in Africa, were used to ensure that as many people

as possible receive an optimal dose of each drug (not an under- or over-dosage). Following completion of large, randomized, controlled trials of artesunate-containing combinations, work is in progress on the feasibility of fixed-dose combinations of artesunate with other companion drugs, such as amodiaquine and mefloquine. ■

#### UPDATE

## Malaria: Do insecticide-treated materials merely delay childhood mortality?

*Results from one of the first studies to address the existence of delayed mortality from use of insecticide-treated materials*



WHO/TDR/Crump

Results from the first study to be completed on the question of whether insecticide-treated materials such as bednets and curtains prevent, or merely delay, childhood mortality recently became available. The study did not turn up any evidence that the predicted phenomenon of 'delayed mortality' exists, even though not excluding the possibility that it might exist. For some years, there has been concern that use of insecticide-treated materials (ITMs) in hyper-endemic malaria areas might merely shift the predominant age of mortality to a higher age-group – that because children may not be infected early in life, they will not build up immunity to malaria, and so will succumb to the disease later on in life. Hence a study with insecticide-

treated curtains was carried out on the site of a previous large-scale trial of the curtains, among a population of 90 000 in 158 villages in Burkina Faso. This study was non-experimental in design – all villages received the intervention for three years (some had previously used the intervention for an additional two years during the earlier trial). The study only aimed to show if significant delayed mortality was occurring, not to measure its extent.

Insecticide-treated curtains (ITCs) were found to provide substantial protection to people who slept in protected houses and also some degree of community protection by reducing the vector population. In the intervention area, the entomological inoculation rates (EIRs) indoors were estimated to be more than 90% lower than outside the area, while outdoors, the EIRs were estimated to be more than 80% lower. There was no evidence of a 'rebound' in vector densities over time.

Interpretation of the mortality data was complicated by the fact that, after a progressive reduction in mortality rate in the first two years, there was a sharp increase of 11% in the final year. However, this did not appear to be due to 'delayed mortality' because it occurred across all 0-5 year age-groups, slightly more so in the youngest, and would have had to have been far greater (more than 50%) to put in question the overall survival rate obtained through the use of ITMs during the first years of the study. ■

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# Roll Back Malaria update: Strategy for Research and Development



Research and development (R&D) features prominently in Roll Back Malaria (RBM), and the following is an outline of the WHO R&D strategy for this global movement. The strategy is based on two main aspects:

- **Provision of evidence to guide actions in rolling back malaria.**
- **Development of new tools, with emphasis on getting R&D results into practice as quickly as possible.**

Training and capacity strengthening are integral components. Whenever appropriate and possible, RBM R&D efforts will build on efforts already under way, e.g. RBM is working very closely with TDR, as its research arm within WHO, and, outside WHO, RBM's major R&D partners include the Multilateral Initiative on Malaria (MIM), research and training institutions and regional R&D networks, foundations and NGOs which support R&D on malaria.

The foci of RBM R&D, and key functions and actions, include the following:

## **Increasing global investment in R&D on malaria through:**

- Providing the necessary advocacy for increased spending on malaria R&D
- Ensuring that increased investment in RBM is reflected in a proportionate increase in R&D expenditure.

## **Providing sound evidence – a cornerstone of the RBM strategy – through:**

- Supporting operational research to guide the planning and implementation of control activities
- Evaluating the impact and cost-effectiveness of control interventions
- Research-based decision support systems to deal with the many complex demands of malaria control.

## **Supporting the development of new tools through:**

- Providing 'seed' funding to initiate high-priority R&D

## *Developing new malaria*

*control tools and providing evidence to guide actions form the basis of the RBM R&D strategy*

- Supporting the acceleration of development of new drugs, vaccines and other products
- Fostering innovative mechanisms for product development such as public/private partnerships
- Ensuring that the needs of malaria control in endemic countries influence priority-setting for R&D, e.g. through RBM presentations at all major R&D forums, from country to international level, and through making RBM country situation analyses widely available.

## **Ensuring quicker uptake of new tools through:**

- Regular review of the latest advances in technology and research products
- Support for multisectoral discussion groups (scientists, technical experts, industry, funders, policy makers, interventionists, public health officers)
- Policy research in developing countries

## **Improving application of existing tools through:**

- Identification of knowledge gaps, and tools and product-needs, for RBM in endemic countries
- Putting existing interventions into wide-scale and appropriate use
- Establishing effective linkages between researchers and control programme staff as an integral part of RBM.

## **Capacity building through:**

- Helping develop the capability to enable malaria endemic countries to be self-reliant in operational research
- Support for a number of scientific and training institutions in advanced developing, and developed, countries
- Strengthening of scientific research in the 'South'
- Support for R&D agencies building this capacity
- Helping develop the capability of the malaria control sector to engage in evidence-based actions for rolling back malaria. ■

## CONTACT

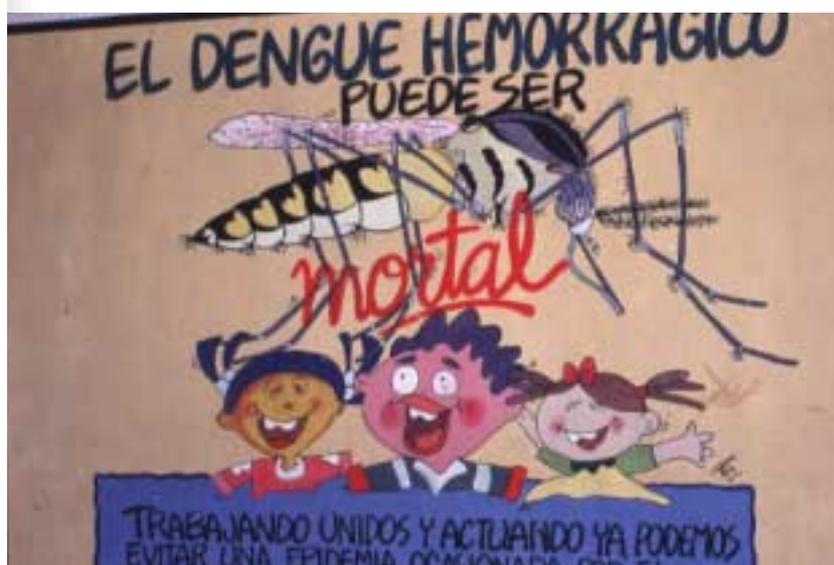
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## SEE ALSO

[www.rbm.who.int](http://www.rbm.who.int)

# Dengue Fever/ Dengue Haemorrhagic Fever in the Americas

By Dr J.R. Arias and Dr Z. Yadon, PAHO, WHO Regional Office for the Americas



the geographical areas that are at highest risk using geographical information systems, use of alternative ovicides (household bleach i.e. chlorine as 5.25% sodium hypochlorite solution) and larvicides (lime), epidemiological risk factors, and knowledge, attitude and practices (KAP) studies. Dengue control in many countries of the Americas has been based on emergency interventions to face epidemics that have appeared in countries such as Paraguay, Ecuador, El Salvador, Guatemala, Honduras, Nicaragua, Dominica

In South America, Dengue health education materials are aimed especially at children.

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Dengue fever/dengue haemorrhagic fever (DF/DHF) is on the increase in most of the countries of the Americas. It appears that the trend of dengue in many countries is very similar to the situation in some Asian countries 20 or 30 years ago: DF epidemics are being seen every three to five years, and the incidence of DHF is ever-increasing, particularly in Central America (in El Salvador, Guatemala, Honduras and Nicaragua). This situation is the result of high densities of *Aedes aegypti*, the vector mosquito, brought about by lack of an adequate supply of water and solid waste disposal, rapid uncontrolled urbanization, and deterioration of the control agencies. The circulation of multiple dengue serotypes and decentralization of health services have compounded the problem.

The PAHO/TDR Small Grant Programme has included dengue in its agenda for the past two years. In the first year (1999), of 110 project proposals received, 11 were on dengue. Of the 16 projects that were funded, four were on dengue. These projects were carried out in 2000. In the second year (2000), 97 letters of intention were received of which 29 were on dengue. Of the total, seven on dengue were short-listed. Project selection for 2000 took place in December 2000 and the projects will be funded and carried out in 2001.

Research activities in the Americas have focused on operational aspects such as determination of

and Costa Rica. Some countries that have a strong base in social communication and community participation (such as Panama) have been spared the major epidemics of recent years. Cuba has a very strong vertical programme and its efforts have given it positive results even though, in 1997, it was the victim of an outbreak in Santiago. Uruguay, even though infested with the vector, has been free of autochthonous dengue since the vector was eradicated prior to 1960. Chile still remains free from the vector (and dengue), also since its eradication before 1960.

The Pan American Health Organization has drawn up a proposal for its member countries, recommending they introduce more intersectoral actions into their prevention and control programmes, including social communication that may lead to behavioural change in individuals and households to reduce vector species breeding sites. Many countries have embraced this plan of action and are in the process of incorporating it into their programmes. ■

# Chiang Mai Declaration on Dengue Fever/Dengue Haemorrhagic Fever

## Considering that

Dengue fever (DF) is the most important mosquito-borne viral disease of humans. There has been a dramatic increase in geographic spread, numbers of cases and severity of disease in the past 30 years. Currently 2.5 billion of the world's population, primarily in tropical developing countries, are at risk. Annually, there are estimated to be tens of millions of cases of the disease. Hundreds of thousands of these are of the more severe dengue haemorrhagic fever (DHF) which is a leading cause of childhood hospitalization and death in many countries. The economic impact of DF/DHF is comparable with that of other major infectious diseases such as malaria, tuberculosis and hepatitis.

## And that

Tools to reduce dengue morbidity and mortality are currently available for appropriate case management and mosquito control. Dengue is an environmental issue, its prevention and control requires collaboration with many sectors. Several countries have demonstrated that, with strong political commitment, the wide and wise use of these tools can result in successful control.

## In recognition

Of the magnitude of this global public health problem, and at the initiative of His Majesty King Bhumibol Adulyadej of Thailand, an international conference with over 700 public health specialists from 41 countries was held in Chiang Mai, Thailand, from November 20 to 24, 2000.

The delegates of the First International Conference on Dengue/DHF in the new millennium

## Recommend

that all countries at risk for dengue transmission develop and implement sustainable prevention and control programmes, and

## Resolve

- To strongly endorse the WHO global strategy for prevention and control of DF/DHF;
- To advocate increased political commitment and resources for improved and sustained prevention and control efforts;
- To promote active intersectoral partnerships involving international, regional, national and local agencies, non-governmental organizations, foundations, private sector and community organizations;
- To build and strengthen capacity of health systems for DF/DHF treatment, surveillance, prevention and control;
- To pursue, encourage and support the development, application and evaluation of new and improved tools and strategies for DF/DHF prevention and control.

*Chiang Mai, Thailand  
November 24, 2000*

# The genetic transformation of a malaria mosquito

Transforming the malaria-transmitting mosquito into a harmless insect which doesn't carry the parasite has been the

goal of the TDR Molecular Entomology initiative since 1991. The insertion of a gene for green fluorescence protein, as a marker, into the malaria transmitting *Anopheles stephensi* marks the beginning of a new phase along the road to this goal.\*

The event is a breakthrough, although there is still a long way to go to reach the goal, which is projected to be ten years away. The green fluorescence gene is used as a model gene. It makes the mosquito glow green when excited with ultraviolet light and might, at a later stage, be replaced by genes which inhibit parasite development.

Genes which inhibit parasite development in the mosquito are being identified in a second line of

research under the Molecular Entomology initiative. Interesting genes have already been found, e.g. immune response genes. Key molecules in the mosquito that are essential for the parasite are also being identified, e.g. xanthurenic acid was identified as a factor essential for activating the gamete stage of the parasite. This work will provide potential target genes for insertion into the mosquito genome. A third line of research under the initiative is to develop mechanisms for driving the selected genes into natural populations of mosquitos. Possible driving forces have already been described e.g. using transposable elements, which spread through natural popula-

Scientists successfully  
insert a functional gene  
into mosquitos



Genetically manipulated larvae fluoresce when exposed to UV light.

tions easily. Genes associated with mosquito choice of food host (animal or human) are also being sought. Proteins

and genes thought to be involved in recognizing human odours, and therefore important in host-finding, have been identified – cloning and characterization of some of these olfactory genes in *An. gambiae*, the main vector of human malaria in Africa, has begun.

*An. stephensi* is one of the major carriers of malaria in urban areas of the Indian subcontinent. Applying this transformation system to *An. gambiae* will speed up understanding of the physiology of the mosquito carriers of the disease and their interaction with the malaria parasite. Ultimately this work could lead to the replacement of wild mosquito populations with 'safe' strains of mosquito unable to transmit malaria.

Of course, numerous and important scientific, ethical, safety and regulatory issues will have to be addressed before such a strategy could be used to control a vector borne disease. The benefits and risks associated with such an approach will have to be carefully assessed, with full consideration given to community, policy and socioeconomic reactions and impacts. The TDR committees of Social, Economic and Behavioural research (SEB) and Molecular Entomology are formulating a joint initiative for this purpose. This will focus on issues of risk perception, assessment and communication, ethics, choice of sites and plans for deployment, and socioeconomic issues associated with such an undertaking. ■

\*2000, Catteruccia F. et al. Stable germline transformation of the malaria mosquito *Anopheles stephensi*. *Nature* 405 (6789): 959-62. 22 June 2000.

Following page:

Example of TDR's Final Reports, a regular series of publications illustrating how TDR-supported research work is breaking new scientific ground, generating new knowledge, developing new tools and making innovative progress in the fight to combat tropical diseases.



## Training

▶ **Arthropod vectors transmit diseases to hundreds of millions of people each year, causing millions of deaths. The morbidity and socioeconomic losses associated with these diseases are overwhelming and, in many instances, increasing. The resurgence of some diseases and failure to control others have a variety of causal factors, including the lack of trained scientists in vector-borne diseases. The Biology of Disease Vectors course was established to try and rectify this shortage of skilled scientists working to control vector-borne diseases.**

Since its inception in 1991, the training course on the Biology of Disease Vectors (BDV) has been supported annually by TDR in partnership with, and under the leadership of, the MacArthur Network on the Biology of Parasite Vectors. The Howard Hughes Medical Institute has also become a co-sponsor.

The BDV course trains highest quality students in molecular, genetic and quantitative approaches to the study of disease-transmitting insects. The course's main objectives are to 1) train a new generation of vector biologists and provide current medical entomologists with a foundation of modern molecular techniques; 2) recruit molecular biologists from other research areas into the field of vector biology; 3) establish a global network of scientists to facilitate collaborative investigations and to enhance progress in the field.

Initially, the course was taught at the Colorado State University in the USA. More recently, it has been hosted in a variety of international venues (Greece, Mali, Brazil and the Czech Republic) to provide easier access for students from regions where vector-borne diseases are endemic.

The course is advertised internationally and attracts hundreds of applicants each year, of which approximately 35 outstanding students are selected. The students come from around the globe,

including a significant number from countries where vector-transmitted diseases are a major problem. Students are typically advanced Ph.D. students, postdoctoral fellows, and established investigators aiming to increase their skills in vector biology or redirecting their careers from other areas. Some 40% of participants are women. As a rule, 20 world-renowned scientists from leading institutions are chosen to give the lectures and supervise the laboratory work.

The BDV course has been an extraordinary success. Small class size and global expert teachers provide an unparalleled learning and networking experience. International collaborations are established and continue to grow. Course evaluations have been overwhelmingly positive. Recommendation from former students and faculty is the primary driving force for new applications. Graduates from the early courses are already emerging as leaders in the field of vector borne diseases, and a number of them have been chosen to teach in more recent courses. The BDV course is helping to train a new generation of vector biologists, who are already playing leading roles in improving the health of millions of people. ■

#### Reference:

"The Molecular Biology of Insect Disease Vectors: a methods manual", (1997) 604pp. Chapman & Hall

**PROJECT No. 910331,  
950885 - 990630**

Training course:  
'Biology of disease vectors'

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**UNDP/World Bank/WHO  
Special Programme for  
Research and Training in  
Tropical Diseases**

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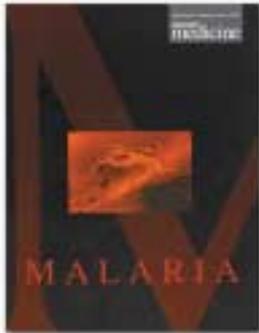
#### Information source:

Dr B. Dobrokhotov  
e-mail: dobrokhotovb@who.int

**TDR FUNDING: US\$ 256 500 (1991-2000)**

## TDR VARIOUS

- **NATURE Medicine. Special focus: Malaria.** Sponsored by MMV and TDR. 30 pages.



- **A focused research agenda to influence policy and practice in home management for malaria.**

Meeting Report (8-11 May 2000, Kilifi, Kenya.)  
*TDR/IDE/MHM/00.1*  
26 pages.

- **Recommendations of a Scientific Working Group on Dengue.**

Meeting Report (3-5 April 2000, Geneva, Switzerland).  
*TDR/DEN/SWG/00.1*  
10 pages.

- **Recommendations of a Scientific Working Group on Strategic Social, Economic and Behavioural Research.**

Meeting Report (31 May-2 June 2000, Geneva, Switzerland).  
*TDR/STR/SEB/SWG/00.1*  
11 pages.

- **Operational Guidelines for Ethics Committees that Review Biomedical Research.**

*TDR/PRD/ETHICS/2000.1*  
31 pages. Available in English, French, German, Spanish, Turkish, Lao, Russian.

- **Prospective Thematic Review of TDR Research Capacity Strengthening.**

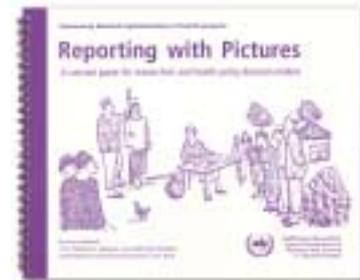
Meeting Report (15-17 November 1999, Geneva, Switzerland).  
*TDR/RCS/PTR/00.1*  
18 pages.

- **Recommendations of a Scientific Working Group on Tuberculosis.**

Meeting Report (9-11 February 2000, Geneva, Switzerland).  
*TDR/TB/SWG/00.1*  
13 pages.

- **TDR Strategy (2000-2005).**

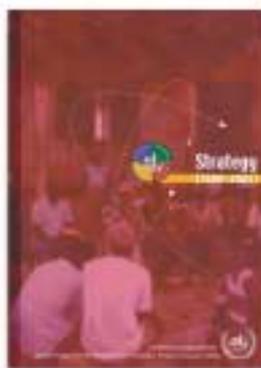
*TDR/GEN/SP/00.1/Rev.1*  
28 pages.



- **Reporting with pictures; a concept paper for researchers and health policy decision-makers,** A. Haaland, O.B. Akogun, O. Oladepo, O.O. Kale.

*TDR/IDE/RP/00.1*  
80 pages.

This manual followed from an operational field research project on Community-Directed Treatment of Onchocerciasis with ivermectin. It explains how communities can undertake their own record-keeping and reporting without illiteracy being a constraint. The manual describes the conceptualization, development, testing and adaptation of a pictorial reporting form used in ivermectin distribution programmes, summarizes the lessons learnt in the process, and relates these lessons and experiences to other research questions and topics. It also summarizes the principles of visual perception among illiterates, upon which the form builds, and which were confirmed by testing in different countries. This publication is a succinct yet comprehensive exposition of how policy makers and health planners, among others, can extend the frontiers of health care at the 'grass roots' level, thus providing a substantial window of opportunity beyond simple drug delivery. ■



**HOW TO OBTAIN PUBLICATIONS**  
All TDR publications are available to download from the TDR website: [www.who.int/tdr/publications/publications](http://www.who.int/tdr/publications/publications) or on request from TDR Communications

## OTHER PUBLICATIONS

- **Bulletin of the World Health Organization, Special theme: Malaria. 2000, 78 (12): 1374-1491**

The theme section of this Bulletin covers a wide range of malaria topics, from combination therapy (a review of its use in South-east Asia, outlining the problems that need to be overcome in order to adopt it successfully in sub-Saharan Africa), insecticide-treated mosquito nets (a review of six studies comparing insecticide-treated bednets with indoor insecticide spraying), to the possible use of genetically modified *Anopheles* for vector replacement (a review of recent progress in molecular studies of malaria vectors in three areas with potential for near-term impact in malaria control: species identification, population genetics and insecticide resistance), from the use of geographical information systems in the planning, execution and monitoring of interventions (computerized mapping and management of data stand to greatly assist the targeting of interventions against malaria), to the potential role of post-genomics research in the develop-



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ment of new anti-malarial drugs (a review of the current status of the *P. falciparum* genome sequencing project

and the unique insights it has generated, and of the application of functional genomics tools to the identification of new therapeutic strategies and targets). A new section 'Public Health Classics', takes a look back at the ground-breaking demonstration by Shortt and Garnham in 1948 of the exo-erythrocytic cycle of the malaria parasite, and includes a commentary on the significance of this discovery from a modern-day perspective. ■

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### Net news

The good news for researchers is that more and more scientific journals are becoming available in full text on the web. The bad news is that, for many, you have to pay for them. So where can you find free online access to full text journals?

Free Medical Journals.com [www.freemedicaljournals.com](http://www.freemedicaljournals.com) is dedicated to the promotion of free access to full text medical journals. It lists links to over 500 journals covering areas such as epidemiology, infectious diseases, pharmacology, public health and tropical diseases. More selective is the new PubMed Central website [www.pubmedcentral.nih.gov/](http://www.pubmedcentral.nih.gov/), which provides a web-based archive of full text life sciences journals. Other sites of interest are SciELO [www.scielo.org](http://www.scielo.org), which focuses on South American science journals, and the recently revamped Parasitology Online [www.parasitology-online.com](http://www.parasitology-online.com), which offers free full text access to certain issues and articles for a range of parasitology journals.

Of course, a trip to the library is likely to open more doors, as many subscribe at an institutional level to services such as OVID [www.ovid.com](http://www.ovid.com), which provide online access to journals for staff working in the institution. Ask your librarian for details. ■

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We welcome feedback  
or any Net sites and  
observations.

## New lease of life for resurrection drug

*Companies agree to make and donate 60 000 doses of eflornithine for use in treatment of sleeping sickness*

The supply of eflornithine, nicknamed the 'resurrection drug' because of its spectacular effect on comatose patients in late-stage gambiense sleeping sickness, may at last be assured. WHO and Médecins sans Frontières (MSF) have been working towards this end since 1999.

Eflornithine was discovered in 1980 by Dr Cyrus Bacchi, Pace University, New York, through a TDR-supported study on polyamine metabolism in trypanosomes (the causative organism of sleeping sickness). This study demonstrated that, in mice, eflornithine was effective against the enzyme ornithine decarboxylase, a key enzyme in the multiplication of trypanosomes. Following clinical trials, eflornithine was registered for the treatment of gambiense sleeping sickness in 1990. But eflornithine is expensive, and unaffordable by the affected countries and consequently, manufacturing of the bulk material ceased in 1995.

However, in December 1999, Hoechst Marion Roussel (now Aventis) granted to WHO the production rights for eflornithine to find a third party manufacturer (*TDRnews* No. 61). Now WHO/TDR, in collaboration with MSF, have identified potential third party manufacturers. Available stocks donated by Aventis (the French-German company holding the patent rights for eflornithine), in 1999, after formulation of all remaining bulk material, are projected to last until June 2001.

As *TDRnews* was going to press, news of the latest developments was breaking. Bristol-Myers Squibb (BMS) – which, with

Gillette, has recently introduced Vaniqa™, an eflornithine-containing cream, for removing facial hair in women – in collaboration with Dow Chemical Co., Akorn Manufacturing Inc., and Aventis had agreed to make and donate to MSF's warehouse in Bordeaux, France, 60 000 doses of eflornithine by June 2001 for use in treatment of sleeping sickness. This supply will last for 3 years. Discussions are in progress between BMS, WHO/TDR and MSF concerning the BMS proposal that, after 3 years, production of eflornithine by Dow Chemical Co. and Akorn Manufacturing Inc. could continue, but would have to be purchased. The most critical part of these discussions relate to price: MSF would like to see this pre-arranged at US\$10 per dose (as compared to, in 1997, a price of US\$20 per dose).

A course of eflornithine treatment is typically one injection a day for 14 days. Currently, preliminary clinical studies are ongoing with an oral formulation of the drug. If subsequent Phase III clinical trials prove its safety and efficacy, oral eflornithine could replace the injectable form and would be less expensive. As well, the ease of administration would allow its use on a wider scale for the treatment of gambiense sleeping sickness. ■

## RESEARCH NEEDS

## Repositioning of leprosy in TDR: notice to leprosy researchers

In December 2000, Carlos Morel, Director TDR, and Bjorn Melgaard, Director WHO Department of Vaccines and Biologicals, agreed that leprosy research previously under the purview of the TDR Steering Committee on Immunology of Mycobacterial Diseases (IMMYC), will in future be integrated into each of the four functional areas of TDR: Basic and Strategic Research (STR), Product Research and Development (PRD), Intervention Development and Implementation Research (IDE), and Research Capacity Strengthening (RCS). This move brings leprosy into line with all the other diseases in TDR's mandate, which have been addressed by the functional units since 1994, and it will make TDR leprosy research more sustainable. Dr Paul Nunn, in his position as TDR Leprosy Disease Coordinator, will coordinate TDR activities with each of these areas. Researchers are invited to submit proposals directly to each areas according to their deadlines. ■

PLEASE SEE FULL DETAILS AND  
DEADLINES ON THE FOLLOWING PAGE

ADDITIONAL INFORMATION  
on research grants as well as  
application forms are also  
available through TDR's website:

[www.who.int/tdr/grants](http://www.who.int/tdr/grants)

# Steering Committee and Task Force meetings

	Meeting date	Deadline
<b>BASIC AND STRATEGIC RESEARCH (STR)</b>		
• Molecular Entomology (BCV)	24-27 September 2001	24 July 2001
• Pathogenesis and Applied Genomics (PATHO)	24-27 September 2001	24 June 2001
• Social, Economic and Behavioural Research (SEB)	4-8 June 2001	23 March 2001
<b>PRODUCT RESEARCH AND DEVELOPMENT (PRD)</b>		
• Drug Discovery Research (DDR)	26-30 March 2001	26 January 2001
• Vaccine Discovery Research (VDR)	28 May-1 Jun 2001	28 March 2001
<b>INTERVENTION DEVELOPMENT AND IMPLEMENTATION RESEARCH (IDE)</b>		
<i>IDE Task Forces may call for specific proposals at any time of the year according to their workplans.</i>		
• Severe Malaria (SEVERE)	March 2001*	
• Research on Drug resistance and Policies (RAP)	March 2001*	
• Malaria Home Management (HOME-MGT)	March 2001*	
• Filariasis Intervention Research (FIL)	Early May 2001*	
• Intervention Research on Chagas Disease (CHA)	2-4 May 2001	
• Intervention Research on African Trypanosomiasis (TRY)	4-6 September 2001	
<b>RESEARCH CAPACITY STRENGTHENING (RCS)</b>		
• Research Strengthening Group (RSG)	2002	31 October 2001
• Malaria Research Capacity Strengthening in Africa (MIM) **	2002	30 November 2001

\* tentative

\*\* progress reports and renewals only

## ***In memoriam***

Sadly did TDR staff learn of the death of two staff members last year, **May Gatan** and **Veronica Vaz**, who are still greatly missed, and of the following TDR associates, **Dr U. K. Sheth** Professor/Director, Department of Pharmacology, GS Medical and KEM Hospital, Mumbai, India; **Dr Robert Mshana**, Organisation of African Unity, Lagos, Nigeria and member of the TDR Vaccine Discovery Research Committee; and PhD Research Trainee **Fred Msadallah Salum**, of the National Institute for Medical Research, Amani Research Centre, United Republic of Tanzania, who passed away in May 2000. ■

# Uzbekistan: Samarkand

(23-30 October 2000)

*Isaev Research Institute of Medical Parasitology*

- *Leishmaniasis Laboratory facilities (where live Leishmania inocula are produced for a leishmanization programme. This offers potential for evaluating vaccine candidates. TDR is improving GMP in the institute as part of an Institution Strengthening Grant).*
- *Institute Medical Clinic – Leishmaniasis ward.*
- *Institute facilities (museum, library, conference room – where WHO Regional Workshop of Malaria was being held).*
- *TB hospitals*
  - *pulmonary*
  - *extra-pulmonary.*



WHO/TDR/Crump

Technicians carefully measure the rate of temperature reduction as live *Leishmania* parasites are killed by freezing in liquid nitrogen.



WHO/TDR/Crump

Participants in the malaria training workshop share data on the malaria situation in their countries and cover all aspects of research and control activities in the region.



WHO/TDR/Crump

A woman taking her DOTS drugs dispensed at the TB hospital.



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#### TO OUR READERS

We are unfortunately unable to accept for publication in *TDRnews* announcements (for meetings, new programmes, institutions, publications, etc.) which readers send us. Announcements which relate to research on tropical diseases would clearly be of interest to our readers. However, because of limited space in the newsletter, we regret that we can publish only those concerning events in which TDR is directly involved.

#### CONTACT

All TDR Image Library images can be viewed on-line: [www.who.int/tdr](http://www.who.int/tdr)

TDR is also able to provide a limited number of CD-ROM of the Image Library to institutions.