INVESTING IN HEALTH AND DEVELOPMENT

Research capacity building
in developing countries

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

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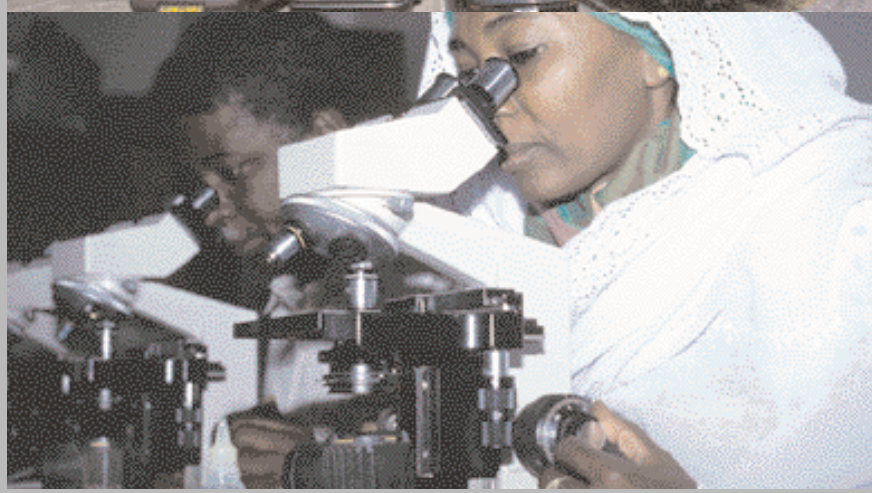

For over 50 years, scientific and technological advancements have created tremendous opportunities for progress in combating tropical diseases. But developing countries cannot find solutions to their public health problems merely by acquiring equipment and medicines. Today, skills and aptitude matter more than ever before. The ability to optimally exploit knowledge and devise solutions to local problems that work in prevailing conditions is paramount. Not everyone needs the latest technological advances. But every developing nation needs capacity. The capacity to identify benefits and opportunities and to adapt them to their own needs and constraints, the ability to initiate and engage in research and apply knowledge and technology to essentially local problems, moving beyond the mere application of results generated by others.

The past decades have witnessed an exponential growth in scientific research capacity in developing countries – where TDR's target diseases have their greatest day-to-day impact, and where solutions to the diseases and their detrimental influence on individual and collective livelihoods and productivity are most urgently needed. This is evidenced by the greater financing of research and development (R&D) and a corresponding increase in the number of people engaged in research in developing nations. TDR has played a significant role in this expansion. The programme has not been alone in promoting and improving individual and institutional R&D capacity in developing countries. However, since it was established over 25 years ago, TDR has continued to invest substantially and strategically in creating or boosting research capacity in developing countries, as an explicit objective of the Programme. While our capacity building strategies have traditionally been flexible, responding to changes in internal and external environments, this goal has remained, and will remain, constant.

TDR has several significant comparative advantages, which separate it from other agencies. One is the continuum of funding opportunities available to scientists resulting in a fundamental long-term commitment to the capacity building process. Researchers can initially obtain support for research training, followed by further specialist grants to facilitate the development of an independent research career, or grants for institutional development, scientific partnerships and networks with the longer term objective of sustainable R&D funding.

Investing in capacity building is not without risk – there have been failures but more often than not success. One of the commonest problems has been that of identifying outstanding individuals, training them and then seeing them simply become part of the 'Brain Drain' of talented individuals emigrating to more attractive situations in industrialised nations. Almost uniquely, TDR has managed to avoid this, with virtually all TDR trainees having returned to their disease-endemic home countries or to their region and established research careers. Consequently, institutions have often grown through the coalescence of often dispersed, isolated, local groups into international collaborative partnerships and centres of excellence. Moreover, some individuals have also exceeded expectations and established exceptional careers in science – and beyond.

Measured in numbers, TDR support for capacity building has encompassed over 1200 individuals from over 400 institutes in 80 countries included in the UN definition of "developing countries". However, this indicates only the 'supply side' of the equation and does not adequately describe the real and comprehensive contribution these individuals have made. In this publication, the careers of a few selected TDR-funded individuals are briefly described, along with the impact of their work on the disease situation in their home countries. They are presented within TDR's current strategic R&D framework. They represent an alumni that would be hard to find an equal to. They represent past successes, present endeavour and substantial hope for the future. TDR is committed to ensure that the paths these proven leaders have pioneered so well are followed by many others over the coming decades.

Carlos M. Morel
Director, TDR

FOR OVER 25 YEARS,

TDR has been at the forefront of global efforts to improve health in developing countries – working through a range of partnerships and networks to target neglected diseases that mainly affect the poor. The programme is a key player in research on the development and implementation of new and existing tools and strategies for the control of tropical diseases and in strengthening research capacity in countries with the highest disease burden. Today, efforts are under way to eliminate four of the diseases targeted by TDR – leprosy, onchocerciasis (river blindness), lymphatic filariasis, and Chagas disease. But other neglected diseases – including TB and malaria – continue to kill or disable millions of people every year and hold back development in the poorest countries.

There is a continuing need for research both to maximize the use of existing tools and strategies and to develop new and better ones to reduce the high burden of infectious diseases.

New drugs are also urgently needed today to counter the spread of antimicrobial resistance. Many first-line drugs are losing their effectiveness as disease agents become increasingly resistant through misuse and overuse of essential drugs.

In addition, widespread infection with HIV/AIDS (unknown when TDR was created) has increased susceptibility to both TB and leishmaniasis and increased the prevalence of both.

Meanwhile, global investment in research on diseases that mainly affect the poor is a drop in the ocean in relation to the high disease burden involved. It is estimated only 10% of global investment in health research is targeted to the diseases which account for 90% of global disease burden. In 1998, for example, less than 1% of the US$70 billion spent on the research and development of new medicines, vaccines, and diagnostic tools was used for HIV/AIDS, malaria, and TB – which together account for almost 6 million deaths a year. A recent report* by the Commission on Macroeconomics and Health – established by WHO Director-General Dr Gro Harlem Brundtland in 2000 – called for a significant scaling up of financing for global research and development on the diseases with the highest disease burden in poor countries.

To make matters worse, most research on neglected diseases is still carried out in industrialized countries, not in countries where the diseases are endemic. While researchers in disease-endemic countries are closer to the problems and may hold the key to solutions, all too often they are handicapped by the lack of essential skills, equipment, access to information, and opportunities to participate in the global health research agenda.

The way forward

In response, TDR has developed a new strategy, designed to bridge the gap between health research and disease control and further strengthen research capacity in the poorest countries. The aim is to speed up the development and implementation of urgently needed tools and strategies for disease control by involving developing country researchers at every stage of the research and development process – from strategic research and product development through product registration and "proof-of-principle" trials to implementation within the health system. This new involvement in implementation research will entail working more closely with disease control programmes and national governments. The new strategy, which is being gradually phased in, places research capacity strengthening at the heart of the programme – underpinning everything it does, from the discovery of new basic knowledge, to the development of new tools, new intervention methods, and new policies for disease control.

This new expanded mandate also involves a corresponding shift in the allocation of resources for research capacity strengthening. While research capacity building in the least-developed countries remains a priority, a greater proportion of resources is now being invested in capacity building in more developed countries to support a TDR-driven research and development agenda. Top of this agenda will be investment in the

*Macroeconomics and Health for Economic Development: Investing in Health for Economic Development: the Report of the Commission on Macroeconomics and Health, December 2001

research and development of new tools for the prevention and control of TB and African trypanosomiasis (sleeping sickness).
By 2005, funding for individual capacity building (through training and research projects) will account for only 10% of funding for research capability strengthening (down from 50%) and institutional capacity building will get 30% of funds. The lion's share (60%) will be spent on strengthening existing research capacity in more developed countries to support research and development in TDR priority areas.
By capitalizing on the research capacity it has helped to build up in developing countries, TDR aims to speed up the implementation of new and existing tools and strategies to reduce the high burden from infectious diseases.

Investing in research capacity strengthening

Over the years, TDR has supported individual career development and institution strengthening involving over 400 research groups and institutions in about 80 disease-endemic countries.
This ongoing development of core leadership and research capacity has enabled individual researchers and institutions in developing countries to be more responsive to public health needs in their own countries and to participate more effectively in the global research agenda.
TDR has contributed to the formation of a new generation of public health leaders – many of them now directing disease control and research efforts in their own countries. Many of the research groups and institutes supported by TDR work in close collaboration with research partners from industrialized countries and play a key role in strengthening research capacity in other developing countries – enabling "best practices" to be shared via South-South linkages.
Meanwhile, several TDR-supported institutes are now world class research centres in their own right. Some of the outstanding individuals and research institutes which have received TDR grants to strengthen research capacity are featured on the following pages.

Among them are leading research and training centres – many of them sited not in major towns or cities but often in remote areas where the disease burden is highest. Some focus on a priority disease, while others focus on a wide range of health problems.
Several have consistently trained and built up wide-ranging multidisciplinary teams of researchers – including social scientists, economists, and demographers as well as a raft of health professionals. Some have used TDR support to develop the expertise and facilities needed to carry out clinical trials of new drugs and vaccines.
Many of the individual researchers featured here were supported by TDR to enable them to study for masters degrees and doctorates in partner institutions in industrialized countries. Today, all of them have returned to work in their own or a neighbouring developing country.
All have contributed to training others.
One research partner in Latin America helped operate a TDR-funded small grants programme which trained and built up a community of over 100 young researchers in the up-till-then neglected area of health and social science research. Some of the researchers are involved in cutting-edge scientific research – making use of new molecular techniques to discover new basic knowledge that will help speed up the development of new vaccines, drugs, and diagnostic tools.
Several have had the satisfaction of seeing new tools and intervention methods adopted by disease control programmes and implemented almost immediately. Others have contributed to greater understanding of the health economics and socioeconomic impact of health policies.
Some are contributing to improved knowledge sharing by establishing regional networks of researchers and carrying out collaborative training and research in countries with a shared disease problem.
All of them are likely to be key partners in the TDR-directed research agenda to improve health and boost development in the poorest countries.

Profile:

SIMA RAFATI

Dr Sima Rafati is using new molecular tools to develop vaccines against cutaneous and visceral forms of leishmaniasis, which are widespread in the Islamic Republic of Iran. With TDR capacity-building support, she has trained and built up a research group at the Pasteur Institute in Tehran. Her latest research aims to limit the spread of leishmaniasis by developing a DNA vaccine to prevent the disease in dogs, one of the main reservoir hosts for visceral leishmaniasis.

Dr Sima Rafati, who heads the Department of Immunology at the Pasteur Institute in Tehran, Iran, works at the forefront of vaccine development. With support from TDR, her research group has used genetic engineering techniques to isolate two genes from leishmania parasites which could form the basis of future vaccines against the cutaneous form of the disease. One of these genes – known as a cpa gene – was a new discovery in this species. The new gene has now been formally registered in the global gene bank. In October 2001, in Paris, Rafati was awarded the Institute Pasteur/UNESCO Medal in recognition of this discovery and of her ongoing contribution to the development of a vaccine against leishmaniasis.

Buoyed by this success, Rafati and her team have now set their sights on the parasite that causes the visceral form of the disease. With renewed support from TDR, they aim to show that the same genes, extracted from a different parasite, can be used to protect dogs – one of the main reservoirs of the disease – and possibly humans, against visceral leishmaniasis.

The stakes are high. There are an estimated 12 million cases of leishmaniasis worldwide and about 2 million new cases every year. An estimated 350 million people in 88 countries are at risk. And visceral leishmaniasis is on the increase today – fuelled by the spread of HIV/AIDS, which increases susceptibility to the disease. In Iran, cutaneous leishmaniasis remains a major public health problem. Most cases – about 20 000 a year – involve the cutaneous form of the disease, which causes extensive lesions and can result in permanent scarring and serious disability. Humans and rodents (gerbils) are the main reservoir for this form of the disease. Visceral leishmaniasis, the most serious, life-threatening form of the disease, accounts for about 5000 cases a year, mainly in the north-west and south of the country. In endemic areas, almost all those affected (97%) are children under 10 years old. The disease involves fever, weight loss, anaemia, and swelling of the liver and spleen. Over time, the parasites destroy white blood cells and severely weaken the immune system. Dogs and humans are the main reservoir for visceral leishmaniasis in Iran. Both forms of the disease are transmitted by sandflies.

Rafati says there is an urgent need to develop a safe and effective vaccine. "A large number of young people develop this disease and to date there are no effective ways of controlling the sandfly vector or the reservoir of the parasite," she says. To make matters worse, resistance to first-line drugs for visceral leishmaniasis is on the increase and second-line drugs are too expensive, difficult to administer, and have unpleasant side-effects. And although a new oral drug, miltefosine, is in the pipeline (see also Sundar page 20), it will not, initially at least, be registered for use in children, who account for the majority of new cases. In the 1980s, during the Iran-Iraq war, over 2 million Iranian military personnel and 6000 refugees underwent "leishmanization", in an effort to immunize them against the disease by injecting live cultured parasites. However, 2-3% of those who returned from the war and were monitored developed large or long-duration lesions (i.e. lasting for more than 12 months), indicating that the widespread use of a "live" vaccine would not be advisable under the

GRANTS

- ***Research Training Grant: 1996***
  Protective capacity of SW3 recombinant protein and synthetic peptides against Leishmania major
- ***Research Group Development Grant: 1997-2000***
  Identify/characterize gene coding a 24 KDa protein of the amastigote stage of L. major, a putative vaccine subunit
- ***Vaccine Discovery Research Grant: 2001***
  Evaluation of immune responses against L. infantum Cysteine proteinases in Kala-azar individual and DNA vaccinated dogs

MEMBERSHIP

prevailing conditions. Consequently, the procedure was discontinued after the war ended in 1989.
Rafati's ongoing search for likely candidate vaccines has involved the development of a team of young postgraduate researchers from different universities in Iran as well as training for staff at the Pasteur Institute in Tehran. "This is very important because leishmaniasis is one of the main health problems in Iran and we need to engage young scientists in efforts to prevent the disease," says Rafati. "One of my main goals is to encourage, train, and involve young postgraduate students in research programmes – especially students from areas where leishmaniasis is endemic."
With TDR funding for research capacity building, a new molecular biology laboratory was established at the Institute, which has enabled the training of seven postgraduate students and five members of staff so far.
Eventually, Rafati hopes the gene discoveries she has made may contribute to the development of a "cocktail" vaccine, comprising protective antigens against the different forms of the disease.

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***Rafati, S.**, et. al. (1997):* Biochemical analysis and immunogenecity of *L. major* amastigote fractions in cutaneous leishmaniasis. *Clinical Experimental Immunology*, 110: 203-211

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***Rafati, S.**, et. al. (2000):* Vaccination of BALB/c mice with 24 kDa antigens of amastigote form of *Leishmania major*. *Clinical and Experimental Immunology*, 120: 134-138

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***Rafati, S.**, et. al. (2002):* Cysteine proteinase type I and II of *Leishmania infantum* are recognized by sera during canine and human visceral leishmaniasis. (Submitted)

Profile:

RODRIGO CORREA-OLIVEIRA

Researchers in Brazil are drawing up the family pedigrees of the entire population of two villages – Melquiades and Virgem Das Gerais in the state of Minas Gerais – in a bid to find out whether natural resistance to the parasitic disease schistosomiasis is an inherited trait. The research team, headed by molecular immunologist Dr Rodrigo Corrêa-Oliveira, is also trying to find out whether people from some family groups are more likely to develop a severe, life-threatening form of the disease once they become infected.

The aim is to discover key antigens which could be used to develop a vaccine against the disease. Although the disease is treatable with praziquantel, the drug is not 100% effective and there are already reports of drug resistance in some areas.

The data which has been collected by the research team over 5-6 years includes four generations of family members. In 2002, when the data is complete a genome scan will be carried out to examine key inherited traits. In addition, Corrêa-Oliveira and his team are studying the contribution of socioeconomic factors and of environmental factors – such as regular domestic or agricultural contact with parasite-infested water – in increasing susceptibility or resistance to the disease. The study which has been jointly funded by TDR, the European Community, the US National Institutes of Health (NIH), and the Brazilian government, involves 3000 people from different socioeconomic groups who live and work in areas where schistosomiasis is endemic.

In 1992, Corrêa-Oliveira was awarded a TDR Career Development Grant to study the role played by cytokines – chemical messengers of the immune system – in determining the outcome of schistosomiasis infection and in natural and acquired immunity to the disease. In most cases, after the initial acute phase of the disease, infection leads to chronic intestinal or urinary forms of the disease, in which the parasitic worms invade the blood vessels of the intestines or bladder. But in some people the outcome can be life-threatening – involving cirrhosis of the liver or bladder cancer. Cytokines play a key role in both determining the progression of the disease and in regulating the immune response.

Dr Rodrigo Corrêa-Oliveira, who received TDR support for his doctoral training almost 20 years ago, is today a leading expert in the role played by cytokines — chemical messengers of the immune system — in both the development of immunity to schistosomiasis and in progression of the disease. His research findings should make a major contribution towards development of a vaccine that could protect the estimated 600 million people who live in areas where the disease is endemic.

Corrêa-Oliveira analysed the cytokine responses of three groups of infected patients from an area in Minas Gerais state where the disease is endemic. They included patients with the initial acute form of the disease, chronic intestinal disease, and severe (hepatosplenic) schistosomiasis. By carrying out blood tests, he discovered that a key immunological messenger known as interleukin-10 was needed to prevent progression from the chronic intestinal stage of the disease to the most severe forms. Meanwhile, another cytokine – interferon – together with key antibodies were associated with the development of immunity in people with natural resistance to the disease. The latest follow-up study involving two large populations in Minas Gerais aims to establish to what extent the different responses to schistosomiasis are genetically determined.

Corrêa-Oliveira, head of the Laboratory of Cellular and Molecular Immunology at the Fundaçao Oswaldo Cruz (FIOCRUZ) in Brazil, works in collaboration with molecular biologists at York University in the UK. The TDR funding has also

GRANTS

- ***Career Development Award: 1992-96***
Analyse role of cytokines in regulation of immune responses and development of resistance to S. mansoni infection in man.
- ***Partnership Grant: 1994-99***
Immunity and immunopathology in schistosomiasis.

MEMBERSHIP

- *Schistosomiasis Committee*
- *Pathogenesis Steering Committee*
- *Schistosomiasis Vaccine Committee*
- *Pathogenesis Committee*
- *Pathogenesis and Applied Genomics Committee*

enabled him to train several doctoral students to work in the field of molecular immunology. In addition, he is collaborating on the latest study with a researcher from Makerere University in Uganda. Corrêa-Oliveira was first awarded a training grant by TDR, which enabled him to study for a doctorate in immunology at John Hopkins University in the United States. Since then, he has received the two most prestigious TDR grants for research capability strengthening – the Partnership Grant (for institutional support) and the Career Development Grant (in recognition of individual excellence). He says these awards have had a "major impact" both on his own career and on the development and growth of the laboratory which he now heads.

"The TDR grant gave an enormous push to the implementation of the most up-to-date technologies available in immunology and molecular biology," he explains. "As a result of the research we have carried out over the years, our laboratory is today one of the leading groups in the research of human immunology, mainly in relation to TDR target diseases."

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***Eloi-Santos, S.M.**, et. al. (1989):* Idiotypic sensitization in utero of children born to mothers with schistosomiasis or Chagas disease. J. Clin Invest. 84:1028-1031

***Bahia-Oliveira, L.M.G.**, et. al. (1992):* Differential cellular reactivity to adult worm antigens of patients with different clinical forms of *schistosomiasis mansoni. Trans. Roy. Soc. Trop. Med. Hyg*, 86: 47-52

***Viana, I.R.C.**, et. al. (1994):* Human immune responses to schistosomal antigens. II Analysis of in vitro interferon-gamma production by lymphocytes from individuals in an area endemic for *Schistosoma mansoni. Trans. Roy. Soc. Trop. Med. Hyg.*, 88 : 446-470

***Vago, A.**, et. al. (1996):* PCR detection of *Trypanosoma cruzi* DNA in esophageal tissues of patients with chronic digestive Chagas disease. *Lancet*, 348: 891-892

***Malaquias, L.C.C.**, et. al. (1997):* Cytokine regulation of human immune responses to *Schistosoma mansoni*: I. Analysis of the role of IL-4, 5 and 10 on peripheral blood mononuclear cellular responses. *Scand. J. Immunol.*, 46: 393-398

***Lemos, E.M.**, et. al. (1998):* Decreased CD4+ circulating T lymphocytes inpatients with gastrointestinal Chagas disease. *Clinical Immunol and Immunopathol.*, 88: 150-155

***Martins-Filho, O.A.**, et. al. (1999):* Clinical forms of human *Schistosoma mansoni* infection are associated with differential activation of T cell subset and costimulatory molecules. *Digestive Diseases and Sciences*, 44: 3, 570-577

***Corrêa-Oliveira, R.**, et. al. (2000):* Natural versus drug induced resistance to *Schistosoma mansoni. Parasit. Today*, 16: 397-399

***Bahia-Oliveira, L.M.G.**, et. al. (2000):* Immunological and clinical evaluation of chagasic patients subjected to chemotherapy during the acute phase of *Trypanosoma cruzi* infection 14-30 years ago. J. *Infect. Diseases*, 182: 634-638

Profile:

FRANCINE NTOUMI

A researcher in Gabon is breaking new ground through genetic analysis of malaria parasites. Dr Francine Ntoumi has used TDR funding to study molecular analysis and train postgraduate students in the techniques – building up a team of young researchers who are now involved in multi-country studies. Their findings are expected to contribute to greater understanding of the impact of antimalarial drugs and candidate vaccines and of the mechanisms involved in the development of drug resistance.

Dr Francine Ntoumi, from the Republic of Congo, is using molecular analysis to gain fresh insights into malaria prevention and treatment. Now working in neighbouring Gabon, Ntoumi is training a new generation of researchers in the same techniques.

Ntoumi received her first TDR grant in 1993, for post-doctoral training at the Pasteur Institute in Paris in the molecular analysis of malaria parasites – in this case, from blood samples taken from the village of Dielmo in Senegal. The technique can be used to measure the effectiveness of antimalarial drugs, insecticides, or candidate vaccines, by establishing which strain of parasites have been killed and which persist after prevention or treatment. On her return to Gabon in 1995 to continue malaria research at the International Medical Research Centre (CIRM) in Franceville, Ntoumi was awarded a TDR Re-entry Grant and began training her first student in the techniques learned at the Pasteur Institute. Other awards followed and by 1998 she had established her own research group and was recruiting African students for postgraduate training. So far, over 10 students have been trained – two of whom have also benefited from TDR funding.

TDR support has been critical for her institution, she says, and given hope to many postgraduate students who might otherwise have abandoned their research. "It is not easy for young African scientists to obtain grants for postgraduate studies," says Ntoumi. "Science students here often say that it is a waste of time doing postgraduate studies because there is no way to go forward. TDR fills this important gap."

Ntoumi used her TDR Re-entry Grant to investigate why people who carry the gene for sickle cell disease (an inherited form of severe anaemia) are less susceptible to severe forms of malaria. Working with postgraduate students recruited through the TDR grant, Ntoumi's team collected blood samples from 100 hospital outpatients aged from 1-76 years in Mounana, a mining region in south-east Gabon where malaria transmission is high. They analysed the blood samples for malaria parasites – comparing parasite strains from the sickle cell gene carriers with those with normal haemoglobin. Using molecular analysis to type the parasites, they discovered that those with the sickle cell gene had both a larger number and greater variety of malaria parasite strains than those with normal haemoglobin. And in a larger follow-up study in 1998, involving over 600 children aged 6-11 years, the group demonstrated that those with the sickle cell gene were less likely to develop severe anaemia because they had developed greater immunity to all the parasite strains in circulation. These findings help shed light on the process of immune response and could be helpful in preparing for future malaria vaccine trials. Meanwhile, in a small pilot study in 1999, Ntoumi's research group has also shown that children whose mothers regularly dose them with antimalarial drugs when they are sick but without prior confirmation of malaria may be putting them at increased risk of developing a severe, life-threatening form of the disease. "The findings suggest", says Ntoumi, "that unnecessary treatment with antimalarial drugs may prevent normal exposure to malaria parasites and the development of natural immunity, leaving children more vulnerable to attacks of severe malaria". In the study, involving about 100 children aged under 5 years, the researchers compared levels of parasite infection among children in Gabon, where few children are exposed to malaria prevention measures, and Benin, where the use of over-the counter antimalarials is widespread. Both studies were conducted in areas where malaria transmission rates are similar. The team found that

GRANTS

- ***Research Training Grant: 1993-95***
  Post-doctoral training in malaria and in molecular biology of malaria parasites
- ***Re-entry Grant: 1996-98***
  Correlations between genetic diversity of P. falciparum, haemoglobin A/S carriage and malaria-associated symptoms
- ***Research Capability Strengthening Grant: 1998-2001***
  Relation between P. falciparum strains parasite factors and outcome of severe clinical malaria in Gabon/Benin children
- ***MIM Grant: 1998-2002***
  Relationship between complexity of infections/ disease/transmission & human red blood polymorphisms in two African countries

the Benin children were infected with a lower intensity and less variety of malaria parasites than the Gabon children. And they were much more vulnerable to attacks of severe malaria. By comparison, the Gabon children had a much higher threshold for severe malaria – which was not triggered until their blood parasite level was two and a half times that of the Benin children with severe malaria. In Benin, a larger follow-up study has now been carried out nationwide by the national malaria programme, involving a TDR-supported PhD student from Ntoumi's research group, and mothers are already being trained to recognize the symptoms of malaria.

"It's very difficult to explain to mothers that by over-protecting their children against malaria they may be making them more susceptible to severe forms of the disease", says Ntoumi. TDR is also supporting the group's ongoing research using molecular tools to monitor resistance to antimalarial drugs, the technique being used to determine which parasite genes are involved in development of resistance. Since 1998, the group (now based at the Albert Schweitzer Hospital in Lambarèné, Gabon) has also received funding through the TDR Task Force on the Multilateral Initiative for Malaria in Africa (MIM) – an alliance aiming to strengthen malaria research capacity and disease control in Africa. Ntoumi's team are now undertaking studies involving research institutions in Gabon, Benin, France and Germany. And students from Benin, Burkina Faso and France are currently being trained in molecular analysis. Ntoumi says that TDR has established a "gold standard" for research in developing countries . "If we are a TDR grantee, our stakeholders know that we are working on a competitive basis with other groups outside the country, and that means that we are doing good work."

MEMBERSHIP

- *Vaccine Discovery Research Committee*

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***Ntoumi, F.**, et. al. (2000):* Site-based study on polymorphism of *P. falciparum* MSP-1 and MSP-2 genes in isolates from two villages in Central Africa. *Parasitologia*, 42: 197-203

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***D. Mawili-Mboumba, P.**, (2002):* Pfmdr1 Gene Alleles and response to low-dose mefloquine treatment in Gabonese Patients. Antimicrobial Agents and Chemotherapy, 46(1) 166-170.

***Ekala, M.T.**, (2002):* Family specific humoral responses to merozoite surface protein 2 (MSP2) in Gabonese residents with *Plasmodium falciparum* infections (In Revision)

***Issifou, S.**, (2002):* Site-based comparison of hematological and parasitological factors of *P. falciparum* infections in young children living in Central and Western Africa (Submitted)

Ekala, M.T., (2002): Sickle cell trait carriage : Prevalence and levels of family specific antibodies to *Plasmodium falciparum* MSP2 peptides in serum samples from Gabonese children (Submitted)

Profile:

ZHOU XIAO-NONG

In China, Dr Zhou Xiao-Nong has used research training support from TDR to adapt state-of-the-art digital technology as a means of predicting – and preventing – outbreaks of schistosomiasis, a disease which afflicts over 200 million people worldwide and which holds back development in some of the poorest countries. The new tool can be used to identify populations most at risk for the disease (and possibly others) and improve the cost-effectiveness of disease control programmes.

Until recently, thousands of people living in the marshland areas along the Yangtze River in China were despatched to the fields in spring every year to search for the small amphibious snails which carry the parasite that causes schistosomiasis. But this "hit-and-miss" method left many snail habitats undetected. Today, a TDR-funded researcher, Dr Zhou Xiao-Nong, of the Chinese Academy of Parasitic Diseases, has developed a more accurate computer-based method for mapping snail habitats and highlighting the "hot spots" for transmission of schistosomiasis. As a result, hazardous snail populations can be destroyed and mass treatment targeted to the local communities – especially children and rural workers – most at risk. The method can also be used to predict the impact on disease patterns of climate change and development projects such as dam-building and irrigation schemes.

Over recent years, deforestation, irrigation schemes, delta subsidence, and climate change have all contributed to an increase in the frequency of flooding in the marshlands along the middle and lower reaches of the river of the Yangtze River, China's longest and the third largest river in the world. When the floods subside, deposits of clay soil and silt provide nourishment for aquatic vegetation and fresh pastures for the schistosomiasis-causing snails. The disease is contracted through contact with parasites in stagnant water sources. Without treatment – an annual dose of the drug praziquantel – schistosomiasis can lead to chronic urinary tract infection, cirrhosis of the liver, and bladder cancer. The new tool, known as a geographic information system (GIS), is based on satellite-based remote sensing techniques and key environmental data. Mapping technologies are used to overlay selected data, for example, temperature, soil, elevation, vegetation, hydrology, population centres, and land use, on to a base map. The result is a tailor-made composite digital map that provides a visual display of critical comparative data which can be used to predict outbreaks of disease. Zhou has developed the tool with capacity-building support from TDR and in collaboration with schistosomiasis experts at the Danish Bilharzia Laboratory, Louisiana State University in the United States, and Nanjing University in China. After graduate studies at the Jiangsu Institute of Parasitic Diseases in China, Zhou received funding from TDR through a Research Training Grant, enabling him to pursue his research in Thailand and Denmark. He studied for his doctorate (on the biology of the schistosomiasis-causing snail) at the University of Copenhagen, returning to China to carry out the fieldwork involved. On his return to work in China, TDR funded a training course on the transfer of the GIS technology to other provinces in China where the disease is endemic. A GIS laboratory was established and training has now been extended to include young researchers from other countries as well.

In 1998, the Yangtze River burst its banks, causing the worst flooding for 100 years and heavy loss of life. With support from TDR, Zhou seized the opportunity to demonstrate the value of using remote sensing techniques and GIS to monitor the ecological impact of the floods and pinpoint the areas at risk for future outbreaks of schistosomiasis.

GRANTS

- **Research Training Grant: 1991**
  Biology and control of snail intermediate host
- **Re-entry Grant: 1992-94**
  Population genetics, cytogenetics, morphology and distribution of O. hupensis, intermediate host of S. japonicum
- **RCS Applied Field Research Grant: 1998-2000**
  Snail distribution/assessment of schistosomiasis risk by remote sensing and GIS in lower Yangtze River basin, China

MEMBERSHIP

If successful, the method would enable disease control measures to be targeted more cost-effectively.

Two study areas were selected, one in the Poyang Lake region, the other along the Yangtze River in Jiangsu province. By using satellite images from the summer flood season and the following spring, together with a range of ecological determinants – such as soil, vegetation, and water – composite images were created to predict potential snail habitats and the risk of disease. Then, two years later, a follow-up survey was carried out to assess the situation on the ground. When the two sets of data were compared, 90% of the potential snail habitats identified by the use of satellite imaging and environmental data were confirmed. They included two new snail habitats in marshland along the Yangtze River – forecast via the GIS tool and later confirmed by disease control staff on the ground.

Today, in a related TDR-funded study, still under way, Zhou is developing new computer models to assess the potential impact on schistosomiasis transmission of the massive Three Gorges Dam project, due to be completed by 2009 in an effort to prevent flooding and improve economic development along the Yangtze River.

The potential for the spread of schistosomiasis into new areas is a major concern, he says. "There is a continuing need to develop new ways to monitor the situation in the Three Gorges Reservoir region and downstream of the Yangtze River during and after construction of the Three Gorges Dam," he says. "Implementation of a GIS model system to manage spatial data on the drainage network, land use, infection sources, and population centres may provide a practical way of accomplishing this."

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Profile:

JOHN GYAPONG

In 1992, a study on the social and economic impact of lymphatic filariasis in Ghana revealed the devastating impact of this disabling disease. The researchers, led by Dr John Gyapong, showed that people with severe forms of the disease suffered acute episodes throughout the year, which left them incapacitated and unable to work for 3-4 days at a time.

In addition to the economic burden, the study also identified the hidden social stresses involved. Second only to mental illness as the world's leading cause of long-term disability, lymphatic filariasis can cause gross enlargement of the limbs and genitals, as well as damage to internal organs. The social and psychological impact can be disastrous, destroying marriages and family relationships.

In Ghana, Dr John Gyapong's work has had a major impact on the development and implementation of the global strategy for the elimination of lymphatic filariasis. Over the past decade, supported by TDR research capacity-building grants, Dr Gyapong has succeeded in shedding new light on efforts to control this disabling disease which afflicts over 120 million people in India, Africa, the Pacific, and the Americas — most of them from poor communities.

But how big a problem was the disease in Ghana? And where should treatment be targeted? To find out, Gyapong carried out night-time surveys, taking blood samples between 22.00-02.00 hours, the only time when parasites are detectable in the blood. But the method, standard procedure at the time, was impractical, time-consuming, and not popular with villagers. Although only a few drops of blood were needed, rumours abounded that the blood was being taken for sale – or worse. A more practical diagnostic tool was needed.

With a Research Training Grant from TDR, Gyapong set out to develop a new rapid assessment tool to replace the night-time surveys. His ground-breaking study revealed an effective rapid method was to assess the number of people in a community with visible impairment – severely distended limbs and genitals due to lymphatic filariasis. When checked against diagnostic (night-time) blood tests for the same communities, this proved to be an adequate gauge in determining high-risk areas for lymphatic filariasis – and was adopted as standard procedure for disease control programmes.

But other questions remained. If the disease was to be eliminated it was necessary to estimate the true disease burden. Without this data it was difficult to estimate the volume of drugs needed or where to target them. Development of a new rapid antigen test – which Gyapong helped to field test in Ghana – was the breakthrough needed to "map" the disease over large areas. The advantage of the new test was its ability to detect an immune response instead of active parasites in the blood, and so it could be used at any time.

Gyapong's team set out to develop a method for rapid geographical assessment of the disease. Screening men in 87 villages in northern Ghana, the researchers established that disease transmission areas were larger than previously estimated and that the prevalence of the disease could be determined by overlaying a 50km grid system on large areas and sampling each section in turn. The study also revealed that the disease was far more prevalent than previously believed. "In Ghana we found that over 4 million people were living in endemic areas, twice the number we thought," says Gyapong. "It gave us a better idea of what we were up against in efforts to eliminate the disease."

With a new disease-mapping tool and unlimited supplies of the dual-drug treatment (ivermectin and albendazole) donated by the manufacturers, Merck and Co Inc. and GlaxoSmithKline respectively, the next hurdle was to find a way of reaching "the unreached". In areas where

GRANTS

- **Research Training Grant: 1993-96**
  Epidemiology and control of lymphatic filariasis
- **Re-entry Grant: 1997-99**
  Evalute impact of combination of ivermectin and albendazole treatment on lymphatic filariasis in Ghana
- **10 TDR R&D grants**
  Onchocerciasis, malaria, lymphatic filariasis

MEMBERSHIP

- *Task force – Community Directed Treatment*

infrastructure was poor, novel delivery methods were needed to ensure that annual mass treatment was available to all who needed it. TDR had already demonstrated that the most effective way to control onchocerciasis was to help communities assume responsibility for distribution of the once-yearly treatment. In one of five country studies carried out in Africa and Asia, Gyapong's team investigated whether it would work in Ghana.

A study involving almost 3000 people found that community distribution succeeded in reaching 75-88% of the population with drugs, while the health service reached only 45% – not nearly enough to ensure elimination of the disease. A major advantage of volunteer community workers is their willingness to deliver drugs on a door-to-door basis, at times that do not disrupt work patterns or daily routines. Community-directed treatment has now been adopted by the global filariasis elimination programme.

Today, as manager of the Lymphatic Filariasis Control Programme in Ghana and director of the national Health Research Unit, Gyapong has a foot in both disease control and research, ensuring that he is well-placed to field-test new drugs, diagnostics, other tools, and new disease control policies. Over the past decade, with support from TDR, he has built up a team of young researchers to work mainly, but not exclusively, on lymphatic filariasis. "Through my involvement with TDR, I have had the opportunity to contribute to the network of scientists providing the evidence-base needed for the elimination of lymphatic filariasis," he says. "It is very satisfying to see operational decisions being implemented and the community benefiting as a result of the research we have done."

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***Gyapong, J.O.**, et. al. (2001):* Validation of a rapid assessment method for the distribution of Bancroftian filariasis. *Trans. Roy. Soc. of Trop. Med. and Hyg.*, 95: 681-686

Profile:

ABOULAYE DJIMDE

A TDR-supported doctoral student from Mali, Dr Aboulaye Djimde, has made a significant breakthrough in the fight against drug-resistant strains of malaria parasites, one of the major threats to malaria control today. He has demonstrated that a newly discovered gene in malaria parasites – known as pfcrt – can be used as a molecular marker to identify resistance to treatment with the first-line drug, choloroquine.

The new technique, involving molecular analysis of parasite DNA from the blood of malaria-infected patients, is much faster than existing surveillance methods. It can be used for rapid identification of areas where choloroquine-resistance is widespread and alternative first-line drugs should be used. And it could lead to major savings in the cost of malaria treatment by avoiding the need to use expensive second-line drugs.

Dr Aboulaye Djimde, a researcher from Mali, used a TDR research training award to develop a new technique to map areas where chloroquine is no longer effective as a first-line drug against malaria. The new technique – using molecular markers to identify drug-resistant strains of parasite – has already been used to prevent malaria deaths by averting the use of chloroquine during an epidemic in northern Mali, and it could lead to major savings in malaria treatment costs.

Up till now, in many African countries, drug resistance has been mainly assessed through monitoring the clinical response to treatment in malaria patients over about 14 days. But about 200 patients are needed to ensure the validity of the findings and the results can be difficult to interpret in areas where re-infections are frequent. It can take up to three months to acquire reliable data using this method, while the new molecular method can yield results within six hours.

The technique was tested by Djimde and other researchers in a 2-year study involving over 1400 malaria patients. The study included people from three different ethnic groups and regions within Mali – the river delta of central Mali, an arid plateau to the east, and a rural village in the south. In each case, a pinprick of blood was taken from the malaria patient before chloroquine treatment was started. Parasite DNA was then extracted from each blood sample and analysed for the presence of the drug-resistance marker. When the positive samples were compared with the treatment outcome, the molecular marker proved to be a good indicator of chloroquine treatment failure in all three settings.

The technique was successfully deployed by Djimde during an epidemic of malaria in northern Mali in 1999, while he was still completing his doctorate at the University of Maryland in the United States.

The epidemic occurred in a normally arid area which had been affected by unusually heavy rains.

It was the first time the technique had been used in an emergency. Working closely with the national malaria control team, he carried out rapid analysis of malaria parasite genes from those infected, revealing that the marker for choloroquine resistance was widespread.

On the basis of these findings, Djimde recommended the substitution of sulfadoxine/pyrimethamine instead of treatment with chloroquine. Since completing his research, Djimde has trained four younger scientists in Mali in the same technique.

He has recently been awarded a TDR Re-entry Grant and is working to develop a similar model to monitor resistance to sulfadoxine/pyrimethamine. He is also working closely with colleagues in Nigeria, Ghana, Uganda, and Tanzania as part of a TDR-funded network designed to assess the value of molecular markers for drug-resistance and their possible application to drug control.

Djimde, who originally worked as a pharmacist in Mali, was awarded a Research Training Grant to

GRANTS

- **Research Training Grant: 1996-2000**
  Microbiology and immunology of malaria
- **Re-entry Grant: 2001-2002**
  Towards a molecular tool for monitoring sulfadoxine-pyrimethamine (SP) resistance in Mali

MEMBERSHIP

study in the United States. He obtained a doctorate in molecular microbiology and immunology in 2001 and has now returned to Mali, where he heads the Molecular Epidemiological and Drug Resistance Unit in the Malaria Research and Training Centre at Mali University. His main achievement, he says, "has been to demonstrate that sophisticated molecular technology can be transferred to developing countries and contribute to the control of tropical diseases."

Dr Christopher Plowe, Associate Professor of Medicine at Maryland University, where Djimde studied, says he is a "talented, bright, and dedicated researcher. If we are ever to make headway against malaria in Africa," he continues, "we must do everything we can to encourage exceptional people like him to devote themselves to this intractable problem."

In 2002, Dr Djimde was awarded the "Fighting Malaria" prize by the Federation of European Societies for Tropical Medicine and International Health (FESTMIH) and Sanofi-Synthelabo. The prize is given to a researcher or research team in recognition of their significant contribution in the field of fundamental or clinical knowledge related to malaria.

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***Djimde, A.**, (2001):* A molecular marker for chloroquine-resistant falciparum malaria. *N. Engl. J. Med.*, 25, 344(4): 257-263

Profile:

SHYAM SUNDAR

Dr Shyam Sundar, an Indian researcher, is at the forefront of efforts to improve the diagnosis and treatment of visceral leishmaniasis. He is also paving the way for local production of a candidate leishmaniasis vaccine and for future vaccine trials. Through efforts to strengthen research capacity, TDR support has ensured that his research group has the full range of skills and facilities needed to conduct large-scale clinical trials of new drugs, diagnostics, and vaccines.

Dr Shyam Sundar, of the Institute of Medical Sciences at India's Banaras Hindu University in Uttar Pradesh, is a man with a mission. He wants to "revolutionize" the diagnosis and treatment of visceral leishmaniasis – or kala-azar as it is known in India – and help speed up development of a vaccine to prevent the disease. There are an estimated 250 000 new cases of visceral leishmaniasis every year in India, half the global total. And in the worst affected areas at least 40% of cases are resistant to treatment with first-line antimonial drugs. The parasitic disease, transmitted by the bite of an infective sandfly, is usually fatal if left untreated. Although effective second-line drugs exist, they have many drawbacks. They can only be given by injection or lengthy infusions and require special treatment centres. The medication has to be given over 4-6 weeks and most patients suffer unpleasant, occasionally life-threatening, side-effects. Meanwhile, the very high cost of the treatment, over US$1000 for a course of injections, puts it out of reach of the people worst affected, most of them poor. "People are dying today because treatment is ineffective and toxic, and second-line drugs are both toxic and expensive," says Sundar. "Any new treatment must be affordable if it is to have an impact."

In 1994, supported by TDR, Sundar and his team began the search for alternative forms of treatment, testing drugs, already on the market for other uses, for effectivness against visceral leishmaniasis.

The first breakthrough came in 1997 when, in small-scale trials, they demonstrated that miltefosine, a drug originally developed for cancer treatment but later withdrawn because of adverse side-effects, was effective against visceral leishmaniasis. The drug, currently used for the topical treatment of breast cancer, had already been shown to be effective against visceral leishmaniasis in animal models. Hopes were raised that it could become the first oral treatment against the disease in humans.

With capacity-building support from TDR to conduct clinical trials, involving training in Good Laboratory Practice (GLP) and Good Clinical Practice (GCP), large-scale, multi-centre trials involving adult patients confirmed the initial findings. Registration of the drug for use in patients over 12 years old is now pending (trials involving children are still under way) and TDR has entered into an agreement with a German pharmaceutical manufacturer, Zentaris (formerly ASTA Medica), to market the drug at an affordable price for use in developing countries. Sundar and his team are delighted. "Once the drug has been registered," says Sundar, "it should become the standard treatment for visceral leishmaniasis, especially in areas where antimonial drugs don't work." Sundar's group is also involved in clinical evaluation of new diagnostic tests for visceral leishmaniasis. Up till now, confirmation of disease has involved taking a sample of cells from the spleen to detect parasites – a dangerous surgical procedure which can result in haemorrhaging.

The researchers succeeded in demonstrating the effectiveness of a new rapid dipstick test – K39 – developed in the United States. While existing blood tests can detect the presence of antibodies, they fail to distinguish between past and present infection. By contrast, the K39 antigen test, which requires only a pinprick of blood, detects antibodies to the antigen and so reveals existing infection. The team is also involved in evaluating another test, developed in England, designed to detect antigen in urine. In addition, Sundar's team are gearing up to conduct clinical trials of candidate vaccines to prevent visceral leishmaniasis. Surveys are being carried out involving

GRANTS

- ***Project Development Grant: 1998***
  Research capability strengthening for Kala Azar Medical Research Center, Muzaffarpur, India
- ***Research Capability Strengthening Grant: 1999-2002***
  Visceral leishmaniasis & PKDL: new therapeutic, immunologic & diagnostic studies & site preparation for vaccine trial

MEMBERSHIP

- *Product Development Team - Miltefosine*

about 50 000 people in 24 villages to gather data for future vaccine trials. Two candidate vaccines will be evaluated, a first-generation vaccine using killed (autoclaved) parasites, developed at the Central Drug Research Institute (CDRI) in India, and a second-generation synthetic vaccine developed at the Infectious Diseases Research Institute (IDRI) in the United States. Sundar spends the working week at the Kala-azar Medical Research Centre which he established in1990 at Banaras Hindu University, Varanasi. This provides free medical treatment for people with visceral leishmaniasis, helps raise public awareness about the disease, and focuses on research and training for postgraduate students. Researchers from Bangladesh and Nepal have also been sent there for training. In 1997, Sundar established a Kala-azar Immunoparasitology Laboratory at the university to support and strengthen the research activities. This also supplies several research institutions with parasites, clinical isolates, and blood or serum for use in research.

At weekends, Sundar travels 350km north to treat patients at the 36-bed treatment centre he set up in 1994 at Muzaffarpur in Bihar state, the epicentre of visceral leishmaniasis in India. About 50 patients a week are diagnosed and treated free of charge. The centre, which has received funding from the Rockefeller Foundation and TDR, is now funded by a local trust. Sundar reflects that his research has been "very fruitful and extremely satisfying" over the last 10-12 years. "Before long we should have a new standard treatment and a rapid diagnostic test for visceral leishmaniasis. And in 10 years' time we could have a vaccine as well."

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Profile:

FRED BINKA

In remote northern Ghana, a health research centre set up by Dr Fred Binka is now a world leader in operational research, with a major focus on child health in developing countries. Following a carefully considered development plan and a mix of TDR capacity-building and R&D support, the Navrongo Health Research Centre now houses a high-calibre, multi-disciplinary research team with a wide range of skills needed for research in tropical diseases and other health-related problems.

The Navrongo-based research team was painstakingly built up and, until recently, directed by Dr Fred Binka, a Ghanaian doctor and health researcher who was the driving force behind the establishment of the Navrongo Health Research Centre (NHRC) in 1992. Originally one of the African field sites for the ground-breaking 1988 study on the positive impact of vitamin A supplements on child health, the centre was set up as a district health research unit linked to the Ghanaian Ministry of Health. Binka, who now teaches at the School of Public Health at the University of Ghana in Accra, used capacity-building support from TDR along with other funds to build up a 50-strong multi-disciplinary team of researchers, 80% of whom come from the Navrongo area. "We have developed local capacity and local ownership," says Binka. "And we can compete in the health research field with any country in the world."

Navrongo is a world-class health research centre sited in a poor, remote area in north-east Ghana. A 12-hour bus ride away from the capital Accra 900 kilometres to the south, the Centre has been established close to the people, mainly poor subsistence farming families, who stand to benefit most from efforts to find practical solutions to major health problems. Health research carried out there during the 1990s has had a major impact on child survival. Over the past decade, infant mortality rates in the surrounding area have been reduced by almost 40% (down from 140 to 85 deaths for every 1000 live births) and fertility rates have fallen as more women have been encouraged to use modern contraceptive methods. Many of the research findings have influenced national health policy in Ghana and are expected to have a lasting impact in other countries as well.

Today, researchers from Asia and other African countries are trained at the Navrongo centre. Although geographically remote from the global scientific community, the research centre is linked to global health resource networks through HealthNet, a global information system, which uses radio- and telephone-based computer networks and ground-based satellite communications to exchange health and medical information with countries around the world. Today, the Navrongo team is involved in a wide range of research. They include a raft of studies on the effectiveness of different drug treatments for malaria, the use of entomological studies to map malaria transmission areas, an investigation into how outbreaks of meningitis are triggered, and a study aimed at finding acceptable alternatives to female genital mutilation as a rite of passage into womanhood. As each successive research project has highlighted the need for researchers from other health-related disciplines, TDR has provided Research Training Grants to help train (or in some cases re-train) new researchers to complement the existing team. As a result, the original core team of 10 researchers has been expanded to include health economists, demographers, a biostatistician, microbiologist, social scientist (formerly a nutritionist), and a parasitologist and entomologist.

Most of those who have been funded and trained overseas have since returned to work at Navrongo. "We can't afford to invest in training people who don't come back," says Binka, who has also recruited expatriate Ghanaians from abroad to fill key research posts in a rare example of reversed "brain drain". Binka's team, cut their teeth on two of the biggest health research studies ever carried out in Africa – first the vitamin A supplementation study and later the multi-centre study on the impact on child health

GRANTS

- ***Research Training Grant: 1994***
  Permethrin impregnated bednets and child mortality in the Kassena-Nankana district of Ghana
- ***6 TDR R&D grants:***
  malaria; bednets and case management

MEMBERSHIP

- *MIM, Malaria Research Capability Strengthening – Chairperson*
- *MIM, Malaria Research Capability Strengthening in Africa*
- *CHILD, Sick Child*
- *MAL-HSR, Malaria and Health Sector Reform – Chairperson*
- *SEVERE, Severe Malaria*
- *PoP, Proof of Principle*
- *IR, Implementation Research*

of the use of insecticide-impregnated bednets. The research revealed that the two interventions had a dramatic effect – slashing the number of child deaths from all causes by 23% and 17% respectively. In addition, bednet use also helped free up hospital beds, reducing malaria admissions by 40%.

Today, in an effort to increase the use and regular re-treatment of bednets in the district around Navrongo, researchers are assessing a range of different distribution systems, including shops, clinics, and the recruitment of 2000 children from brigade schools over the next 2-3 years to work on a commission basis during school holidays.

In 1994, Binka's team set out to implement and assess a novel community health and family planning project in three villages. Auxiliary nurses were mobilised as volunteer community outreach workers to provide comprehensive family health care and family planning services on a house-to-house basis in a rural area. The scheme was based on the premise that uptake of family planning services was likely to remain low as long as infant mortality rates remained high. If child deaths from diseases such as malaria, pneumonia, diarrhoea, and measles,(the major childhood killers) could be reduced, it was argued the use of modern contraceptive methods would increase. The study also involved social research to better understand the cultural barriers to acceptance of family planning. Within five years, contraceptive use had increased in all the areas involved and fertility rates had declined by an average of one birth for each of the women enrolled in the study. By contrast, fertility rates in control groups were unchanged. The scheme has now been included in the government's current 5-year development plan as an effective way of delivering health and family planning services in rural areas.

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Profile:

ABDUL FAIZ

A small, low-profile malaria research group established in 1993 by Dr Abul Faiz, a professor of medicine at Chittagong Medical College, is today conducting clinical trials on behalf of TDR to evaluate the effectiveness of a new emergency treatment for severe malaria.

"If the drug trials are successful," says Faiz, "artesunate could prove to be a life-saver in malaria-endemic areas of Bangladesh."

People living in the remote Chittagong Hills, for example, where standard emergency treatment by injection is not readily available, face a journey of up to 18 hours to the nearest health facility – even longer at night or during the rainy season.

A TDR-supported malaria research group established by Dr Abdul Faiz in Bangladesh has been selected to carry out clinical trials of a new emergency treatment aimed at reducing the high death toll caused by severe malaria.

Use of a new suppository drug – rectal artesunate – by people in remote rural areas is intended to help keep people alive until they can reach the nearest hospital and receive appropriate treatment.

Malaria is one of the main causes of sickness and deaths in the Chittagong district in south-east Bangladesh. Over 80% of malaria cases in Bangladesh occur there, and almost all malaria-related deaths. An estimated 5-6 million people in Chittagong district are at risk and multidrug-resistant malaria is on the increase.

The district receives a regular influx of migrant populations – many of them with no resistance to malaria. When sporadic epidemics of malaria occur they involve thousands of cases and a high death toll. The disease accounts for a high percentage of hospital admissions.

In 1997, over 50% of hospital beds in some areas were occupied by people with severe malaria. But many malaria deaths occur because people are unable to get to a hospital in time to receive life-saving drugs.

The new suppository drug – rectal artesunate – has the potential to reduce the death toll from severe malaria from 5-35% to less than 1%. The suppository is intended for use at community-level as an emergency form of treatment for patients with severe malaria who are too sick to take oral medication and unable to reach a health facility in time to receive life-saving treatment by injection. The aim is to "buy time" by keeping people alive until they can reach a hospital.

The Phase IV clinical trials are being carried out in six regions (thanas) in Chittagong district. A team of about 30 researchers is involved and about 1200 malaria patients have been enrolled so far. Most of the people taking part in the study live in villages of a few thousand people with relatively stable populations. Once enrolled in the trial, people with severe malaria are given rectal artesunate before being referred to the nearest hospital for follow-up treatment.

Parallel trials of rectal artesunate are also being carried out on behalf of TDR by researchers in three African countries – Ghana, Nigeria, and Tanzania. TDR has submitted an application for registration of the drug with regulatory authorities in Switzerland, the United States, and the UK.

Working in close cooperation with the national malaria control programme, Dr Faiz's research team conduct a range of malaria studies designed to improve the diagnosis and treatment of malaria at the local level. The team is also involved in training doctors, nurses, medical students, laboratory workers, and other health workers from both the private and public sectors in the management of malaria.

In 1998, Faiz was awarded a 3-year Capability-Strengthening Grant by TDR to help build up the research capacity of the malaria research group while carrying out a range of operational research studies.

GRANTS

- ***Research Capability Strengthening Grant: 1998-2001***
  Malaria research group development to strengthen malaria control programme of Bangladesh
- ***ANTIMALS R&D: 1999-ongoing***
  Evaluate impact of rectal artesunate on resolution of severe malaria and mortality

MEMBERSHIP

These included the development of guidelines for clinical and laboratory diagnosis of malaria, an assessment of the risk factors for the development of severe and complicated malaria, and studies on the effectiveness of different forms of malaria treatment. At the same time, the Chittagong team forged close collaborative links with the Faculty of Tropical Medicine at Mahidol University in Bangkok, Thailand – a stronger institution, also based in the South, that continues to provide practical support. The operational research provided hands-on experience for the research team in research methodology, data analysis, report writing, and the process of submitting papers for publication in peer-reviewed journals. It also gave them the confidence to compete for research funding.

"In a developing country like Bangladesh, one of the major obstacles to conducting research in the field of tropical diseases is lack of funds," says Faiz. "Through support from TDR, the group also acquired the skill of writing applications for research grants, and a couple of them have already been funded."

TDR support has been critical, says Faiz, in establishing the research capacity and confidence of the malaria research group.

"Our ability to plan, organize, and confidently manage a project through a team approach has improved," he comments. "We have a greater understanding of how to present evidence-based research and of how to carry out research in a developing country under severe resource constraints."

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Profile:

ROBERTO BRICEÑO-LEÓN

A Venezuelan sociologist, Dr Roberto Briceño-León, has helped establish a dynamic and highly-skilled scientific community of health and social science researchers in countries throughout Latin America through an innovative small grants programme funded by TDR. The 7-year programme was designed to improve disease control through recruitment and training of researchers to focus on the neglected social and economic aspects of tropical diseases in the region.

Over 100 young researchers from countries throughout Latin America have benefited from 12-month grants in an effort by TDR to develop research capacity in the up-till-then neglected social and economic aspects of tropical disease control. One of the main driving forces behind the scheme, Venezuelan sociologist Dr Roberto Briceño-León, says the scheme has helped "establish a scientific community of health and social science researchers throughout the region".

A critical element in this success, he maintains, was the decision by TDR to devolve decision-making power for the Small Grants programme to a regional group. An executive committee of regional experts, including biomedical and social science researchers as well as disease control experts, was established to evaluate research proposals, and a small secretariat set up at the social science laboratory (LACSO) which Briceño-León directs at Venezuela's Central University in Caracas.

" This meant that the regional group was able to lead a process and adapt it to the conditions in which it would be developed," says Briceño-León. "As a result, this programme was both from and for Latin America." The Latin American Small Grants Programme, in operation from 1989-96, was designed to attract mainly junior professionals at the outset of their career. However, funding was also extended to more senior professionals, such as biomedical researchers with no previous work experience in health-related social sciences. Research proposals were accepted from undergraduate and postgraduate students, provided they had backing from an institution such as a university, government, or non-governmental organization.

The small size of the projects ensured that younger, less experienced researchers were encouraged to apply, together with a proportionately higher number of female researchers than those who normally compete for larger awards in the international arena. Grants were awarded for one year, and only renewable in exceptional circumstances. The majority of projects approved focused on malaria and Chagas disease – the tropical diseases with the highest disease burden in this region. Other priority diseases studied included leprosy, leishmaniasis, and onchocerciasis. Although important biomedical and social science research was conducted in Latin America before the scheme was launched, there was little collaboration between the two disciplines. "Today we can look at a group of new investigators who have been incorporated in an area in which many would never have thought of working," says Briceño-León. Over one third (35%) of proposals came from doctors, about 16% from sociologists, and about 11% from biologists. The rest involved people from a wide range of professions, including architects, economists, anthropologists, engineers, historians, psychologists, political scientists, and archaeologists. This shift in research focus is mirrored by Briceño-León's own varied career.

A sociologist by training, his early career – and first three books – centred on urban sociology. His doctorate involved an award-winning study of the social impact of Venezuela's overwhelmingly oil-based economy, which he argued had triggered a sharp reduction in other economic activities and encouraged social dependency on the state.

GRANTS

- **Programme-based grant: 1991-97**
  Individual, social and political aspects of the control of tropical diseases with community participation
- **Social and Economic Research: 1989-96**
  Social and economic aspects of tropical diseases: Small grants programme for Latin America

MEMBERSHIP

- *Social Economic & Behavioural Research*
- *Socioeconomic Research*
- *Applied Field Research*
- *Chagas Disease*

The major turning point in his career was participation in a TDR-funded study on the role of traditional housing in transmission of Chagas disease. While traditional housing materials such as mud, leaves, and timber had long been blamed for attracting vector triatomine bugs, entomological research had demonstrated that the critical factor was not the materials themselves but the degree of finishing involved. If the roof was tiled or covered with corrugated metal, the walls and floor plastered with mud and cement to seal the cracks, the bugs would have nowhere to hide.
Briceño-León investigated why the poor left their houses unfinished and suggested ways of motivating people to improve their building work in a bid to prevent infection with this chronic incurable disease. The critical factors he identified were lack of regular income and a fatalistic view of disease which excluded the possibility that they could have any control over transmission. With financial support from the government, people were encouraged to improve their own houses, using traditional techniques and knowledge, a solution far more acceptable and sustainable than provision of industrial housing units alien to their way of life. Briceño-León says the process has helped empower people and made them active players in disease prevention. "We succeeded in demonstrating that traditional houses could be both beautiful and healthy, while still being affordable," he says. The research findings have also been used by the Chagas disease control and housing programmes in Argentina, Bolivia, Guatemala, Honduras, and Paraguay.
In 2001, the Venezuelan government and UNDP awarded Briceño-León the National Habitat Award for his research – on what came to be known as The Sick House (La Casa Enferma) – and for his practical contributions to improving the housing conditions of the poorest groups.

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Profile:

OBINNA ONWUJEKWE

Nigerian researcher, Dr Obinna Onwujekwe, has used a TDR Re-entry Grant to determine whether community funding and distribution of ivermectin for the treatment of onchocerciasis could be a sustainable solution to the shortfall in government and donor funding needed to distribute the drug.

Ivermectin (under the brand name Mectizan®) is supplied free of charge by the manufacturer, Merck and Co. Inc. But in 1994, the National Onchocerciasis Control Programme in Nigeria estimated that, if the government provided the drug to all those who needed it, the distribution costs alone would almost swallow up the entire national health budget. At the time, less than 30% of affected communities were covered by the mass distribution.

Dr Obinna Onwujekwe, a TDR-funded health economist in Nigeria, has demonstrated the feasibility of a novel community funding system for mass distribution of ivermectin for the treatment of onchocerciasis. The study in south-east Nigeria revealed that people are both willing and able to contribute to the modest running costs involved, meaning that the treatment programme, which would otherwise be beyond government budgets, should be viable in the long term.

An estimated 7 million people are infected with onchocerciasis in Nigeria – the worst affected country in the world – and about 40 million people are at risk. In some areas, over 90% of the community are infected. The parasitic disease, transmitted by blackflies, causes visual impairment, blindness, unbearable itching, skin lesions, and gross swelling of the genitals. Although once-yearly treatment with ivermectin prevents the harmful effects of the disease, it has to be continued for 10-15 years, the life-span of adult worms inside the body.

Today, ivermectin procurement and distribution in Nigeria is funded by the African Programme for Onchocerciasis Control (APOC) – an international partnership established in 1995 to develop sustainable community-directed treatment programmes in 19 African countries where the disease is endemic. But APOC funding will come to an end in 2010. From then on, communities will be expected to assume responsibility not only for distributing the drug but also for the costs involved. But are communities willing and able to pay for the local distribution costs? Do they have the capacity to organize and run a community financing scheme? And is it likely to be sustainable for the 10-15 years of continued mass treatment needed to eliminate the disease?

Onwujekwe set out to determine whether such a system is viable in Nigeria. A medical doctor by training, he had just completed a Masters degree in Health Economics at Chulalongkorn University in Bangkok, Thailand, supported by a Research Training Grant from TDR. The study was carried out in Achi and Nike, two areas in south-east Nigeria where onchocerciasis is endemic. In both areas, the drug was provided through APOC by the non-governmental organization Sightfirst. An estimated 18 000 people were eligible in Ache and 20 000 in Nike. Each community established committees to organize distribution and determine how the communal funds should be raised. Fundraising methods included a community levy on all adults, a levy on large extended family groups, donations, and a fee for administering the drug. Community-directed distributors were selected and trained to administer the drug and monitor and manage adverse events. None was paid but some had their travel costs reimbursed.

The distributors succeeded in reaching almost 60% of those eligible in Achi and over 60% in Nike. In both areas, the unit cost of delivering the drug was US$0.39 – including both the direct costs of the provider (Sightfirst) and the direct and indirect costs (mainly time-related costs) of the community. However, the unit cost is expected to be much lower in subsequent years, since a high percentage of the costs were incurred in determining the ability and willingness of the community to pay.

In his report, Onwujekwe recommends that

GRANTS

- ***Research Training Grant: 1993-94***
  Master's in health economics: onchocerciasis
- ***Re-entry Grant: 1996-98***
  Design, implement and evaluate a novel scheme for community financing of onchocerciasis control using ivermectin in Nigeria
- ***Research Training Grant: 1998-2002***
  Health economics and financing aspects of malaria control

MEMBERSHIP

communities should be given grants to cover the costs of collecting the ivermectin from distribution points and that community organizers and drug distributors should be given incentives such as travel allowances, annual payments, scholarships, prizes, and certificates. The Ministry of Health is also urged to carry out entomological and epidemiological studies once a year and report to the community the effectiveness of the distribution system.

If community financing is well promoted, Onwujekwe says, it is likely to be successful in Nigeria. "The sense of social contract and social obligation is strong in Nigerian culture," he says. "Because of the close-knit social set-up, communities are expected to ensure equity by making the drug available to those who lack the ability to pay."

Community financing is a way of empowering communities to take control of their own health, says Onwujekwe. "Communities with endemic diseases might possess the ability and willingness to take control of their destiny, but invariably they need both logistic and technical support to realize their aspirations. When this support is lacking, the result is a vicious cycle of disease in their communities."

Since returning to Nigeria, Onwujekwe has trained colleagues and students in health economics and helped establish a Health Policy Research Unit at the University of Nigeria where he teaches. He is also a co-founder of a West African Health Economics Network which brings together other TDR grantees.

In 1998 he was awarded a Research Training Grant by TDR to enable him to study for a doctorate in health economics at the London School of Hygiene and Tropical Medicine.

Onwujekwe hopes that his research will lead to greater understanding of how individuals and society value different health care commodities and services. "To make decisions about resource allocation, governments and donors need to know where and how to intervene in order to maximize the benefits to society while at the same time ensuring equity."

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Profile:

FENG ZHENG

Established in 1999 with initial capacity-building support from TDR, the Regional Network for Asian Schistosomiasis (RNAS) brings together researchers, international experts, and disease control authorities from six countries: China, Cambodia, Indonesia, the Lao People's Democratic Republic, and The Philippines (countries where the disease is endemic), and Japan (where it used to be).

Dr Feng Zheng, until recently head of the Institute of Parasitic Diseases in Shanghai and now Director of the Central Laboratory of Parasite and Vector Biology, was one of the prime movers behind the establishment of the schistosomiasis network and is the lead researcher. "Until recently, there has been little communication and exchange on schistosomiasis in the region, where the countries share the same problems and have similar conditions," he says. "This unique network will enable us to share information and to carry out collaborative research and training activities in areas where the disease is endemic."

TDR is supporting a regional network for Asian schistosomiasis, established by China's Dr Feng Zheng, to promote information exchange and collaborative training and research on the disease in countries in south-east Asia. Over the next five years, the network will carry out collaborative research projects across the region to evaluate new diagnostic techniques and to investigate the role of animals in maintaining the cycle of transmission of schistosomiasis in the region.

In China, the prevalence of schistosomiasis has been reduced as a result of mass treatment carried out from 1992 to 1998 during a World Bank Loan Project. By 1996, the disease had been eradicated in Zeijiang Province. Elsewhere, the number of villages where the disease was endemic had been reduced by 20-50%. However, there has been no reduction in the breeding grounds of the snails which harbour the disease-causing parasites and no reduction in transmission rates. Today, an estimated 40 million people are at risk. Worst affected are those who live along the flood-prone middle and lower reaches of the Yangtze River.

In The Philippines, about 6.7 million people in 24 provinces are at risk of schistosomiasis. In the three worst affected provinces almost 20% are infected. In Indonesia, a 1999 study in two areas found that average prevalence was 0.46-1.55%. Elsewhere, in the Lao People's Democratic Republic and Cambodia, where surveillance is poor, an estimated 60 000 and 90 000 people respectively are estimated to be at risk.

The RNAS, which is also supported by national governments and by the Danish Centre for Experimental Parasitology in Copenhagen, facilitates information exchange among researchers throughout the region and promotes training and research on priority issues. There are plans to establish a database of researchers from a range of disciplines working on Asian schistosomiasis, and several of the institutions involved are setting up internet websites which will be linked to the main RNAS website (www.RNAS.org) and to other schistosomiasis research institutes worldwide.

In areas of Cambodia, Lao People's Democratic Republic and The Philippines where the disease is endemic, the network is to evaluate a new rapid dipstick dye test, which has been developed to speed up large-scale population screening for schistosomiasis in the field.

The new easy-to-use kit, developed at the Jiangsu Institute of Parasitic Diseases in China, takes 5-10 minutes to use, can be stored at room temperature, and costs less than other cold chain-dependent and lengthier diagnostics such as ELISA tests.

Meanwhile, a new rapid, easy-to-use, and low-cost ELISA test developed in China is to be tested in other disease-endemic countries in the region.

GRANTS

• ***Research Capability Strengthening grant: 1999-ongoing***
Establishment and strengthening of a regional network for Asian schistosomiasis

MEMBERSHIP

While currently-used ELISA tests require special equipment and reagents, cold chain storage, and laboratory facilities, the new ELISA is rapid, easy-to-use, low-cost, and not cold chain-dependent. A 1998 evaluation of the test by the Chinese Ministry of Health found that it succeeded in detecting 90% of schistosomiasis infections.

Another priority research area is the role played by animals such as cattle, goats, pigs, dogs, and rats in disease transmission. The aim is to establish which animals are involved in transmission in a range of different geographical settings so that disease control measures can be tailored accordingly. In China, for example, cattle and water buffaloes are a major source of infection, while these animals play a minimal role in The Philippines – due, possibly, to cross-resistance from infection with a liver fluke.

RNAS researchers will also be evaluating new formulations of the drug praziquantel for animal use in an effort to improve compliance among livestock owners, and the possible role of alternative drugs such as trichlabendazole.

One novel solution – currently supported by TDR in a related project – is the development of a timed-release dose of praziquantel in the form of a giant capsule ("bolus") for use in ruminant animals such as cattle. Once the drug has been released in the stomach (rumen), the empty bolus is regurgitated. The network is also planning to carry out research to develop a protocol for the use of ultrasound technology to assess damage to organs such as the liver and bladder caused by schistosomiasis infection. Does the Chinese strain of the schistosomiasis-causing parasite (*Schistosoma japonicum*) cause more organ damage than the Philippines strain, for example? And how does this compare with the outcome of infection in Cambodia and the Lao People's Democratic Republic, where a different parasite (*Schistosoma mekongi*) is responsible?

The study will also compare internal organ damage caused by Asian schistosomiasis with that caused by *Schistosoma mansoni*, which occurs in countries in Africa, the Caribbean, the Eastern Mediterranean, and South America.

PIMRAT

A small pharmacology research group at he University of Ibadan in Nigeria, which received an institutional strengthening grant from TDR almost 25 years ago, is today a leading multidisciplinary malaria research and training centre and a key research partner within the Multilateral Initiative on Malaria in Africa (MIM), carrying out significant work in the field of antimalarial drugs, molecular biology and analysis of traditionally-used antimalarial treatments.

In 1978, TDR awarded an Institutional Strengthening Grant to a small group of malaria researchers at the Department of Pharmacology and Therapeutics at Ibadan University in Nigeria, to help build up research capacity on the pharmacology of malaria drugs. It turned out to be a sound investment – leading to the training of a new generation of researchers and expansion into a wide range of new malaria-related research activities.

The initial study – focusing on the use of quinine – led to related studies on the way the body responds to treatment with different antimalarial drugs.

As the research group expanded in the early 1980s, it moved to new premises at the Postgraduate Institute of Medical Research and Training (PIMRAT) – a university institute donated by a private pharmaceuticals company. TDR provided Research Training Grants to help build up the malaria research group – most of them awarded to young physicians who had obtained their first degrees.

By the mid-1980s, the group had extended its focus to include studies on the effectiveness and toxicity of antimalarial drugs and the treatment of drug-resistant malaria. Within 10 years of its launch, some of the younger scientists who had been recruited assumed leadership of the group and set about further expanding the range of malaria research activities.

These included studies on the biology of malaria parasites and evaluation of the effectiveness of new antimalarial drugs including halofantrine, mefloquine, and artemisinin derivatives.

The group also received TDR funding for an investigation of the potential of two non-antimalarial drugs in boosting the efficacy of chloroquine against chloroquine-resistant parasites. While one of these drugs, verapamil (used in the treatment of cardiac arrhythmias), proved to be unsuitable for widespread use, co-treatment with the antihistamine drug chlorpheniramine proved to be effective against laboratory-cultured chloroquine-resistant parasites.

The chlorpheniramine discovery was made by scientists at PIMRAT working in collaboration with scientists at the Walter Reed Army Institute for Research (WRAIR) in the United States. Although studies are still ongoing, co-treatment is believed to have great potential in delaying the development of resistance to chloroquine, in areas where chloroquine resistance is not yet widespread.

With an inevitable move into the rapidly expanding field of molecular biology in the early 1990s, the group has since built up expertise in this area and is now involved in studies on the molecular biology of antimalarial drug-resistance. More recently, in 1997, a group of social science and health education researchers from Ibadan University joined the malaria group at PIMRAT. Today, the core team of about 24 researchers is drawn from a range of disciplines including: pharmacists, pharmacologists, paediatricians, community physicians, parasitologists, phyto/chemists, biochemists, molecular biologists, health economists, health educators, and social scientists.

Ongoing malaria research projects involving PIMRAT researchers include three funded by TDR through the Multilateral Initiative on Malaria in Africa (MIM). One study is looking at ways of developing a more effective interface between

the scientific research community, policy-makers, and disease control programmes in an effort to improve the detection, diagnosis, and treatment of drug-resistant malaria. This study is being carried out in close collaboration with the Ministry of Health and hospitals in the state of Oyo.

Another project is aimed at identifying new anti-malarial compounds from plant products used in traditional medicine for the treatment of fevers. A multi-disciplinary team is working in collaboration with traditional healers. About 20 medicinal plants are being studied.

A third project is focusing on ways of improving home-based treatment of uncomplicated malaria. This involves consultation with care givers, primary health care workers, and community drug vendors, such as patent medicine stores and pharmacies, which sell over-the-counter drugs. The aim is to ensure that communities have rapid access to appropriate treatment.

The malaria group at PIMRAT is now well-established as a training facility and offers training for scientists and students from countries throughout Africa. Close links have been maintained with students on return to their home country, leading in some cases to continued collaboration and shared laboratory facilities.

PIMRAT works closely with other institutes in West Africa – benefiting from shared training opportunities and shared facilities for multi-centre trials. Another area of strength is the group's ongoing collaboration with scientists at Harvard University and WRAIR, which offer short-term training opportunities for PIMRAT scientists and students.

THE HEALTH INTERNETWORK

is a new global initiative aimed at bridging the information technology gap – the so-called "digital divide" – that handicaps health professionals, researchers, and policy-makers in developing countries.
Launched in September 2000 by Secretary-General Kofi Annan as part of the United Nations Millennium Action Plan, it is designed to improve health service delivery, support policy-making, and boost health research capacity in low-income countries.
The new venture is a public-private partnership involving international agencies, the private sector, foundations, non-governmental organizations, and governments. It aims to establish and equip more than 10 000 Internet access sites in hospitals, clinics, research institutes, and public health facilities in developing countries, ensuring more equitable access to up-to-date health information and IT software applications, and more widespread exchange of health information around the globe. The logistics of supplying and installing computer hardware and software, internet connectivity, and computer maintenance are being undertaken by a technological advisory group which involves non-governmental organizations as well as corporate and private sector partners.
Health professionals, policy-makers, and researchers in many developing countries are severely disadvantaged by the lack of access to communications technology and to the latest health and medical information online. In addition, they are prevented from contributing to global knowledge sharing through networking on the internet with colleagues from around the world.
In some countries the communications infrastructure is poor and internet access severely limited. Even where computers are available, they are often out-of-date and poorly maintained. And without basic computer training and information management skills, computer technology cannot be fully exploited. To make matters worse, in some countries health professionals are further handicapped by their poor knowledge of English – the main internet language but the mother-tongue of less than 10% of the world's population.
The first stage of the Health InterNetwork is a ground-breaking "Access to Research" initiative, launched in January 2002, which offers free Internet access to over 2000 biomedical journals for use by health professionals, researchers, and policy-makers in about 70 developing countries. WHO Director-General Dr Gro Harlem Brundtland said the new publishing initiative was "perhaps the biggest step ever taken towards reducing the health information gap between rich and poor countries." With many of the key publications involved costing over US$1500 a year and an average subscription costing several hundred US dollars, most journals were hitherto out of reach for financial reasons, even in health and research institutes with good computer facilities. Regular online access to biomedical publications in the poorest countries will help ensure that health professionals, researchers, and policy-makers have ready access to the latest research findings and can contribute to the global health research agenda.
The new breakthrough follows an agreement reached last year between WHO and six major medical journal publishers: Blackwell, Elsevier Science, the Harcourt Worldwide STM Group, Wolters Kluwer International Health and Science,

TDR is a key partner in the Health InterNetwork – a new global initiative spearheaded by WHO to strengthen public health services in developing countries through opening up access to health information via the Internet. First off the ground is a new initiative which offers free Internet access to full-text research papers in key international biomedical journals. The aim is to help improve health care, research capacity, training, and policy-making in low-income countries around the world.

Springer Verlag, and John Wiley. The aim was to seek a more affordable price structure for online access to their international medical journals. Under the agreement, which will last for three years, online publications are being made available free of charge or at greatly reduced cost, depending on the level of GNP. When the agreement ends, WHO will negotiate a longer-term reduced price agreement with the publishers involved. Through the creation of a public health portal on the internet, the Health InterNetwork is opening up access to state-of-the-art health and medical information, tools, and training programmes online – in the local language wherever possible. The academic and private sectors, together with local partners, are advising on the development and publishing of information as well as contributing content.

The new network will make available evidence and information for health policy and practice, statistical data, software applications such as geographical information systems ("disease mapping"), electronic resources for networking and publishing, and online education and training.

TDR is playing an active role in implementing the Health InterNetwork initiative as part of the programme's commitment to capacity building. TDR's contribution includes infrastructure support for selected institutes and the provision of training programmes to help define and promote the best means for accessing, organizing, managing and applying the vast amount of material and knowledge available via the internet. The latter includes an International Training Course on Health Internetwork Access to Research Initiative (HINARI). It is envisaged that such initiatives will increase the capacity of scientists and health care workers from developing nations to influence the global research agenda, to better set national research priorities and to increase their self-reliance in developing sound strategies for the control, treatment and prevention of disease in their home countries.

FOR OVER A DECADE,

In the small mountainous Kingdom of Nepal, one of the poorest and least accessible countries in the world, TDR is involved in efforts to establish a sustainable network of health researchers who can contribute new knowledge to the prevention and control of tropical diseases.

TDR has provided grants to both individual researchers and institutions in Nepal to help strengthen the country's health research capacity. Research findings on malaria in Nepal have contributed to surveillance of the disease, while research on visceral leishmaniasis (kala-azar) has provided a useful information base for future research and helped policy-makers in drawing up the current disease control programme. In the late 1980s, TDR funded studies by researchers from the Epidemiology and Disease Control Division of the Ministry of Health on visceral leishmaniasis – a major problem in the Terai region of Nepal along the border with northern India. They included studies on the epidemiology of the disease and on the effectiveness of diagnostic tests. Then, in 1991, the government division was awarded an Institutional Strengthening Grant by TDR to further improve research capacity. This 5-year award was initially used to support research on the use of bednets and later for studies on visceral leishmaniasis. Meanwhile, Research Training Grants for doctoral studies were awarded to two young researchers from Tribhuvan University in the capital Kathmandu, enabling them to study at the Liverpool School of Tropical Medicine in the UK and at Mahidol University in Bangkok, Thailand, before returning to work in Nepal. Since then, six additional Research Training Grants have been awarded leading to masters degrees and doctorate students, in topics ranging from gender-sensitive interventions for leprosy, and the molecular epidemiology of malaria, to Japanese encephalitis and malaria-related health education, and the health economics of tuberculosis and leishmaniasis control. Professor Hari Govind Shrestha, Dean of the Institute of Medicine at Tribhuvan University, says the Nepalese recipients of TDR training grants have made good use of their training. "All former trainees are now involved in research and teaching and have contributed significantly to their respective fields," he says, "not only within the Institute but also outside it, acting as consultants for local agencies on the Institute's behalf." TDR's involvement in Nepal has helped forge close links between local research institutes and international collaborators. Today, tropical disease researchers collaborate closely with colleagues from government disease control programmes, Tribhuvan University, the Vector-borne Disease and Research Centre in Hetauda, the B.P. Koirala Institute of Health Sciences in Dharan, district hospitals, and local non-governmental organizations. TDR is also seeking to establish links with the South-east Asia Centre for Tuberculosis in Nepal. Meanwhile, international collaboration has been extended to the Liverpool School of Tropical Medicine in the UK, the US Centers for Disease Control and Prevention (CDC), United States Agency for International Development (USAID), and the Japanese International Cooperation Agency (JICA). TDR has also organized local workshops involving over 80 researchers from institutions throughout Nepal. Recent topics have included the use of computer applications in health research and the design of research proposals. In 2000, a joint workshop was organized in collaboration with the University Institute of Medicine and the Ministry of Health to test a new TDR training package on research epidemiology. In 2001, a CDC-led workshop was held to advise researchers on how to write scientific papers for publication.

Research capacity building
in developing countries

"Over the years, TDR has supported individual career development and institution strengthening involving over 400 research groups and institutions in about 80 disease-endemic countries"

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