TB or not TB?
The latest in TDR’s research from diagnosis to disease treatment | PAGE 14

Also in this issue

4 RESEARCH BRIEFS
7 TDRbriefly
11 Stewardship
22 MIM Pan-African conference
24 ANDI
25 Global Health Histories
28 Artemisinin’s discovery
30 World of TropiKA.net

MEETINGS
32 • Quality management
  • New tools for VL elimination
33 • Community-based interventions
34 • Strategic alliances
35 • Empowerment
  • Diagnostics
36 • Tropical medicine conventions
37 PUBLICATIONS

Targeting visceral leishmaniasis eradication

PAGE 4
When I set off for Dar es Salaam to write about TDR research into earlier initiation of anti-retroviral therapy in HIV-positive TB patients, I had no idea that I would be spending so much of my time in the tropics in an over-air-conditioned hotel conference room.

But along with field visits to hospitals, laboratories and clinics, our group of clinical trial team members from four countries also sat for several days in a darkened room exhaustively reviewing slide presentations. The team analysed in painstaking detail the critical steps related to good clinical practice (GCP) and good clinical laboratory practices (GCLP) that are essential to any clinical trial.

While meetings in some instances can be perceived as bureaucratic encumbrances, in fact they have important consequences, and can shape what happens in health research and hospital services.

While the glamour of research may be associated with huddling over a microscope or a field sample of insect vectors, meetings are important too. They are essential for training and improving field services and procedures, as well as for sharing knowledge and discoveries among expert peers.

Take the interview by one of the Chinese scientists who was a leader in the international development of the first artemisinin combination therapy, the fastest-acting antimalarial available today.

In an interview on page 28, Professor Zhou Yiqing recounts how a TDR-organized 1981 meeting in Beijing was the turning point that introduced artemisinin to the world.

From there, the rest is history.

In 2009 and 2010, TDR’s Stewardship function is convening meetings all over the world to take a fresh look at target diseases and thematic issues with critical relevance to control of infectious diseases most prevalent in poor countries (see article, page 11).

This series of meetings adds another dimension to the discussion of research gaps and priorities.

On the eve of each meeting of these “disease and thematic reference groups”, an even wider range of stakeholders gathers. Representatives of government, NGOs, the private sector and academia meet with the expert group to share knowledge and views about the diseases or themes being examined.

There, history is yet to be written. Perhaps the next artemisinin will emerge from one of those meetings.

Elaine Ruth Fletcher
Managing Editor, TDRnews
Innovation in action

Innovation is the first time that you put a new idea into practice – that was a theme sounded in the recent Global Forum for Health Research meeting Forum 2009 in Havana, Cuba.

The term innovation typically conjures up images of new tools, new products and new patents. However, our understanding of the concept as it applies to global health has become much more broad in recent years.

In fact, there can be many different facets of innovation.

As our cover story reflects, TDR has been on the cutting edge of efforts to develop and assess new forms of TB diagnosis and treatment. Some of these involve new tools, such as the use of light-emitting diode (LED) microscopes in TB diagnosis. Some efforts test strategies for the improved use of existing tools – for instance, the earlier initiation of ARV therapy for HIV-positive TB patients.

Innovative institutional networks and groupings can also be part of the innovation drive. Over the past year, TDR has been involved in the development of a new African Network on Drugs and Diagnostics Innovation (ANDI), which held its second stakeholders’ meeting on 4-7 October in Cape Town, South Africa. Inspired by ANDI, a new China Network on Drugs and Diagnostics Innovation (China-NDI) held its initial meeting, 24-25 October, in Shanghai.

These are both important contributions to the Global Strategy on Public Health, Innovation and Intellectual Property approved at the World Health Assembly in 2008.

Meanwhile, innovation in health systems and in access to health service delivery are other topics receiving increasing focus within WHO and among donor agencies.

Major donors such as the GAVI Alliance (Global Alliance for Vaccines and Immunisation) and the Global Fund to fight AIDS, Tuberculosis and Malaria are examining how they might direct new resources into health systems strengthening.

Here too, TDR is involved. We are working with others in WHO to organize the first Global Symposium on Health Systems Research, 16-19 November 2011 in Montreux, Switzerland.

In the widening discussion around innovation, the competition can at times become intense between diverse groups pitching for innovative new tools; approaches to networking and knowledge management; and investments in health systems innovation.

In TDR’s view, the entire continuum of innovation is important and should be viewed holistically. Those actors concerned with R&D and those concerned with health systems and access are working together towards a mutual goal – the elimination of diseases of poverty and the improved welfare of people globally.

Dr Robert Ridley
TDR Director
VISCERAL LEISHMANIASIS
Shorter, easier treatment shows promise in India

For nearly a century, the standard treatment for visceral leishmaniasis (VL), or kala azar, has been a painful 30-day course of intramuscular injections with sodium stibogluconate. In addition to the prolonged regimen, the treatment is associated with serious side effects including pancreatitis, myalgia (muscle pain) and cardiac failure.

Over the past decade, TDR and partners in India successfully brought to registration a 28-day oral drug, miltefosine, for VL. The only existing oral treatment, miltefosine has proven highly effective in both children and adults. However, at roughly US$ 72 per treatment, miltefosine is costly.

Now it appears that a shorter, easier and lower-cost treatment for VL may be on the horizon. Preliminary results of a TDR-sponsored clinical trial of Gilead’s AmBisome® (liposomal amphotericin B) followed by 14 days of oral miltefosine treatment are very promising. Publication of final results is expected in 2010.

The trial, led by Banaras Hindu University and Rajendra Memorial Research Institute of Medical Sciences, is being conducted in two sites in India, one in Varanasi and the other in Patna. The latter is the capital of Bihar, where close to 50% of the Indian subcontinent’s VL cases occur.

According to TDR scientist Byron Arana, combining one injection of AmBisome® with the 14-day miltefosine course appears highly effective as a treatment. This regime also improves patient adherence to the therapy, which helps stave off parasite resistance to the new VL drugs. “Patients tend to feel much better after a short time of taking miltefosine—and then they often stop taking the pills. That’s a recipe for resistance,” Arana says, “and the patient is never cured.”

FOR MORE INFO
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TB DIAGNOSIS
More rapid and accurate smear microscopy

New techniques to make diagnosis of TB much faster and easier in developing countries have shown good results in TDR-supported trials, and are likely to be endorsed soon by WHO.

One procedure is a new “front-loading” smear sampling technique that would permit same-day TB smear diagnosis with two sputum smear samples. Currently, sampling over two or three days is required, imposing a burden not only on laboratories but on patients having to make repeated clinic visits.

TDR also recently sponsored clinical trials of low-cost LED (light-emitting diode) fluorescent adapters to microscopes. LED fluorescence microscopy is rapidly becoming popular in developing country settings. Expert review, as well as controlled trials, indicates that the LED microscopes make the analysis of TB smears faster and easier.

The Scientific and Technical Advisory Group of WHO’s STOP TB Department reviewed experiences with both front-loading and LED fluorescence microscopy in a November meeting and will issue findings shortly. Nearly half of suspected TB patients do not get a confirmed TB diagnosis currently. A major factor is the dropout rate of poor patients who cannot afford the travel and time off work for repeated clinic visits. (See TB update, p. 14).

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Microscopic examination of a TB specimen at St Peter’s TB Clinic, Addis Ababa, Ethiopia.
A shorter miltefosine course would be less costly and would reduce gastrointestinal side effects often experienced with the 28-day oral miltefosine regime.

Still, as VL researchers know too well, no single drug regime is a cure-all for this neglected disease of poverty. Active case detection efforts as well as improved access to care, disease surveillance, integrated vector management and social mobilization all are critical. “There are many pieces to the leishmaniasis puzzle,” says Arana. “This combination treatment is a big one. But it’s only one.”

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VISCERAL LEISHMANIASIS
Vector control critical to VL elimination

Achieving lasting vector control in poverty-stricken areas, where poor sanitation and housing facilitate insect breeding, is a goal that has long eluded visceral leishmaniasis (VL) disease control programmes.

In parts of South-East Asia, VL was virtually eliminated with DDT fifty years ago, only to return once mass spraying campaigns ended. Indoor residual spraying (IRS) with DDT is still practiced in India while in Bangladesh, vector control is largely reliant on use of bednets.

A TDR-supported study published in October in BMC Medicine illustrates how a renewed vector control effort could potentially make an enormous impact on sandfly vector breeding sites around homes. Effective vector control could thus make a critical contribution to the elimination by 2015 of VL, a disease that affects some 500,000 people on the Indian subcontinent.

The study, a cluster randomized control trial carried out in villages in Bangladesh, India and Nepal, found that all three vector control interventions tested had very significant impacts on reducing sandfly vector densities – but IRS spraying either with DDT (in the case of India) or pyrethroids (Nepal and Bangladesh) had the most pronounced effect.

Environmentally-friendly wall plastering of homes with lime as well as the use of long-lasting insecticide treated bed nets (LLIN) also had very good outcomes. In sites where the lime had an appropriate acidity, the plastering, a traditional practice in festival seasons, had a particularly strong effect in reducing sandfly densities.

The study was part of a WHO/TDR implementation research program designed to support elimination of VL by 2015 on the Indian subcontinent through integrated vector management.

The authors conclude that IRS should be strengthened immediately in India and Nepal, while IRS plus the renewed insecticide treatment of bednets in Bangladesh (where bednet coverage exceeds 90 percent in endemic districts) has the best potential there for rapidly reducing insect bites.

The next stage of studies aims to help national vector control programmes administer IRS spraying of homes more effectively.

“In ideal conditions when our researchers spray, you can say this works well. In real-life situations, the challenges are very different,” observes Axel Kroeger, one of the study’s co-authors and a professor of International Community Health at Liverpool University. “A vector control programme may spend millions of dollars and then wind up spraying water on the walls, if, for instance, the insecticide is sold illegally to farmers. Or spraying may not happen because the monsoon comes too early or there are elections.”

Along with the health and ecological impacts of long-term reliance on IRS particularly with regards to DDT, insects may also develop resistance if it is used over a prolonged period.

“So IRS is always best used in a campaign period, while a combination of measures would always work better over the long-term,” Kroeger concludes.

FOR MORE INFO
For link to the article see: www.biomedcentral.com/1741-7015/7/54
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Impregnating bednets with insecticides in order to prevent VL transmission from sandfly bites.
SCISTOSOMIASIS
Researchers uncover parasite’s DNA blueprint

An international research consortium led by University of Texas researchers and supported over the years by TDR has sequenced the genome of Schistosoma mansoni, a parasite that infects some 200 million people in 76 countries as one of the major agents of schistosomiasis.

As reported in the cover article of Nature’s July 16 edition, the sequencing of S. mansoni is the largest of any parasite to date. Although associated with low mortality, S. mansoni causes severely debilitating illness in populations throughout Africa, the Eastern Mediterranean, South-East Asia and eastern South America, constituting a public health burden second only to malaria in terms of parasitic diseases.

the parasite known as a miracidium, which develops from eggs passed in the urine or faeces of infected people.

An estimated 400 million people worldwide are at risk of schistosomiasis infection. Because existing drugs don’t confer lasting protection, many of those people will likely become re-infected. However, for unknown reasons, others will not. The research team seeks to identify the genes responsible for severe infections in some groups and the development of immunity in others.

The project is supported in part by the National Institute of Allergy and Infectious Diseases of the USA-based National Institutes of Health, the John E. Fogarty International Center for Advanced Study in the Health Sciences, the Burroughs Wellcome Fund and TDR.

FOR MORE INFO

AFRICAN INSTITUTIONS INITIATIVE
TDR improving public health doctoral programmes

TDR is helping initiate model doctoral programmes in Africa in public and population health in collaboration with a new African Institutions Initiative. The £30 million programme, funded and spearheaded by the Wellcome Trust, is designed to strengthen health research capacity on the continent through the creation of seven pan-African consortia. A meeting to launch the initiative was held 6-8 October in Arusha, United Republic of Tanzania.

Comprising more than fifty universities and research institutions from eighteen African countries as well as partners outside Africa, the consortia will advance the development of viable research hubs at African universities through new academic programmes, networks and other strategies.

Members of the seven consortia will be responsible for focus areas such as networking, research capacity strengthening and training while also working towards common goals.

TDR is a member of the Consortium for Advanced Research Training in Africa (CARTA), which plans to develop doctoral programmes in nine African universities. CARTA builds upon past TDR collaborations within Africa that successfully built master’s-level programmes in epidemiology, health economics and health social sciences. These laid the groundwork for the doctoral-level programmes.

Steven Wayling, the TDR representative on the CARTA consortium, says: “CARTA is an example of how TDR works with other groups with similar objectives to raise money for capacity development, and how TDR leverages its intellectual resources to benefit a wider audience.”

“TDR will provide technical guidance and contribute materials central to the training programme,” Wayling said. “Each cohort of students will come together every academic year to be trained in skills not always taught in formal academic programmes. This may include grantwriting, publication and negotiating skills.”

CARTA is led by Alex Ezeh, executive director of the African Population and Health Research Centre in Kenya. Sharon Fonn, dean of the School for Public Health, University of Witwatersrand, South Africa, is CARTA’s deputy director. Fonn is a member of TDR’s Research Strengthening Group and of TDR’s Scientific Advisory Committee for integrated community-based interventions.

TDR also is involved in a second consortium being supported by the African Institutions Initiative – the Research Institute for Infectious Diseases of Poverty (IIDP) Consortium, directed by Margaret Gyapong in Ghana.

TDR Director Robert Ridley says, “The African Institutions Initiative is aligned with TDRs focus on ensuring researchers and institutions in disease-endemic countries play a pivotal role in shaping health research agendas. We are looking forward to contributing to this important new programme.”

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Dr Margaret Gyapong.
Focus on global public health: a first for ECOSOC

Due to the global economic crisis, some 23 African countries may not meet a single Millennium Development Goal, including goals for reducing child mortality and improving maternal health (MDGs 4 & 5) and for combating HIV/AIDS, malaria and other diseases (MDG 6).

Sudan issued that somber warning on behalf of the world’s least-developed countries (Group of 77) at the annual United Nations Economic and Social Council (ECOSOC) in Geneva. The meeting was the first ECOSOC annual session to make global health issues the leading topic of a high-level ministerial review.

The global health review, conducted over the first four days of the 6-31 July meeting, focused on how policy-makers might attain international goals and commitments related to the 1948 “health for all” declaration of the International Conference on Primary Health Care at Alma Ata, in what is now Kazakhstan.

WHO Director-General Margaret Chan charged that the global economic system is failing to address critical health issues, and that poorer nations are bearing the brunt of financial, environmental and health-related crises.

“Globalization has not turned out to be the rising tide that lifts all boats.”

For more on the Global Forum:
www.globalforumhealth.org/
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Instead, wealth has been created and spread in waves that lift the bigger boats but swamp or sink many smaller ones,” Chan said in her keynote speech.

Neglected tropical diseases, noncommunicable diseases and maternal health all were discussed as factors impacting attainment of the MDG goals.

Other topics included ways to improve health systems and retain health workers in developing countries, inequities in health among and within countries (including gender inequality), the importance of technologies in improving health outcomes and the role of philanthropy and public-private partnerships in global health.

ECOSOC brings together ministers and government officials, UN organizations, non-governmental organizations (NGOs) and others to discuss international economic, social, humanitarian and environmental issues.

“This year’s focus reflected a growing perception among policy-makers of health’s relevance to sociopolitical and economic agendas,” said Meinrad Studer, TDR external relations coordinator.

“Due to the recognition that health and sustainable development are intrinsically linked, health policy-makers are shifting towards a more holistic approach to health,” Studer observed. “Ministries of health must work closely with ministries of finance, food and agriculture, foreign affairs, environment and development. Health NGOs must work with development NGOs.”

Along with participating in forums such as ECOSOC, TDR engages politicians and policy-makers through a range of other stewardship, strategic alliance and advocacy activities.

“TDR is in a position to lead the way on such intersectoral cooperation in light of the fact that its co-sponsors (UNICEF, UNDP, the World Bank and WHO) are key actors in various aspects of development,” Studer said.

TDR has long been a leader in research on socioeconomic aspects of neglected diseases. For instance, socio-economic research has shed light on why women may have greater difficulty in accessing leprosy treatment than men. TDR-supported scientists also have used socioeconomic analysis in field trials to improve access to health tools such as antimalarials and bednets.

TDR recently initiated a series of disease and thematic reference groups to examine emerging needs in research on neglected diseases. A Global report for research on infectious diseases of poverty, planned for 2011, will synthesize these findings with particular reference to health systems, biotechnology and the environment.

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CRIMALDDI to coordinate malaria drug search

The European Commission is funding a two-year, US$ 800 000 project to coordinate European and international research to develop new malaria drugs.

Led by the Liverpool School of Tropical Medicine (LSTM), the CRIMALDDI project (Coordination, Rationalisation and Integration of Antimalarial Drug Discovery and Development Initiatives) brings together key players in antimalarial drug discovery. These include WHO/TDR, the Medicines for Malaria Venture (MMV) and Europe’s leading research organizations.

LSTM Deputy Director and Professor Steve Ward is CRIMALDDI’s scientific coordinator. He explains the project’s mandate thus: “New drugs to prevent, treat and eventually eliminate malaria are desperately needed if we are to make an impact upon the millions needlessly dying from this disease each year. Antimalarial drug research and development programmes are in operation across Europe and throughout the world, but too often these initiatives are uncoordinated, and time and money are spent going over old ground.”

CRIMALDDI will survey the current state of antimalarial research across Europe. A roadmap for antimalarial drug discovery efforts there and a five-year action plan for delivering on the roadmap will be based on the survey’s findings. An expert advisory group will provide external validation and ensure that the plans are practical and appropriate. CRIMALDDI also will formulate strategies to better coordinate R&D, to remove barriers to drug development and to facilitate dissemination of results.

Ward explains that this streamlining will improve the use of limited antimalarial funding: “Coordinating research will mean that resources are better directed towards faster development of drugs to treat and eliminate malaria. We will look at the global status of antimalarial drug discovery to ensure that the research agenda for antimalarials in Europe over the next decade is properly aligned with what’s going on elsewhere in the world.”

For more info: www.liv.ac.uk/lstm/about/communications/press_releases/crimalddi.htm

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Tunisia, Guizani has made significant contributions to the understanding of the pathogenesis and population genetics of leishmaniasis at the molecular level.

Taking a “gene-to-patient” approach, her research has resulted in several milestones: the development of a bioinformatic tool kit for in silico characterization of potential targets; validation of an antigenic Leishmania target, LeIF protein; and development of a prototype diagnosis kit based on DNA chips using targets identified by comparative genomics. Over her 20-year career, Guizani has received several TDR grants, served on TDR’s Research Strengthening Committee and published more than 30 peer-reviewed articles. She is a founding member of the Tunisian Women and Science Association and a founder and African coordinator of the TDR-sponsored South-South Initiative for Tropical Disease Research.

Another outstanding scientist, Lizette Koekemoer, has been awarded the Southern African Association for the Advancement of Science (S2A3) British Association Medal (Silver) for 2009.

Koekemoer is director of the Vector Control Reference Unit at the National Institute for Communicable Diseases in Johannesburg, where she investigates the molecular basis of insecticide resistance in malaria vector mosquitoes including Anopheles funestus and An. gambiae complex. Her work has demonstrated that the resistance mechanism is metabolic and she has identified two genes that are unregulated in resistant individuals.

Koekemoer discovered two species of Anopheles mosquitoes, a rare feat given the century of in-depth research on the genus. She has introduced new technology to vector research, including a multiplex PCR assay to identify five An. funestus mosquitoes in Africa. The assay is now the standard method for identification of this group of mosquitoes worldwide.

As principal investigator on TDR-funded projects for biological control of vectors and MIM/TDR malaria research, Koekemoer was recognized for “high-quality science, with a sound background and straightforward analytical methodology.” She also is a member of the TDR Empowerment Research Strengthening Group (RSG).

Past TDR grantees recognized for research excellence

Abdoulaye Djimdé, a researcher with the Malaria Research and Training Center at Mali’s University of Bamako and a former TDR grantee, was named Best Pharmacist in the Francophone World by the National Academy of Pharmacy of France in May. Presented during the 62nd World Health Assembly in Geneva, the award recognized Djimdé’s outstanding contributions to antimalarial therapeutics development.

Djimdé began his career by researching herbal medicines traditional healers used to treat jaundice in his native Mali. Several years later, he served as principal investigator on a Multilateral Initiative on Malaria (MIM)/TDR Antimalarial Drug Resistance Network in Mali.

One of the world’s leading experts on the molecular characterization of malaria parasite resistance to antimalarial drugs, Djimdé has published 38 peer-reviewed articles and oversees 12 scientists at the University of Bamako. (see also: www.edctp.org/Announcement.403+M52f6b37568e.0.html).

Elsewhere in the Francophone world, Tunisian scientist Ikram Guizani, also a former TDR grantee, was awarded a prize for Best Female Scientific Researcher by the President of the Republic of Tunisia in recognition of her contributions to leishmaniasis control.

As head of the Laboratory of Epidemiology and Ecology of Parasitic Disease at the Pasteur Institute of Tunisia, Guizani has made significant contributions to the understanding of the pathogenesis and population genetics of leishmaniasis at the molecular level.

Taking a “gene-to-patient” approach, her research has resulted in several milestones: the development of a bioinformatic tool kit for in silico characterization of potential targets; validation of an antigenic Leishmania target, LeIF protein; and development of a prototype diagnosis kit based on DNA chips using targets identified by comparative genomics. Over her 20-year career, Guizani has received several TDR grants, served on TDR’s Research Strengthening Committee and published more than 30 peer-reviewed articles. She is a founding member of the Tunisian Women and Science Association and a founder and African coordinator of the TDR-sponsored South-South Initiative for Tropical Disease Research.

As principal investigator on TDR-funded projects for biological control of vectors and MIM/TDR malaria research, Koekemoer was recognized for “high-quality science, with a sound background and straightforward analytical methodology.” She also is a member of the TDR Empowerment Research Strengthening Group (RSG).

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Dr Jean Paul Chiron, Secretary General of the National Academy of Pharmacy of France (left), extends award to Dr Abdoulaye Djimdé (right). In the middle: Dr Djimdé’s wife, Mama Assa Diba-Djimdé.

Dr Ikram Guizani, on right, receives her award for Best Female Scientific Researcher from Leila Ben Ali, wife of the President of the Republic of Tunisia.
TDR veterans receive high honors

Former TDR Director Adetokunbo Lucas was awarded an honorary doctor of medicine degree by the University of Sussex in the United Kingdom at a ceremony in July. It was the first such honorary degree in medicine following the university's establishment of the Brighton and Sussex Medical School. Lucas, a medical doctor and senior health policy expert in Nigeria, served as TDR’s second director from 1976-1986, guiding the new programme at a time when discoveries in biology, genetics and immunology transformed medicine.

Under Lucas's leadership, TDR set out to translate those discoveries into tangible benefits for the victims of neglected diseases. Lucas later served as chair of the Carnegie Corporation’s Strengthening Human Resources in Developing Countries grant programme, chair of the Global Forum for Health Research and professor of international health at the Harvard School of Public Health. On 2 December, Lucas presented at WHO in Geneva on TDR’s early history and achievements, as a guest speaker of the Global Health Histories series (see p. 25).

Another TDR veteran, CP Ramachandran, has recently been named professor emeritus by the University of Science, Malaysia (USM) in Penang. Ramachandran, a pioneering researcher into lymphatic filariasis (LF), served for ten years as professor and dean of USM’s School of Biological Sciences, overseeing a period when the school developed into a major research institution. After joining TDR in 1975, Ramachandran became head of the Research Capacity Strengthening Unit. “Effectively, I became a salesman for TDR,” he recalls. “In Southeast Asia my name went from ‘CP Ramachandran’ to ‘TDR Ramachandran’.”

From 1985 until his retirement in 1996, Ramachandran was secretary of TDR’s Filariasis Steering Committee, where he was instrumental in initiating the Global Program to Eliminate Lymphatic Filariasis. He continues to serve as a Global Alliance for the Elimination of Lymphatic Filariasis executive group member as well as chair of the Mekong Plus Program Review Group and chairperson of the Pacific Island Countries Programme Review Group for Elimination of LF.

Poverty Related Diseases College opens doors

A first-of-its-kind international programme in biomedicine and development has opened at Cameroon’s University of Yaoundé I.

The Poverty Related Diseases College (PRDC) offers students from developed and developing countries an educational curriculum that bridges biological sciences, health and development, according to Professor Wilfred Mbacham, a former TDR trainee and University of Yaoundé public health biotechnology expert who is coordinating the new programme.

The programme is the first such initiative to be led by an African institution under the auspices of the 7th Framework Program (FP7) of the European Commission Directorate General for Research, a major European Union funding instrument for international research.

The PRDC is targeted at PhD candidates or post-doctoral researchers worldwide. The college’s inaugural class comprises 24 advanced PhD students and post-docs, with 12 from Africa and 12 from Europe. Via a curriculum-based scientific exchange program, the students will participate in three intensive courses at research and university centres in Uganda, South Africa and Cameroon.

While based in Cameroon, the PRDC involves a partnership with Makerere University in Uganda, the International Centre for Genetic Engineering and Biotechnology in South Africa, the Tropical Diseases Research Centre in Zambia and the Mbeya Medical Research Programme in the Republic of Tanzania. The college’s collaborating European partners include Sweden’s Stockholm University, Germany’s Max Planck Institute, Italy’s National Research Council and the Academic Medical Centre at the University of Amsterdam, Netherlands.

For more info:
www.prd-college.eu and www.u1.uninet.cm.
Global report for research on infectious diseases of poverty

Country-led dialogue guides review of issues

Since its founding in 1975, TDR has convened expert groups to stimulate action on critical research agendas. Now, TDR is expanding and enhancing this effort in the context of its Stewardship function and a new European Commission partnership. Ten expert groups are preparing reports on specific areas of neglected disease research. A Global report for research on infectious diseases of poverty is to be launched in 2011. Underlying these reports is a new emphasis on broad dialogue among stakeholders and more active leadership by developing countries.

Co-chairs of the TDR-sponsored expert reference groups met 2-4 September in Geneva to agree on a framework for the planned disease and thematic reference group (DRG/TRG) report series. They also discussed how the series would contribute to the subsequent Global report for research on infectious diseases of poverty, to be published in mid-2011.

The reference group reports are intended to be “unique, authoritative, and credible overviews” of the status of research in a particular area, highlighting top-level research priorities, while the global report should be an “action-oriented report, identifying areas useful for accelerating development and applications of interventions,” said Catherine Davies, Global report scientific coordinator.

The reports also are a key element in a new European Commission-TDR partnership to provide an overview and top-level, stakeholder-endorsed strategic recommendations on priorities for research on neglected diseases, notes Ayoade MJ Oduola, coordinator of TDR’s Stewardship function, which is leading this effort.

Currently, less than 10% of the global health research budget of both the public and the private sectors is earmarked for health problems in developing countries and only 2% of global R&D funding is allocated to research on major communicable diseases, according to data published by the European Commission1.

Six TDR-sponsored reference groups are addressing disease-specific areas of research in which TDR has been engaged for over 30 years, while four more groups address cross-cutting research themes particularly relevant to diseases of poverty: social sciences and gender; innovation and biotechnology platforms; health systems and implementation research; and environment, agriculture and infectious diseases.

Each DRG/TRG report will stand alone. The Global report will focus on three cross-cutting themes – biotechnology and innovation, health systems and access, and environment/climate change.

“The challenge is to make our report rigorous enough to function as a one-stop repository of up-to-date information, yet flexible enough to permit the exchange of novel ideas,” said Felipe Guhl, co-chairman of the group (continued on page 13)}


Disease reference groups (DRGs) and thematic reference groups (TRGs) hosted in WHO country offices (WCO)

DRGs/TRGs to be developed

DRG 1: Malaria – WHO Regional Office for Africa (AFRO), Republic of Congo
DRG 2: TB, leprosy and Buruli ulcer – WHO country office, Philippines
DRG 3: Chagas disease, human African trypanosomiasis and leishmaniasis – WHO country offices, Sudan & Brazil
DRG 4: Helminth infections & Ivermectin Resistance Initiative – African Programme on Onchocerciasis Control (APOC), Burkina Faso
DRG 5: Dengue and emerging viral diseases of public health importance – WHO country office, Cuba
DRG 6: Zoonoses and marginalized infectious diseases – WHO Regional Office for the Eastern Mediterranean (EMRO), Egypt
TRG 1: Social sciences and gender – WHO country office, Ghana
TRG 2: Innovation and biotechnology platforms for health interventions – WHO country office, Thailand
TRG 3: Health systems and implementation research – WHO country office, Nigeria
TRG 4: Environment, agriculture and infectious diseases – WHO country office, China
BOX 1. Better environmental management can reduce climate change impacts on diseases, experts at Shanghai meeting conclude

Case studies of how climate change may impact infectious diseases prevalent in agricultural areas were a focus of the October meeting of TDR’s Thematic Reference Group (TRG) on Environment, Agriculture and Infectious Diseases.

Presentations included a review of how better ecosystem management could aid in prevention and control of snail-borne schistosomiasis, avian influenza, mosquito-borne dengue, the foodborne trematode *Clonorchis sinensis* and echinococcosis, a disease transmitted to shepherds via livestock and dogs.

The second annual stakeholder consultation and meeting of experts, 26-28 October in Shanghai, China, was hosted by the National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention (China CDC), in collaboration with the WHO Representative Office in China and the Shanghai Municipal Government.

Experts at the meeting reviewed linkages between environment, agriculture and disease for a range of parasitic diseases and viral infections, including schistosomiasis, dengue fever, and avian influenza.

Modeling of climate change trends by Chinese scientists, including TRG members, has led to forecasts that the transmission zone of the parasite *Schistosoma japonicum* will expand by some 783,883 km² by 2050, due to the northward shift of the “freeze line” – where January temperatures exceed 0°C. Rising temperatures are expected to promote the development of snails that are intermediate hosts of *S. japonicum*.

However, climate change impacts can be mitigated through disease control, surveillance and ecosystem measures, said Li Shizhu and Qian Yingjun, of the National Institute of Parasitic Diseases, China CDC. These include surveillance of snail populations, of the parasite in human populations and reduction of snail habitats through the design of water carriers that inhibit snail breeding and mobility.

In a keynote address, Cris Tunon, acting WHO representative in China, noted that the TRG’s work responds to the increased interest in environmental health issues among both national and UN agencies in China.

China CDC Vice Director-General Weizhong Yang underlined the need for further research into the control of environmentally-induced infectious diseases.

Case studies reviewed by the TRG will contribute to a report on *Environment, agriculture and infectious diseases*, planned for 2010. The TRG’s work, in turn, will also contribute to the *Global report for research on infectious diseases of poverty*, said TDR’s Johannes Sommerfeld, who is responsible for coordinating the group.

“We forecast an expansion of schistosomiasis transmission into currently non-endemic areas in the north, with an additional risk area of 783,883 km² by 2050, translating to 8.1% of the surface area of China. Our results call for rigorous monitoring and surveillance of schistosomiasis in a future warmer China.”


Further info: www.who.int/tdr/svc/topics/environment

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“Retention tanks inhibit snails’ spread via water carriers.”
examining Chagas disease, human African trypanosomiasis (HAT) and leishmaniasis in an integrated manner, something rarely done although the same family of trypanosomatidae parasites cause all three diseases.

All three diseases are strongly associated with poverty: “In addition to severe health impact, they have enormous socioeconomic impacts,” said Guhl, who is director of the Center for Research in Microbiology and Tropical Parasitology (CIMPAT) in Bogota, Colombia.

“Knowledge about the trypanosome genome and the disease-transmitting vectors (triatomine bugs for Chagas, tsetse flies for HAT and sandflies for leishmaniasis) has greatly expanded in recent years,” he adds. “But this has not translated into more effective tools for prevention and treatment.

“The reasons for this include the one-dimensional summing up of scientific developments in different sectors of activity, ill-defined stakeholder roles and very narrow approaches to the identification of priority research areas and gaps,” Guhl said. “These are the challenges we want to address.”

Stakeholder and DEC involvement

Great emphasis is being placed on encouraging the active leadership of scientists, decision-makers and institutions from disease-endemic countries (DECs) in the formulation of recommendations.

Each DRG/TRG, while international in membership, is being hosted in a developing country and co-chaired by national experts from that country or region (see map p. 12). Corresponding WHO country or regional offices serve as partners coordinating the overall effort.

Each DRG/TRG expert group also has been launched with a broad consultation forum of government officials, industry leaders and representatives of civil society and NGOs, who discussed the relevance of the initiative and issues important to their work.

“All are being encouraged to provide input to the framework and activities of the disease and thematic reference groups so that the reports will be useful to their work,” said Oduola. “And when the work is finished, they’re encouraged to utilize those reports.”

In his presentation to the co-chairs of the DRG/TRGs in Geneva last September, TDR Director Robert Ridley stressed the importance of stakeholder involvement in the review process – as evidenced by a number of past findings in neglected diseases research.

For instance, when insecticide-treated bed nets were first marketed for malaria prevention, they were uniformly white. That changed, Ridley noted, when it was reported that in some cultures white is strongly associated with death, as it is the colour of a shroud.

“Each DRG/TRG report will have to resonate with a particular community of both experts and stakeholders,” he observed. At the same time, the global report should paint a “big picture” that can resonate with the worldwide community of scientists and policy-makers.

Contributing to WHO/TDR research agendas

The Global report will be the first in a planned series of biennial reports on top-level priorities for research on neglected infectious diseases of poverty, including:

- identification of the most pressing public health priorities in developing countries;
- recommendations for high-impact, targeted science/implementation research.

The report’s focus is on three themes currently resonant in international policy dialogues: health systems, interplay between the environment and neglected diseases, and potential impact of biotechnology/innovation.

It will build upon key findings from the DRG/TRG reports as well as taking a fresh look at the issues, Davies said.

The TDR report is expected to contribute to the World Health Report 2012, which will be dedicated to the topic of research for health for the first time in WHO history. Its analysis will also contribute to European Commission strategies around funding for infectious diseases of poverty.

“The Global report, along with the disease and thematic report series, comprise key elements in TDR’s aim of building a platform for dialogue and debate about research priorities,” Oduola said. The other element in this neutral platform is the TropIKA net knowledge management portal designed for sharing research information.

“Together, these resources should establish an effective framework for continuous assessment of research and control needs, progress analysis and provision of information useful to foster coherence, collaborations and effective action on priorities amongst stakeholders on infectious diseases of poverty,” Oduola said.

“These reports should frame recommendations in a way that is relevant to countries, to those working in the field, and to those making decisions on funding,” Davies said. “They will set out ‘options for actions’ illustrating how agreed priorities might be taken forward.”


For more information:
www.who.int/tdr/svc/stewardship/research-think-tank

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TB or not TB?

Closing the gap between evidence

TB is one of the world’s most widespread infections – one of every three people is a carrier. Over the past two decades TB resurfaced worldwide, along with TB co-infections with HIV/AIDS and drug-resistant TB. Daunting gaps in knowledge about how to manage the new epidemic left TB diagnostic and treatment practices in dire need of improvement, and health services overwhelmed. Yet new evidence generated by TDR is making a major difference in TB diagnosis and treatment.

DAR ES SALAAM, UNITED REPUBLIC OF TANZANIA:
At a busy TB clinic, Freddie waited to pick up his drug prescription for the next two weeks. The Tanzanian military band member was leaving to perform in Zanzibar, and wanted to make sure he would not miss a dose.

A tall man who looks much younger than his 44 years, Freddie (his nickname) just a few months ago was mostly bedbound and coughing up blood. Married with two children, ages 25 and 9, he knew his life was at risk.

Then he was referred to Dar es Salaam’s Mwanan-Jamala Hospital TB clinic, which is collaborating with TDR on a trial to improve treatment of TB patients infected with HIV.

A sputum smear was positive for TB. But at the same time the clinic staff asked him to take HIV as part of an innovative TDR-supported trial. The trial, TB-HAART, is testing whether HIV-infected TB patients who also begin antiretroviral (ARV) therapy together with TB treatment, and much earlier than ARVs typically are offered, have better recovery rates and overall health than those who only receive TB drugs.

After a few soul-searching conversations with the nurses and his brother, Freddie decided to brave the HIV test, which turned out to be positive. The upside was that he was registered for the TB-HAART trial, which he credits with restoring his health.

In fact, Freddie still does not know if he has been receiving ARV drugs right from the start or a placebo for the first six months plus the TB course (after the first six months everyone receives ARVs and is guaranteed a lifetime supply). But he has observed a rapid and remarkable change in his overall health.

“My weight has gone up from 65 to 75 kilos and my CD4 blood cell count [a measure of immune system strength] rebounded from 400 to 500 [cells/mm³]. Overall, I am feeling much better, so(185,110),(808,815) I am convinced that I am already receiving ARVs along with my TB treatment,” he said. “I have hope and have been able to resume my normal life” (see Freddie, p.16).
While the data has yet to be unblinded, rebound stories like Freddie’s provide strong indications that initiation of ARVs simultaneously with TB treatment is not only safe but also can improve patient survival and overall health. As a result, there may be interim review of patient data from the four participating countries in late 2010, according to Philip Onyebujoh, coordinator of TDR’s Evidence for TB/HIV Treatment Policy business line.

Ultimately, the trial holds the potential to significantly influence TB/HIV treatment policy and even HIV treatment – particularly since evidence is scant on when to begin ARV therapy for HIV-infected populations in developing countries.

Many African countries, including Tanzania, begin ARV treatment after CD4 count falls below 200 – although the Ministry of Health is considering an upward shift of that threshold in line with worldwide trends. On 30 November, WHO issued guidelines recommending that ARV treatment be offered for anyone with CD4 counts of 350 or lower. WHO guidelines noted, however, that the quality of evidence regarding that threshold is still only “moderate” – relying largely upon one randomized control trial in Haiti and one post-hoc analysis of data from another trial.1

Beyond the current WHO recommendation, the TB-HAART trial is testing if TB-infected HIV patients with CD4 counts higher than 350 – people like Freddie – also might benefit from earlier initiation of ARV therapy. If evidence reflects a significant benefit, the case for raising the threshold even further could be made.

“All in all, the thresholds we have right now still lack evidence about optimal treatment for developing country populations, who also are frequently malnourished and beset with other parasitic, bacterial and viral infections,” says TDR’s Mahnaz Vahedi, a medical doctor and TB-HAART project manager.

Vahedi’s polite demeanor belies an intellectual intensity and professional drive that has led her to ply the air routes between Geneva and Africa countless times over the past
two years to ensure the trial’s smooth progression. Large-
dly due to such efforts, the trial has nearly reached its
halfway point in recruitment.

Value-added TB research

The addition of TB to TDR’s portfolio of neglected diseases
is relatively recent. In 1998, in response to rapid world-
wide surge in TB cases, TDR’s governing body decided to
develop a targeted series of research activities.

“TDR does not aspire to be the lead actor on either TB or
HIV/AIDS,” Director Robert Ridley said. “We are working
alongside the STOP TB Partnership and the Global Fund
to Fight AIDS, TB and Malaria as well as with WHO’s
STOP TB Department.

“We identify needs for new evidence, and then make
optimal use of our networks and experience in field set-
tings to fill these critical gaps.” Key areas of TDR focus
so far have included:

• **TB-HAART (highly active anti-retroviral treatment):**
The four-country trial has enrolled 720 of a planned
1800 patients. The halfway mark – 900 patients
having undergone at least six months of treatment –
should be reached in 2010. At that point, the trial’s
safety oversight committee might decide to review
preliminary results, which are urgently needed as
evidence for treatment policies.

• **TB treatment in four months:** Cutting treatment
time from six to four months with a gatifloxacin-
containing TB drug combination is the focus of a piv-
otal TDR co-sponsored Phase III trial. This research
is under way in collaboration with the national TB
control programmes of Senegal and Benin, research
institutions in Guinea, Kenya and South Africa, and
the European Commission-funded Ollotub Consorti-

um. The last of the 1836 volunteers were completing
treatment at the end of 2009 with analysis forthcoming
in 2010 (see TDRnews 82, p. 4).

• **“Fixed-dose” drugs:** This trial tests TB treatments
that combine multiple drugs into a single-dose pill.
Already on the market in many countries, these fixed
dose combinations had not previously been evaluated
for safety and efficacy. A single-blinded randomized
clinical trial involving 1000 patients in Ethiopia and
Nigeria is to end in 2010 (see TDRnews 78, p.16).

• **More rapid and accurate smear microscopy:** New
ways to speed up smear diagnosis of tuberculosis are
likely to be recommended by WHO following large
TDR-led multi-country clinical trials of “front-load-
ing” methods. Front-loading means that two sputum
smears are collected and analyzed on the same day.
Currently, patients must return to a clinic over two
or three days to provide sputum samples, and many
do not receive treatment due to patient drop-out.

• **LED fluorescence microscopy for easier diagnosis:**
TDR also has been a leader in testing light-emitting
diode (LED) adapters for microscopes, another new
technology likely to be recommended soon by WHO.
The use of LED causes bacilli to glow in specially-
stained smears. This makes them appear larger than
usual, considerably reducing the time required for
examining each smear.

• **A rapid TB blood test:** Not one commercial TB blood
test on the market performs as well as smear micros-
copy. However, a combination of antigens identified
in a systematic review by TDR and partners last year
shows promise. These will be evaluated in the coming
year to see if a truly revolutionary rapid blood test for
TB could be developed.

Freddie: ‘I am proud to be an advocate’ for HIV testing

“When I was first supposed to get tested, I left the clinic and ran away, I was so afraid,”
Freddie says. “I went to my brother’s house and talked with him; he convinced me that I
should go through with it. ‘Better to know and to get treated than not to know,’ he said.
‘There are drugs now to treat HIV.’

Freddie returned to the TB clinic at Mwanan-Jamala Hospital TB clinic, talked with the
nurses there, and braved the test.

The United Republic of Tanzania recently instituted a policy of offering HIV tests and
ARVs free-of-charge to HIV-positive people with CD4 counts of 200 cells/mm³ or below. But since Freddie’s
initial CD4 count was higher, he would not have been eligible. As a member of the study he is now assured of
receiving anti-retroviral drugs after six months, but he is convinced that he is already receiving them now.

He has meanwhile become a quiet advocate for getting tested among his relatives and his friends. (His wife
has tested negative for HIV, and they are now careful to use condoms). At a recent military festival, he spoke
to many people at the AIDS testing booth.

“I feel so sorry for the former generation of Tanzanians who died of AIDS without having access to such
treatments,” he says. “Now people are less afraid of being tested and finding out. There are the drugs for
treatment and the stigma has been reduced. Until now, I had read about the stories of others who have
become advocates for getting tested,” he adds. “I am proud now to have become an advocate.”
TDR’s training and coordination roles

Before the TB-HAART trial started, it took up to two weeks to get a sputum sample from a peripheral site to the national laboratory in Dar es Salaam, according to Saidi Egwaga, manager of the Tanzanian National Tuberculosis and Leprosy Programme (NTLP) and a principal investigator of the TB-HAART trial. “Now we can speak about same-day delivery of smear samples to the laboratory,” Egwaga said. He was leading an August visit to the Muhimbili National Hospital Laboratory by members of TB-HAART research teams. This mixed group of investigators, clinical trial coordinators, trial managers and monitors came from the four country sites – Zambia, Uganda, South Africa and Tanzania.

The tour of the hospital laboratory was part of a “refresher course” in good clinical laboratory practices (GCLP) and good clinical practices (GCP), organized by TDR’s Vahedi for the country teams. The four-day course was a step-by-step review by safety physicians, trial monitors, TDR staff and the participants themselves of all aspects of procedure.

“Pressure to generate data from this trial is enormous,” stated Onyebujoh, speaking to the group on the first day of the week-long session. Bulky and spectacled, Onyebujoh has a presence that is a cross between academic-physician and artist. He never met Freddie in person, but he shares his love of jazz, and a keen personal appreciation for how the TB and HIV epidemics have ripped through Africa’s best and brightest. He approaches his clinical trial teams like a coach urging players to score a goal against death.

“Globally, there are four trials ongoing looking at optimal timing for the start of ARV therapy,” he says. “But this trial is large enough to make a stratified analysis of outcomes among patients with different CD4 blood counts.”

“We have almost hit our halfway point for enrolment,” he adds. “By late 2010, we might be in a position to generate preliminary findings that can support policy recommendations.

“But to do that, it is critical that every single aspect of the trial be conducted strictly according to international GCP and GCLP standards, and that any review will confirm the robustness of the data.

“Not only that, but there is a need to ensure procedures are the same across all countries so data are completely comparable. This trial, if you look at any aspect, must pass any kind of audit or inspection. The data have to be clean – completely clean.”

From field site to laboratory

The ensuing three days are filled with presentations on step-by-step trial recording, reporting and data management processes, as well as related issues of patient safety, particularly adverse events. Sessions are highly interactive and led by clinical monitors, safety physicians and country trial staff as well as by Vahedi and Onyebujoh.

Every link in the diagnostic and treatment chain is discussed: from the procedures for taking and labeling sputum or blood samples to microscopy examination in field sites. Other topics include packaging and transport, follow-up cultures in reference laboratories, reporting back, treatment processes, patient records and discrepancies, and adverse events.

Getting the patient data right

Misrecording data is not just a matter of a technical error – it can be a life-changing event for the patient, according to Getnet Yimer. The young Ethiopian doctor who is a roaming clinical monitor in the trial recalls how
the wedding engagement of a young man he knew was cancelled due to an incorrect report of an HIV diagnosis.

Yimer reviewed some of the common problems in recording that can be encountered from field site to laboratory. Those include issues such as transcription errors in case record forms; lack of proper transport logs for sample movements; inconsistencies between patient details in laboratory reports and source documents; and documents that are not filed, signed or followed-up properly (see Yimer below).

Yimer devotes countless hours traveling from one clinical trial site to another throughout Zambia, Uganda and Tanzania. There he will sit for hours, paging through documents with a registered nurse or a clinical trial associate, and making detailed notes and corrections where needed.

Vahedi oversees the trial with daily calls to trial monitors and other staff. Every few weeks she also arrives at the far-flung trial sites to provide a double quality control.

“"If you are not there, you just do not really see the picture,” she says. “If you are there, you can overcome roadblocks, and people feel that they are being backed by WHO/TDR at headquarters.”

Ensuring patient safety

Vahedi expresses satisfaction that the trial has improved patient care at participating clinics, which observe a strict routine of follow-up appointments for 24 months, including contacting those who miss appointments.

Underlying strict observance of trial procedures, is a concern for the patient, points out Catherine Magezi Muwonge, the trial’s chief safety physician, speaking at the GCP refresher course.

So while it is important to report a serious adverse event within 24 hours to clinical trial investigators and sponsors as per GCP standards, even more critical is the health of the person involved, she points out.

“If you have abnormal results, the issue is not just about rapid reporting. It really is about the safety of the individual, another human being. So you have to...”

Yimer: “Get the signature right”

Mosquitoes hover around Getnet Yimer in a tiny airless room at the Mwanan-Jamala Hospital TB clinic. He is checking hundreds of pages of clinical trial ‘case record forms’ (CRFs) against original ‘source forms’ that were filled in during patient visits.

He is hunting for discrepancies, often tiny, in the transcription of dates, times and blood counts. He also observes the real-time intake of patients by TB-HAART clinical trial associate Maliwaza Mganga.

The issues he notes are illustrative of the level of detail that must be addressed in order for the trial to reflect international standards.

Yimer says a common problem is slight inconsistencies between signatures, particularly in the cases of illiterate patients. In the latter case, an accompanying witness is supposed to co-sign the consent form, alongside the patient’s “identifying mark.”

“Consent is a major component of a clinical trial,” he notes. “See here, the trial associate has been writing the date on the consent form for those who cannot read and write. I am telling her that it is the witness who should be writing in the date, not herself, because that witness is, in effect, signing in the place of the patient.”

Yimer peers at the source form again. In the initial physical exam, the associate had noted the patient’s musculo-skeletal condition as “normal.”

However, there is no such exam in the TB trial, so Yimer shows her how she should put “not applicable” and sign with her initials.

“Height,” he says, “if you did not get it the first time, you can catch it on the next visit. It is not a variable that will change. However, if you missed weight the first time, you cannot fill it in later.

“Date and month of birth: if they do not know, then put 99/99. Don’t guess.”

And then, there is the issue of the signature. “When you have to sign the bottom of the form, write your full signature, not just initials,” he instructs her, “that is, unless you really do use your initials as your signature.”

“And if you are going to change that practice from an initial to a full signature, then please make a note for the file!”
relate the abnormal results to the clinical condition. You have to manage the patient, to treat them.”

All in all, the bottom line is to adopt a critical, questioning stance vis-a-vis data – and particularly abnormal data, concludes Onyebujoh.

“If a patient’s blood count upon treatment was normal and then it becomes abnormal, clearly something is wrong. So you have to ask: are we dealing with a sample that was too long in the laboratory or a meaningful pathological situation?

“You ask that question and you review the information holistically, in context. You need to be thoughtful, you need to be a clinician. That is what it is all about.”

**Embedding research culture in TB control programmes**

Muhimbili Hospital’s TB laboratory is one of three reference laboratories in Tanzania. It is the laboratory to which samples are sent from all four TB-HAART trial sites in the country.

The laboratory is tucked into a cramped series of rooms on the hospital’s third floor and demand on its facilities is heavy. Every tenth TB sputum sample nationally is supposed to be referred for a follow-up culture; in reality, only about one sample out of 100 is thus confirmed.

This is the first time that the laboratory has participated in such a major piece of research, and good practices adopted for the trial have extended to routine work, says Egwaga. He cites improvements as follows:

- specimen quality as a result of capacity-building in periphery;
- rapid transfer of samples from clinics to laboratory;
- quality control in laboratories, external and internal;
- supply of materials like reagents for analysis and tests;
- documentation of samples.

“TB-HAART has helped us develop standard operating procedures for reporting. People now appreciate more the importance of reliable and accurate source data. The study also has helped us build confidence that we can undertake other clinical trials,” Egwaga says.

Muhimbili Hospital’s experience shows how TB-HAART is more than a clinical trial: it “embeds” a culture of research into national disease programmes.

Essentially, says Onyebujoh, the strategy works on three levels to strengthen health systems:

- It builds improved laboratory and treatment procedures in key national health laboratories and hospitals, such as Muhimbili, which can then introduce those same practices elsewhere.
- It involves national TB programme managers directly in the research creating confidence in findings and support for adoption of new practices.
- Opportunities to participate in research can be a professional stimulus for health workers in developing countries, where “brain drain” is a chronic problem.

“No only does this trial provide people with an additional allowance, it opens up opportunities for continuing education – and this improves staff motivation and retention, which we know is a major problem in Africa,” Egwaga observes.

“I now have my eye on future opportunities for us to become involved in other such trials. This way, everyone knows that there is something new coming along.”
New LED microscopes shed light

One new tool aiding performance of clinics in outlying areas, says Egwaga, is light-emitting diode (LED)-based fluorescence for TB microscopy. This includes purpose-built LED fluorescent microscopes or ordinary light microscopes converted to LED with adapters.

TDR has led testing of the inexpensive adapters. Based partly on these studies, LED fluorescence microscopy may soon become a recommended procedure, following a meeting in November 2009 of the Scientific and Technical Advisory Group (STAG) of WHO’s STOP TB Department.

Conventional fluorescence microscopes are expensive, and their mercury vapour lamps are both short-lived and toxic. LED-based fluorescence is simple, non-toxic and can be operated on solar-powered batteries.

“It’s the same kind of light that campers often wear on bands around their heads,” says Andy Ramsay, a TDR scientist who is also secretary of the Stop TB Partnership’s Working Group on New Diagnostics.

The use of LED causes bacilli to glow in specially-stained smears. This reduces examination time and increases sensitivity of the diagnosis.

“We believe that very considerable gains in TB case detection could be achieved with existing laboratory staffing levels and the addition of this low-cost equipment,” Ramsay says. He cites a recent TDR study that modeled how LED-based microscopy could improve existing TB services in Malawi.

‘Front-loading’ smear microscopy

“Front-loaded” sputum specimen collection – making possible a same-day smear diagnosis of TB – is another procedure likely to be recommended soon. TDR recently completed a large multi-control trial of the approach, tested earlier in a small study conducted by the Liverpool School of Tropical Medicine.

The TDR study, funded by the Bill and Melinda Gates Foundation and the USA’s Agency for International Development (USAID), found that a single-visit, two-specimen approach is as effective as a diagnosis that requires two visits and two or three specimens. The results were presented to WHO in late 2009.

For patients, making multiple visits to a TB clinic for diagnosis is the costliest part of TB treatment, largely due to the travel and lost work time involved (see graphic).
It is thus a huge burden on patients who are poor and a factor in high rates of patient dropout.

“A same-day, patient-centered approach would significantly increase the numbers of people who get treated, particularly among the poor,” says Ramsay.

**Future research needs and aims**

Yet even with more optimized smear microscopy services, as many as half of those with active TB still may never get a smear-positive diagnosis, Ramsay points out.

So the search continues for a “point-of-care” test simple enough to be administered by a lay person. A 2008 TDR-supported evaluation of commercially available rapid diagnostic tests (RDTs) for TB revealed that none performed sufficiently well to do the job.5

However, a combination of antigens identified in a systematic review by TDR and partners in early 2009 show promise, says Ramsay.6 These antigen combinations are being incorporated into an RDT format that will be evaluated with TDR support in 2010.

TDR is also working with the Foundation for Innovative New Diagnostics (FIND) to systematically identify other candidate antigens – using high-tech analysis of most of the nearly 4000 proteins in the *M. tuberculosis* proteome.7

“We are not only dealing with diagnostics that can give incremental gains but also participating in the quest for diagnostics that could revolutionize TB care,” he says.

A TB drug treatment that does not generate adverse interactions with second-line ARV therapies used by HIV patients is another urgent need, Onyebujoh says.

“The current standard TB course is much less effective in HIV-positive patients who are on second-line ARVs because of drug interactions,” says Onyebujoh. “In particular, the TB drug rifampicin interacts.”

Vahedi, meanwhile, is leading a TDR effort on research into new TB biomarkers; the focus of a joint TDR-European Commission expert consultation in 2008.8

“Not only blood samples, but also sputum and other fluids, may contain biomarkers that are easy to collect and can give us valuable information regarding the progress of TB treatment,” she says.

Cost-effectiveness of new interventions is another issue Onyebujoh would like to address more deeply. For instance, there is clearly a cost associated with the raising of CD4 thresholds, adding tens of millions more HIV-positive people to the already long ART treatment waiting lists. However, early initiation of ARVs may also generate savings for health systems – delaying the time when HIV-positive patients need to go on more expensive and difficult-to-tolerate second-line ARV drugs.

“This issue cuts across everything we are doing,” Onyebujoh observes. “If we look at TB-HAART, or use of new biomarkers in studies, or at the replacement of rifampicin with rifabutin for TB patients already on second-line ARVs, we have to be able to say that it is not only safe and effective, but also feasible and cost-effective – particularly for a developing country.”

— Reported and written by Elaine Ruth Fletcher

from Dar es Salaam, photos by Muhidin Issa Michuzi

For more information:

- [www.who.int/tdr/svc/research/quality-assured-diagnostics](http://www.who.int/tdr/svc/research/quality-assured-diagnostics)

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2. [www.theviva.org](http://www.theviva.org)
7. For more information: [www.finddiagnostics.org/media/newsletters/articles/issue13_sstructural_point_of_flow.html](http://www.finddiagnostics.org/media/newsletters/articles/issue13_sstructural_point_of_flow.html)
Nairobi, Kenya – Eradicating malaria is the goal. To get there, research is essential. That was the main message from the 5th Multilateral Initiative on Malaria (MIM) Pan-African Conference. From 1-6 November, some 2000 researchers and policy-makers reviewed the latest in disease control issues and research needs.

“We all know why this meeting is so important,” said Robert Newman, WHO Global Malaria Programme director, in his plenary speech at the 5th Multilateral Initiative on Malaria (MIM) Pan-African Malaria conference in Nairobi.

“In 2008, there were an estimated 232 million malaria cases and 841 000 malaria deaths, with close to 90% of those occurring in sub-Saharan Africa,” he noted, declaring: “We have an unfinished agenda.” Despite the fact that some 80 countries now recommend artemisinin combination therapy (ACT) as frontline treatment for malaria, few malaria patients in sub-Saharan Africa are treated with ACTs. The challenge of increasing access to ACTs, which are the fastest-acting antimalarials available, was a key focus of sessions.

In a symposium co-sponsored by UNICEF and TDR, TDR scientist Franco Pagnoni led with a review of how TDR-supported research on home management of malaria (HMM) is modeling scaled up access to antimalarials. This is also combined with use of rapid diagnostic tests (RDTs) so that drugs are not used unnecessarily.

Then, scientists from Senegal, Ethiopia, Ghana, Uganda, and the WHO Regional Office for Africa presented research testing strategies for integrated community case management of malaria, pneumonia and diarrhoea. Together, these childhood illnesses cause three-quarters of mortality in children under five years of age.

A pre-conference field trip also allowed journalists to witness two related clinical trials in Uganda led by TDR-supported scientists. Makerere University’s George Pariyo is assessing mortality impact, cost-effectiveness, and acceptability of integrated community-based treatment of fevers with antimalarials and antibiotics.

At Iganga-Bugiri, site of an integrated malaria and pneumonia trial managed by Makerere’s James Tibenderana, journalists had a chance to observe epidemiology in action, as researchers tracked malaria cases via household interviews.

**Combating parasite resistance**

Paradoxically, while promoting access to artemisinin combination therapies (ACTs) in Africa was high on the agenda, an equally hot topic was the reports of widening *plasmodium* parasite resistance to artemisinin in Asia.

Recent reports of such resistance along the Thai-Cambodia border region are a sobering reminder that without adequate regulatory structures and surveillance, today’s most effective antimalarial drug could go the way of chloroquine. This would rob malaria control programmes of their most powerful weapon – which, as the Gates Foundation’s Regina Rabinovitch put it, “is a panic-inducing prospect that we simply cannot afford.”
“Strengthened surveillance is one important response,” said TDR scientist Andrew Kitua in a press conference on the resistance issue.

Kitua called for greater surveillance of uncontrolled use of artemisinin, citing recent reports that less than 25% of artemisinins used worldwide are in fact combination therapies (ACTs) – designed to blunt resistance. Counterfeit antimalarials also flood developing country markets.

“We need to have regulations and enforcement of regulations in order to prevent this,” said Kitua. “The community must be educated and the media must play a role.”

**Mosquito resistance to insecticides**

The growing resistance of *Anopheles* mosquitoes to insecticides used in the impregnation of bednets and in other vector control operations looms as another huge threat, meeting participants noted.

Since 2001, the proportion of African households owning an insecticide-treated bednet (ITN) has increased by more than 30% across the continent. Most nets are impregnated with pyrethroids, a class of insecticides with particularly low toxicity. Yet now, mosquito resistance to pyrethroids is a growing problem in parts of the developing world.

“We have too many of our eggs in one basket,” said Newman. “And we don’t have any alternatives in the pipeline for the near term.”

In a pre-conference press tour to a Burkina Faso field study on mosquito resistance, journalists observed scientists documenting insect resistance to two common pyrethroids – permethrin and deltamethrin. The research was subsequently presented at MIM.

The study is being conducted by the Centre National de Recherche et de Formation sur le Paludisme (CNRFP), based in Ouagadougou. CNRFP is part of a TDR-sponsored network studying insecticide resistance in Angola, Benin, Chad and Sudan, as well as Burkina Faso.

Most mosquitoes still remain susceptible to the carbamate, bendiocarb, and to the organophosphate, fenitrothion, network coordinator Hilary Ranson of the Liverpool School of Tropical Medicine, reported to the *Lancet’s* Adele Bleta. Those chemicals, however, have greater toxicity and ecosystem impacts than pyrethroids.

Use of dichlorodiphenyltrichloroethane (DDT) among farmers poses another dilemma for vector control efforts, observed Sodimon Sirima, interim director of CNRFP.

The Stockholm Convention, which came into effect in 2004, outlawed the farm use of DDT, while permitting continued vector control use for public health – until alternatives can be found. However, illicit DDT use in agriculture in the developing world remains widespread, contributing to mosquito resistance.

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1. According to the findings of a new study co-sponsored by the London School of Hygiene and Tropical Medicine and Population Studies International.


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**Genetic modification**

Against these gloomy reports, genetic modification of mosquitoes offers one entirely new tool for vector control. TDR scientist Yeya Touré discussed how genetically modified (GM) *Anopheles gambiaca* mosquitoes may soon begin field trials. The trials would likely involve sterile insect strategies long employed with agricultural pests, but with a GM twist. Currently, a GM-modified mosquito is being tested, in which the GM male would be released to mate in the wild and pass on a fatal genetic defect to offspring (see TDRnews 81, p. 30).

Certain aspects of GM development and deployment lie beyond the scope of existing national or international regulatory schemes. With the support of the Gates Foundation and the USA-based Foundation for the National Institutes of Health (FNHI), TDR is collaborating with scientists in Brazil, Kenya, India and Mexico to develop guidelines on safety and efficacy testing. TDR also recently initiated a network of biosafety centres and courses for developing world scientists (see TDRnews 82 p. 32).

**Strengthening African research**

In comparison to the first MIM conference in 1997, involving only 100 African scientists, the size of the turnout to this year’s event was perhaps one indicator of how scientific capacity on the continent is growing.

The new African Network for Drugs and Diagnostics Innovation (ANDI) aims to bolster capacity in a related arena – R&D that would produce marketable pharmaceutical products. TDR’s Solomon Nwaka, coordinator of ANDI, led a MIM symposium that described ANDI’s plans to increase collaboration among African R&D institutions and to establish a major endowment fund for product development (see ANDI, p. 24).

Meanwhile, TDR’s longstanding contributions to MIM were recognized in awards presented to Director Robert Ridley as well as to TDR/MIM coordinator Olumide Ogundahunsi – for promoting development of young African researchers. Plans to move the MIM secretariat from Tanzania to the University of Yaoundé 1, Cameroon, in January 2011 also were announced. Selected from an open competition, the site’s central African location and bilingual university facility will position MIM at the crossroads of East and West Africa, and strengthen outreach to Francophone African researchers. Professor Rose Leke at the University’s Biotechnology Centre will serve as secretariat chair.

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*Reported and written by Patrick Adams and Jamie Guth from Nairobi*
Business plan endorsed for African innovation network (ANDI)

Some 300 high-level researchers and policy-makers endorsed an ambitious business plan, including a proposal for a US$ 600 million endowment fund, for the new African Network for Drugs and Diagnostics Innovation (ANDI) at the second stakeholders’ meeting in Cape Town.

The ANDI network aims to support and promote research by African institutions for new drugs and diagnostics to address the diseases most affecting Africans. The concept was launched by several African institutions, through TDR, in October 2008 in Abuja, Nigeria.

The turnout at Cape Town, South Africa, reflected the support for the ANDI initiative that has since developed among governments, research institutions, Africans in the diaspora, and international and multilateral agencies, including the African Development Bank and the European Commission.

Currently, there is a “valley of death” between product R&D and the marketplace where most innovation falters, said South Africa’s Minister of Science and Technology, Naledi Pandor, in a keynote address at the 4-7 October event, attended by several health and science ministers.

“That’s where innovation needs the most support, and where it is least likely to get it from the only agents available – venture capitalists or ‘business angels,’” she added. “The establishment of ANDI will help us deal with the crisis in R&D for neglected diseases and develop human capital for sustainable development.”

Following the 2008 meeting, an ANDI Task Force was formed to develop a strategy and the new business plan. The Task Force is led by Ambassador Tom Mboya, of the Permanent Mission of the Republic of Kenya to the United Nations Office in Geneva.

While TDR has provided seed monies, endowment support is now being recruited from multiple donors. Negotiations are being conducted with the African Development Bank to host the fund. The call for funded projects is anticipated in 2010, with a third stakeholders’ meeting planned in October as a formal launch of the network.

The ANDI Task Force estimates a need for an additional US$ 2.4 billion investment in R&D for health products for Africa just to reach the median of global expenditures. Africa bears a disproportionate 25% of the global disease burden; it has only 15% of the world’s population.

A TDR-supported analysis in 2008 of African R&D efforts underlined the fragmented nature of existing initiatives. Most African-based researchers are better linked with Europe and North America than within Africa. ANDI will stimulate more intra-African collaboration, enhancing leadership, ownership and sustainability of African R&D, said Solomon Nwaka, TDR coordinator of the initiative. ANDI also will facilitate networks, IT infrastructure development, and management of intellectual property rights.

“We need African-based solutions with African-based institutions,” said Anthony Mbewu, president of the South African Medical Research Council, which hosted and organized the event with support from TDR and the Government of South Africa. Mbewu, an ANDI Task Force member, also recently became head of the Global Forum for Health Research (TDRbriefly, p. 7).
Global Health Histories seminars frame contemporary research in a long-term perspective

From Patrick Manson, the 19th-century Scottish physician who discovered that a parasitic disease could be carried by insects, to Carlos Chagas, the 20th-century Brazilian researcher who discovered the disease that bears his name, tropical disease research has had a long and distinguished history of bravery and boldness, rigorous science and serendipity. Examining the past in the light of contemporary health issues is the goal of the Global Health Histories series, co-sponsored by WHO, the Wellcome Trust and the Wellcome Centre for the History of Medicine at University College London.

The Wellcome Trust-WHO history collaboration began in 2008 as part of the events surrounding WHO’s 60th anniversary. That series was co-organized by Thomson Prentice, former editor of the World Health Report, whose interest helped ensure its continuity beyond the lifespan of the WHO anniversary year.

Bringing together a diverse group of medical historians, policy-makers and researchers, the 2009 series focused on themes in tropical disease research and control. It was co-organized by TDR along with WHO’s Department of Neglected Tropical Diseases.

The series highlighted how interchange between social scientists and scientists can lead to new ways of looking at disease control challenges – identifying issues from the past with modern-day relevance.

From the Wellcome Centre side, Sanjoy Bhattacharya has been another key driving force in the initiative. “The series is a wonderful way of getting social scientists and scientists involved with policy management,” says Bhattacharya, adding: “it has even brought together people in WHO who might not normally interact!”

Bhattacharya is now hoping that tropical diseases will become the focus of a Wellcome Trust-sponsored series of Witness Seminars, to begin in 2011. In the popular Witness format, experts gather to exchange views on a specific theme; the sessions are recorded and proceedings are printed and then distributed in book form as well as on the Internet.

He and WHO colleagues are now also planning a 2010 series on “emerging issues and trends in global health and disease control.” Plans call for a focus on climate change, environment and health in 2011.

Past meets present across disciplines

Along with seizing a compelling theme, the 2009 series on tropical diseases broadened its appeal through use of new internet technology.

Seminars were broadcast live as “webinars.” This permitted researchers around the world to tune into WHO in Geneva, the ‘nerve centre’ of global health, hear world-class presenters, and then fire questions at them live. The webinars are now being converted to podcasts.

The tropical disease sessions also had a unique format. Each involved two speakers – one an academic historian or social scientist, and the other a scientific expert fluent in current issues of research and control.

Often, the historian chose to speak his or her mind on topical policy themes, while WHO research and policy figures demonstrated their fluency in historical retrospective.

No doubt the inherent drama of the material also helped.

From the practice of research volunteers self-infecting with malaria and yellow fever, to the combing of swamps and deserts to collect insect vectors of disease, the philosophical, ethical and scientific layers of dialogue offered a welcome step-back perspective.
The 2009 seminar series began in March with a focus on leprosy and a historical examination of the political and social forces that drove the elimination campaign. The series then moved onto dracunculiasis (guinea worm), trypanosomiasis (sleeping sickness), onchocerciasis (river blindness), malaria, Chagas disease, leishmaniasis (kala azar) and tropical disease vectors (see p. 27).

Former TDR director Adetokunbo Lucas was one of two guest speakers to close the 2009 series, presenting on the changing role of pharmaceuticals in world health at a 2 December session. Lucas, director from 1976-1986, spoke of the innovative role that TDR played in research on new drugs and diagnostics – a quest so successful that it overtook, in some cases, the quest for vaccines.

“Three major advances occurred in response to WHO/TDR initiatives,” Lucas said. “Global networks of scientists generated new knowledge, with a noticeable impact. New models of collaboration with the pharmaceutical industry demonstrated the value of public-private partnerships for product development, and pharmaco-philanthropy emerged as a new phenomenon.”

History’s value to research today

Despite massive advances in technology, transport, communication and education, the series has highlighted how contemporary scientists face many of the same challenges as their predecessors. Author Aldous Huxley’s comment on history seems to sum it up: “From age to age, nothing changes and yet everything is completely different.”

In particular, lessons learned from history are not always remembered. That was all too evident in a November session on the topic of vector control for tropical diseases, co-presented by Randall Packard, Institute of the History of Medicine, Johns Hopkins University, and Axel Kroeger, a Liverpool School of Tropical Medicine scientist working in TDR.

Packard noted that malaria was widespread in southern England, the southern USA and Italy until agricultural and socioeconomic development virtually eliminated the disease from these regions.

Current malaria control efforts, however, focus mostly on drug treatment, bednets and chemical vector control. A key history lesson – that malaria control and effective vector control succeeded as a result of an integrated package of approaches that also emphasized environmental management and socioeconomic development – needs to be reinforced in modern-day programmes, both Packard and Kroeger emphasized.

Other speakers highlighted the dynamic nature of disease control, even in the so-called “elimination phase.” In his presentation on the history of sleeping sickness, Jean Jannin, coordinator in the Department of Neglected Tropical Diseases, noted that elimination is not a static state. Sleeping sickness was thought to have been virtually eliminated in the 20th century, only to rebound again.

History’s lesson, Jannin observed, is that even when “elimination” is reached, “what-next” scenarios need to be examined, new tools honed and strategies planned to maintain the achievement.

History has also underlined how political stability is an essential ingredient of disease control – time and time again, control campaigns suffered major setbacks after civil war or strife created conditions in which the parasitic vectors of disease could once again thrive.

Such defeats, however, can contain lessons – if they are studied and absorbed, notes Hooman Momen, WHO focal point for the seminar series: “Failure is not bad for research; in many instances more can be learned from failure than from success.”

Yet while failure can teach a great deal, success is better. In his presentation on the campaign against river blindness (onchocerciasis), Janis Lazdins-Helds focused on how the campaign to control and eliminate onchocerciasis achieved many of its goals due to the constant interaction between control officers and researchers who tested and refined strategies for treatment and distribution of the drug, ivermectin, via community-based channels.

Not only that, but Africans led much of the contemporary research and control effort.

“I wonder if the success of the oncho control programme also then had something to do with the African perception of the past,” he later asked.

The ex-colonial era medical officers involved in modern-day onchocerciasis control also were keenly aware of history, adds Jesse Bump of Harvard University, who spoke about the colonial and post-colonial forces that thrust onchocerciasis onto the international stage. “Key programme advocates, including ex-French and British colonial staff who were core advocates to the international agencies in the early days of the global programme, were aware of how previous control efforts had failed and were eager to overcome those barriers.”
End of the ancient dragon? Eradicating guinea worm disease
- Anne Marie Moulin, research director, Centre National de la Recherche Scientifique, France
- Dirk Engels, coordinator of preventive chemotherapy, Department of Control of Neglected Tropical Diseases, WHO, Switzerland

Looking sickness: The controversy continues
- Guillaume Lachenal, lecturer, History and Philosophy of Science, University of Paris Diderot, France
- Jean Jannin, coordinator, Innovative and Intensified Disease Management, Department of Control of Neglected Tropical Diseases, WHO, Switzerland

River blindness: The keys to control
- Jesse Bump, fellow, Harvard University, USA
- Janis Lazdins-Helds, former coordinator of drug development, TDR, Switzerland

Malaria treatment and control: A cultural history of institutions, methods, and metaphors
- Peter Brown, professor of Anthropology and Global Health, Emory University, USA
- Andrea Bosman, scientist, WHO Global Malaria Programme, Geneva, Switzerland

100 years of Chagas Disease: A continuing public health challenge
- Simone Kropf, professor of history, Oswaldo Cruz Foundation, Brazil
- Gabriel Adrián Schmunis, formerly of Communicable Diseases Unit, WHO American Regional Office, USA

Kala azar: Can visceral leishmaniasis ever be controlled?
- Robert Killick-Kendrick, honorary research fellow, Imperial College, UK
- CP Thakur, emeritus professor of medicine and former health minister, India

Tropical disease vectors: Identification and control
"How malaria became a vector-borne disease"
- Randall Packard, chair and William H Welch professor of history of medicine, Institute of the History of Medicine, Johns Hopkins University, USA
- Axel Kroeger, professor of international community health at the Liverpool School of Tropical Medicine, UK, and scientist, TDR, Switzerland

Essential and inessential medicines: The changing role of pharmaceuticals in world health
- Jeremy A Greene, assistant professor, Harvard University, Brigham & Women's Hospital and Harvard Medical School
- Adetokunbo Lucas, former director, TDR, Switzerland, and former professor of international health at the Harvard School of Public Health.

A subjective past
In the early days of tropical disease campaigns, elimination strategies and surveillance expeditions often were shadowed by colonialist goals, laced with a certain sentiment of European cultural superiority, and organized along the lines of military campaigns.

Historical records and archives often reflect the biases of cultural, socio-economic and political forces dominant at the time, Bhattacharya notes.

Even maps, sometimes used as a comparison point for contemporary research, were often created with political agendas in mind. "When carrying out research now, such subjectivity must be re-visited," Bhattacharya points out.

As Simone Kropf, who spoke about Carlos Chagas, observed: "The neglected disease debate can only gain from exploration of how certain health topics have been given varying degrees of political and social relevance over time, depending on national contexts and interests involved."

Learning from each other
Free exchange stimulated by the Histories series has permitted a fresh look at such records, and debate around conventions that evolved.

Guillaume Lachenal, of the University of Paris Diderot who spoke about the politics of international health, commented: "The seminars provoke, allowing us to hear fresh things about global health – which has sometimes the tendency not to question its words and categories."

Added Bump, "I came to provide perspectives in river blindness control. I left with a much deeper appreciation of the science and personalities involved. The dialogue between historians, policy-makers, scientists and practitioners is as valuable as it is rare. The organizers of this wonderful forum are to be commended for their vision."
What was your first experience of malaria?

Prof. Zhou: In the battle to cross the Yangtze River in 1949, I contracted the disease for the first time and suffered recurring bouts. No effective medicine was available. The pain left a sharp impression on me. I received an arsenic injection and, later, Atabrine (quinacrine) pills. The pills made me turn bright yellow. Although the side-effects were serious, I survived.

Is that what spurred you to do research to find anti-malarial drugs?

Prof. Zhou: While I worked as a battlefield doctor, one thing bothered me most: wounded soldiers begging me to save their lives, but sometimes I just could not help them. However, my official participation in the research project stemmed from the Viet Nam War... I witnessed rampant malaria that reduced the combat strength by...
half, sometimes by up to 90% when the soldiers became ill. There was a saying, “We’re not afraid of American imperialists, but we are afraid of malaria,” although in fact the disease took a huge toll on both sides. Later, we submitted a report to China’s Central Military Committee stressing the importance of developing China’s own antimalarials. Taking our advice, the central government set up a panel of more than 500 medical military and civilian experts to develop new antimalarial treatments for stricken soldiers. This was classified as a top-secret state mission named Project 523 after the date, 23 May 1967, when it was established.

What made you and your team think of using artemisinin to treat malaria?

Prof. Zhou: Project 523 included two groups engaged in antimalarial drug development: one to devise chemical medicines, another to examine traditional Chinese medicines. The latter group included researchers as well as traditional Chinese medicine doctors, who as part of Chairman Mao’s barefoot [doctors] scheme scoured the nation to collect folk remedies. Experts screened a list of herbs and folk remedies, a few of which were found to have a curative effect against malaria. In the end, Artemisia annua was chosen for further research.

In the early 1970s, a Project 523 team first isolated artemisinin from the plant. Clinical trials confirmed its antimalarial effects. Between 1976 and 1978, the molecular structure of artemisinin was identified and more artemisinin derivatives were developed. In 1979, artemisinin-based antimalarial drugs were first used in the battlefield in the Sino-Vietnamese War (the Third Indo-China War).

What role did the World Health Organization (WHO) play in the early development of ACT?

Prof. Zhou: In the early 1980s it seemed that antimalarial research was over for good. Fortunately, essays published by Project 523 scientists caught the eye of WHO. In around 1979, TDR expressed interest in cooperation on antimalarial research. But after Project 523 was disbanded in 1981, there was no one to negotiate the issue.

In 1981, TDR held the first international conference in Beijing on artemisinin and its variants. The next year, thanks to WHO/TDR’s efforts, the National Chinese Steering Committee for Development of Qinghaosu [sweet wormwood] and its Derivatives was set up under the Ministry of Health to replace Project 523. The project was saved. Although the cooperation between the National Committee and WHO and TDR was suspended, they continued to provide support.

Why did you introduce ACT outside China?

Prof. Zhou: Today, our discovery, Coartem®, has proven to be highly effective and well tolerated, with high cure rates of over 95%, even in areas of multi-drug resistance. But in an emerging economy like China, nobody has the money to support development of a medicine that has no domestic market and is mostly consumed by poor people outside China. Yet I knew it could cure patients and bring hope and health back to those suffering from malaria. How could I watch such a good medicine die silently in the laboratory and do nothing about it?...I went to the Ministry of Science and Technology, which introduced me to China International Trust and Investment Corporation (CTIC). With the state’s approval and CTIC’s help, we were introduced to Novartis [which co-sponsored the drug’s development].

Looking back, you must be proud of your achievement.

Prof. Zhou: I am proud of what we achieved with our partners. To date, Novartis has provided over 250 million treatments at cost to patients in the developing world, helping to save an estimated 630 000 lives. The credit goes to my country and the thousands of scientists, researchers and barefoot doctors – some of them died before they could see the great things Coartem® could do – together with government officials and our partnership companies and organizations. Coartem® would not have been possible without them.
The world of TropIKA.net

TropIKA.net is a web portal that aims to foster innovation and knowledge application relating to research on infectious diseases of poverty. Recent selections are presented here.

As we mark TropIKA.net’s second year, considerable progress has been made towards our goal of becoming the leading web portal for research on infectious diseases of poverty.

This progress is due in large part to contributions from a growing circle of contributors, web browsers and forum/meeting participants.

We will continue to dedicate ourselves to the task of bringing different research constituencies together to share knowledge and dialogue. We hope that the wide range of new content in all website sections will stimulate further participation in this exciting venture while our expansion continues.

A key element of the TropIKA.net initiative is interactivity. Every item appearing on TropIKA.net includes a “comment” facility for feedback. We welcome comments on the portal as a whole as well as on the issues presented in blogs, commentaries, and meeting forums. Suggestions will be incorporated into our development plans.

Knowledge hubs

TropIKA.net’s “knowledge hub” initiative provides opportunities for participants to contribute more effectively to large health forums. People who are not at the meeting can use the knowledge hub to be virtually present.

Visit the TropIKA.net knowledge hub’s coverage of three major meetings in 2009. The most recent was Forum 2009, the annual meeting of the Global Forum for Health Research, 16-20 November in Havana, Cuba. The 5th Multilateral Initiative on Malaria (MIM) Pan-African Malaria Conference was held 2-6 November in Nairobi, Kenya, and the 2nd Meeting of the African Network for Drugs and Diagnostics Innovation, in Cape Town, South Africa, 4-7 October 2009.

The Forum 2009 meeting, 16-20 November, was attended by some 800 scientists, policy-makers, health care workers, funders and other stakeholders. Its theme was “Innovation for the health of all”. Highlights of the comprehensive TropIKA.net coverage included an interview with the Global Forum’s next executive director, Anthony Mbewu.

Carlos Morel, director of the Center for Technological Development in Health at FIOCRUZ in Brazil, also was interviewed. He said Cuba’s innovations in technology can be exported to other developing countries, with adjustments made for differing levels of infrastructure development.

The diversity of topics discussed in Havana is clear from such TropIKA.net articles as “What will happen to primary care in Cuba when the US embargo comes down?” and “Digital health care in rural India: the costs and benefits of broadband.” Readers can comment on all session reports.

The Multilateral Initiative on Malaria (MIM) conference, 2-6 November, was the largest-ever gathering of malaria researchers, control managers and decision-makers, involving some 2000 participants. During the conference week, the number of visits to TropIKA.net nearly doubled due to the interest generated in the meeting fora.

TropIKA.net interviewed ten MIM delegates on their malaria research endeavours. High-profile delegates interviewed included: Rose Leke, chair of the new MIM secretariat at the University of Yaoundé I Biotechnology Centre in Cameroon, Sanjeev Krishna from St George’s Hospital in London and Pedro Alonso of the Malaria Eradication Research Agenda (malERA).

MIM-related guest blogs included contributions from Roma Chilengi, head of clinical trials at the KEMRI/Wellcome Trust Research Programme in Kilifi, Kenya; Ashley Birkett, director of pre-clinical development at the PATH Malaria Vaccine Initiative; and Kevin Marsh, director of the Wellcome-KEMRI-Oxford Collaborative Research Programme. We welcome invitations to create TropIKA.net Knowledge Hubs at upcoming health fora or scientific conferences.
Reports

Reports by global health agencies and institutions are another important source of information on new health and health research developments. TropIKA.net has so far summarized and commented on 60 such reports. Recent examples include the joint UNICEF/WHO report, Diarrhoea: Why children are still dying and what can be done, and a report from the International Federation of Red Cross and Red Crescent Societies on the damage done by infectious disease epidemics in the South. A report from a workshop held by the UK Academy of Medical Sciences, Global health diagnostics: research, development and regulation, also appeared in our reports section.

News

TropIKA.net aims to provide timely reports on key news in research on infectious diseases of poverty. The more than 400 stories published in TropIKA.net News also relate to news of disease outbreaks; for example, the new epidemic of leishmaniasis in the southern Sudan and West Africa’s largest-ever dengue fever outbreak. Claims from expert groups that the most neglected of all infections of poverty are pneumococcus and Haemophilus influenzae B were also covered in TropIKA.net. Not all of the news is bad; genetic mapping of Schistosoma mansoni has opened new opportunities for research into schistosomiasis. Encouraging new reports suggest the North–South research gap is narrowing.

New initiatives reported have included the African Leaders Malaria Alliance and a new effort to combat neglected tropical diseases in Latin America and the Caribbean. The Centenary anniversary since the discovery of Chagas disease was also featured.

Original articles

These items are especially written for the site. For example, the TropIKA.net team examined recent reports on fake and substandard medicines, describing the huge numbers of these products in circulation as a “neglected epidemic of poverty.” We hope to expand the number of original articles we publish. Contact TropIKA.net if you would like to write for us.

Editor’s choice and blogs

Something new appears on the TropIKA.net blog nearly every day. The blog offers readers an opportunity to comment on TropIKA.net articles and on developments elsewhere. The blog editorial team also alerts readers to interesting items they have spotted on the internet. The blog includes an “Editor’s choice” section highlighting content added to the website and new developments, sometimes controversial. See, for example: A time to honour commitments; Too many organizations, too much talk; All controversy is good controversy … perhaps.

The future

Looking ahead, new initiatives are planned to enrich your visit to TropIKA.net. These include the publication of the TropIKA Reviews – rigorous assessments of the available evidence on key research questions and issues relating to policy and practice on meeting challenges of the infectious diseases of poverty.

From the journals

TropIKA.net has highlighted nearly 400 published medical articles in the form of summaries and commentaries. Some examples of the diversity of articles:

• Barriers to the effective treatment and prevention of malaria in Africa: a systematic review of qualitative studies.
• Prevalence study of yaws in the Democratic Republic of Congo.
• Genomic diversity and evolution of Mycobacterium ulcerans revealed by next-generation sequencing.
• Decreased motivation in the use of insecticide-treated nets in a malaria-endemic area in Burkina Faso.
• Cost of dengue cases in eight countries in the Americas and Asia: a prospective study.
• Mapping the health research landscape in sub-Saharan Africa: a study of trends in biomedical publications.

As well as articles reporting new findings, we have highlighted reviews, discussions and opinion articles, including:

• The global burden of trachoma.
• Malaria and vitamin A deficiency in African children: a vicious circle?
• Access to antimalarial therapy: accurate diagnosis is essential to achieving long term goals.

Profiles

Twenty experts have been profiled since the project’s launch. We chose a diverse range of interviewees from developed and developing countries, including specialists in industry, academia and global health agencies. For example, Professor Brian Greenwood – probably best known for his pioneering work against malaria – spoke about the neglect of two major infectious killers of the poor, meningitis and pneumonia. And Professor Wen Kilama of the African Malaria Network Trust (AMANET) talked of the pressing need for more African scientists on the front lines of research.

Other recent interviews:

• Professor Alan Fairlamb of Dundee University (UK)
• Larry Geiter and Charles Wells of Otsuka Pharmaceuticals
• Michael Gottlieb, head of the Grand Challenges project at the Foundation for the National Institutes of Health (USA)
• Professor Ogobara Doumbo of Mali’s Malaria Research Training Centre
• Professor Christopher Plowe of the University of Maryland (USA)
• Awa-Marie Coll-Seck, executive director of the Roll Back Malaria Partnership
• Jimmy Whitworth, head of international activities at the Wellcome Trust (UK)
• Professor Rose Leke, of Cameroon’s University of Yaoundé.

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Meetings | Quality management • Visceral leishmaniasis

TDR’s Quality Management Advisory Committee (QMAC) recommended that a TDR ‘quality council’ be established and a quality manual be developed to help provide oversight and monitoring of TDR’s quality management activities. The QMAC met 14-15 September in Geneva.

Quality management aims to enhance the quality of TDR-supported scientific research. The concept embodies elements of quality assurance, quality control and quality improvement.

In practical terms, this translates into accountability for the quality of both research processes and deliverables – including issues such as patients’ protection during clinical trials and quality-assurance of data and research findings.

Positioning
A TDR “quality council” would facilitate buy-in and ownership of QM processes, driving continuous improvement and providing direction on strategic quality issues, QMAC members stated.

The proposed council, composed of TDR members, would both reflect and reinforce a broad-based organizational commitment to continuous quality improvement. Such a group could identify actions and specific quality management initiatives to be implemented across the research programme’s activities, as well as monitoring and reporting on quality management-related aspects of performance.

The proposed council should also develop a feedback cycle, using evidence and quality indicators that would be developed. This would assist TDR in identifying opportunities and goals for improvement, QMAC members stated.

Quality manual
The committee also recommended that a TDR quality manual be developed, including a description of programmatic policies, quality objectives and instructions regarding processes and practices.

Such a manual would be useful not only for the quality management team, but across TDR as a whole. It should reflect a broad-based sense of ownership, and be perceived as speaking ‘on behalf of’ research teams to whom it is addressed.

Organizational commitment
Openness, transparency and communications are essential for an effective quality management process, as are effective and timely feedback, the committee members emphasized.

Indeed, quality management is best practiced as a positive feedback loop driven by the achievement of clearly-defined goals.

The need to allocate appropriate resources, autonomy, authority and accountability to the quality management team was also underlined.

It was noted that TDR’s senior management is committed to quality management, including simplicity, consistency with goals and objectives, and emphasis on outputs and outcomes.

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SAC discusses new tools for visceral leishmaniasis elimination

Efforts to eliminate visceral leishmaniasis (VL) on the Indian subcontinent are at a pivotal moment, thanks in large part to TDR-supported development and evaluation of new drugs and diagnostic tools. That was the consensus of the Scientific Advisory Committee (SAC) on Elimination of visceral leishmaniasis (BL 10) at the group’s second meeting 6-8 July in Geneva.

The SAC noted that new tools have made the ground ready for more active case detection efforts supported by the rapid diagnostic test rK39. Clinical trials also are underway of a potential new combination treatment of miltefosine and AmBisome® (liposomal amphotericin B). Quality-assured vector management was also discussed as another important dimension of strategies.

Based on these elements, a comprehensive VL elimination approach can be developed. This can be specifically tailored to highly endemic areas where the majority of VL cases occur, in line with recommendations by national programme managers and principal investigators in the target countries: Bangladesh, India and Nepal.

As these new tools are deployed, research should also monitor their effectiveness in reducing VL caseloads as well as the number of cases of post-kala azar dermal leishmaniasis (PKDL) following treatment.
The presence of asymptomatic VL infections, which remain untreated, would be another important focus, SAC members recommended.

SAC members underlined that VL elimination, and subsequent maintenance of very low levels of parasite transmission, would not be possible without a better understanding of the role of both PKDL and asymptomatic individuals in VL transmission.

With regard to vector control, the SAC recommended that efforts should build on existing capacities and opportunities in country health systems, especially in the field of malaria control and other vector-borne diseases. To guide these efforts, the SAC urged the development of a monitoring and evaluation manual detailing standard operating procedures on key project elements. The document should be developed jointly by research teams and programme managers, and its use should be supported by a training programme.

As recent research shows that impregnated bednets can serve as a strong complimentary intervention to indoor residual spraying (IRS) in endemic areas, the SAC recommended research examine combining IRS with either long-lasting insecticide-treated nets and/or environmental management through lime plastering of walls.

In view of the huge challenges posed by vector-borne diseases in the region, the SAC recommended that a vector biologist should be included on the committee.

Turning its attention to case detection, the SAC reiterated the need for better diagnostic tools, particularly for PKDL. The committee also endorsed formulation of diagnostic criteria for asymptomatic infection and urged support for implementation research using geographic information systems (GIS) data. Finally, the SAC recommended the strengthening of kala azar and PKDL surveillance. Overall, the SAC urged that TDR’s VL research:

- support close coordination among national, district and local programme and health personnel;
- involve the private sector;
- enhance current passive case detection;
- incorporate geographic information;
- establish and utilize standardized case definitions;
- include mechanisms for data analysis and timely feedback to public health and vector control programmes and local health facility personnel.

An analytic framework for ‘community-based’ health interventions (CBI) should be developed

An analytic framework for ‘community-based’ health interventions (CBI) should be developed to see how various strategies, including school-based health programmes and other social marketing approaches, relate to the Community directed interventions (CDI) strategy tested by TDR in onchocerciasis-endemic areas of sub-Saharan Africa.

This was a key recommendation from the Strategic and Scientific Advisory Committee (SAC) meeting of TDR’s Community-based interventions business line (BL 11), 23-25 June, in Geneva.

In a major research milestone, a TDR study published in 2008 demonstrated that poor, rural communities in Africa can dramatically improve access to antimalarial treatments and bednets when given the means to direct the the distribution of an integrated package of health treatments.

The approach, dubbed community-directed interventions (CDI), was tested in communities that already had experience with such annual distribution of ivermectin treatment to combat onchocerciasis.

TDR’s BL 11 has since been spearheading new research on guidance and tools for the scale-up of the CDI approach. While CDI should remain TDR’s main focus, an analytic framework examining the wider range of community-based interventions...
Meetings | Strategic alliances

Deferred pending availability of funds and further development and testing of interventions in African settings.

The SAC also urged BL11 to strengthen collaborations with other TDR research teams whose activities make use of CBI-type approaches or might benefit from using such methods in the future. These include TDR business lines in:
- drug development and evaluation for helminths and other neglected tropical diseases (BL 6);
- evidence for antimalarial policy and access (BL 9);
- research to support the elimination of visceral leishmaniasis (BL 10).

Strategic Alliances Advisory Group recommends moves for strengthening TDR partnerships

A newly formed Strategic Alliances Advisory Group (SAAG) has called for development of a specific framework and communications strategy as initial steps towards enhancing TDR’s partnerships with external bodies.

The multidisciplinary group’s broad range of expertise – spanning medicine, law, government, business, corporate and international relations, innovation, journalism and artistic creativity – is expected to build alliances that will increase the sustainability, effectiveness and growth of TDR-backed initiatives. Key recommendations from an inaugural meeting in Geneva (8-10 June 2009) covered a broad range of topics, including:

**Partnership tools:** Communications is central to building new partnerships. Communication of ‘challenges and impacts’ should be emphasized and TDR outreach to the media should be expanded. Stories collected from people whose lives have been changed by TDR-supported activities will help partners appreciate the value of work undertaken. Documentary film/video production can be an important vehicle, highlighting successes as well as gaps in funding and political decision-making.

**Potential partners:** The SAAG experts highlighted venture philanthropy and the important role that the private sector (including non-pharmaceutical commercial organizations and private academic and research institutions) can play in helping TDR meet its goals both through funding and advocacy. As charities, foundations and individuals can also aid in TDR’s activities, TDR should continually scan the horizon for ways to develop partnerships with these potential sources of support.

**Geographical outreach:** The Middle East, China, Africa, Eastern Europe and the Americas were all seen as areas where TDR should expand interactions. Researchers, academics, non-governmental organizations, federal bodies, United Nations agency heads and ministers of health also were highlighted as groups with which TDR should build stronger links, depending on the region. Assisting countries in communicating research results through symposia and other supportive efforts, and helping to ‘sensitize’ political leaders about science were also seen by the group as valuable activities. SAAG encouraged TDR to take advantage of existing regional and sub-regional initiatives in building these suggested links.

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would help place the range of available strategies and experiences into a more holistic context, the SAC said. That would help guide coherent future research directions.

The SAC recommended that the new analytic framework also include a section devoted to ethical issues relative to public health practices in disease-endemic countries.

Resources on this topic would be drawn from the disease and thematic reference group reports to be published in 2010 (see Stewardship, p. 11). The committee recommended that all future calls for proposals issued by BL 11 call attention to ethical issues in public health research.
Empowerment SAC endorses new moves to address inequities in health research

TDR needs to strengthen ties and share experiences on empowerment of developing country researchers within WHO as well as with outside institutions and agencies.

This was a key recommendation emerging from the Strategic and Scientific Advisory Committee (SAC) of the Empowerment function, at a 2-3 July meeting in Geneva.

As part of this effort, TDR should strive to work more closely with the Council on Health Research for Development (COHRED), the Global Forum on Health Research and other organizations, with which TDR shares common aims and goals.

In terms of practical support for research, training, networks and leverage, SAC also issued the following recommendations to the Empowerment function:

Research: Progress in this area was welcomed, with the committee being particularly encouraged by inter-country research collaborations such as the South Africa-Zimbabwe collaboration to strengthen capacity in entomology. Looking ahead, Empowerment should identify new institutions and health researchers with which to partner. It also should develop a list of potential funders and their areas of interests – so as to help match researchers with potential funding sources. Development of mentorship schemes between established researchers and less experienced colleagues also were encouraged. Workshops and guidance on the writing of grant proposals also were suggested as tools that would help empower researchers.

Training: Decentralization of high-quality courses met with committee approval, although SAC recommended that MSc/PhD and short course programs run for and by disease endemic countries should be examined for excellence, relevance and inclusion of key scientific standards. SAC also encouraged institutional cooperation on training initiatives between developed and developing countries as this can increase training efficiency and benefit candidates from small countries.

Networks: The committee encouraged Empowerment to analyse the nature and extent of TDR’s relationship with the various networks that it has fostered and, in some cases, continues to manage, and to review the characteristics of such networks (in terms of portfolio, best practices, etc.). This will allow Empowerment to find ways that the networks can work together to advance research leadership development.

Leverage: SAC endorsed Empowerment’s new strategic leverage function, which allows TDR to capitalize on its knowledge and expertise to secure resources and commitments for effective, high-quality global research on infectious diseases of poverty. SAC also urged the business line to identify pivotal individuals or institutions that can create conglomerates of leaders with those in other developing countries, and so help reduce inequalities in health research.

Diagnosics SAC recommends expanded advocacy effort

With validated rapid diagnostics tests now available for a number of major tropical diseases, TDR’s diagnostic activities have leveraged impressive results with modest investment, according to the Strategic and Scientific Advisory group (SAC) on Accessible, quality-assured diagnostics (BL 7).

Along with ongoing work to advance testing and evaluation of more rapid diagnostics for a range of diseases, the cross-cutting issues of regulation and advocacy need to be addressed in the coming two years, the SAC stated in a meeting 2-3 September in Geneva.

In terms of regulatory issues, there is a need for more effective regulation of diagnostics at the country level in order to prevent these markets from being dominated by cheap and unreliable products that discourage quality manufacturers. The committee recommended that the Diagnostics BL should explore with key countries options for providing quality standards and improving the regulation of diagnostics tests.

In terms of advocacy, there is a need to raise the profile of TDR’s diagnostics work. The committee recommended that communications (e.g. web portal, advocacy brochures) be enhanced in order to improve awareness of the activity and its impact.

Concretely, the SAC approved a new project to develop a set of “assured” product specifications for new diagnostics in various disease specific areas. The test specifications, endorsed by international and scientific and medical communities, would then be made widely available to test developers via the TDR website and other communications channels. SAC also approved a proposed study of the health impact of bad diagnostics to be undertaken by the London School of Hygiene and Tropical Medicine (LSHTM).

In terms of disease-specific issues, the SAC reviewed the progress of diagnostics research in a range of areas.
Tropical medicine meetings highlight health equity and access

Early treatment of severe malaria in the community with rectal artesunate is most effective when carried out by mother coordinators, according to the results of a new TDR-sponsored study presented at the 58th annual meeting of the American Society of Tropical Medicine and Hygiene (ASTMH) 18–22 November in Washington.

Widely considered the premier forum for advances in tropical medicine and global health, the meeting explored links between global health and the safety, security and economic performance of countries around the world. Sessions were devoted to the relationship between nutrition and infectious disease; new malaria diagnostics and treatments; the spread of pandemic influenza A (H1N1) and infectious diseases’ socioeconomic impacts.

In a special symposium on rectal artesunate, TDR scientist Melba Gomes described the multi-country study of treatment at the community level by: village health workers, traditional healers, mother coordinators and a mix of the three. “The results show that providing early treatment through mother coordinators was more successful than village health workers,” Gomes said.

The symposium examined the challenges of making the drug available in remote communities, addressing the perceptions of patients (or their parents) about the need for hospitalization after receiving a suppository, and the intervention’s cost-effectiveness.

Earlier, TDR scientists also participated in the 6th European Congress on Tropical Medicine and International Health in Verona. With its theme of Equity, human rights and access to care, the meeting 6-10 September addressed topics ranging from ethical challenges in clinical research to gender-based violence in refugee populations.

The meeting culminated in the Verona Declaration – calling for stronger European policies to address social determinants of health, and in particular, risks to migrants and refugees “that directly or indirectly put at risk the life of migrant people and hamper their access to health.” The declaration also asked donors to place the strengthening of health systems at the centre of global health initiatives.

TDR-related presentations at ASTMH

- Pre-referral rectal artesunate in rural African communities: experience in use, Chair, Melba Gomes, TDR & Co-chair Malcolm Molyneux, Liverpool School of Tropical Medicine, UK
- Rapid diagnostic tools in theory and practice; Chair, Jane Cunningham, TDR & Co-chair, Rosanna Peeling, London School of Hygiene and Tropical Medicine, UK
- Getting a rapid TB-diagnosis: What can we do with what’s available? Chair, Luis Cuevas, TDR
- A systematic review of the accuracy of rapid diagnostic tests for malaria in endemic areas; Presenter, Piero Olliaro, TDR
- Parasitological impact of one-year preventive mass chemotherapy on soil-transmitted helminthiasis and schistosomiasis in northern Rwanda; Presenter, Piero Olliaro, TDR

For further information: www.astmh.org/Abstracts_and_Education.htm

TDR-related presentations at the European Congress on Tropical Medicine & International Health

- Home/heat-home treatment: is this the way forward? Moderator, Franco Pagnoni
- Translating research into practice: using systematic reviews in policies, guidelines and influencing change: Chair, Francesca Infectious Diseases Group; Chair, Paul Garner, Liverpool School of Tropical Medicine, UK & Piero Olliaro, TDR
- Antimarial treatments: registration & beyond, Chair, Piero Olliaro, TDR

For further information: www.festmih.org/verona2009/
Print and multimedia publications now available from TDR

**Good laboratory practice training manual: Trainee (2nd edition)**
A tool for training and promoting good laboratory practice (GLP) concepts in disease-endemic countries

268 pp., 2008 (ISBN 978 92 4 154757 4)
DOI 10.2471/TDR.09. 978-924-1547574

This manual provides resource material for good laboratory practice (GLP) training. It is based on the Organisation for Economic Cooperation and Development (OECD) principles of good laboratory practice, which are recognized as the international standard. The manual is designed to be used by trainees at TDR-GLP training workshops. It contains an introduction which highlights the history and fundamental points of OECD principles of GLP.

Now available in hard copy, or for download at: www.who.int/tdr/publications/training-guideline-publications/good-laboratory-practice-manual-trainee

**Handbook: Good laboratory practice (2nd edition)**
Quality practices for regulated non-clinical research and development

328 pp., 2008 (ISBN 978 92 4 154755 0)
DOI 10.2471/TDR.09. 978-924-1547550

Good laboratory practice (GLP) is the recognized rules governing the conduct of non-clinical safety studies. They ensure the quality, integrity and reliability of study data.

This 2nd edition handbook is designed to aid countries upgrading their laboratories to GLP status. Based on the Organization for Economic Cooperation and Development (OECD) principles of GLP, the handbook provides laboratories and trainers in disease-endemic countries with technical information necessary to implement GLP programmes.

Now available in hard copy, or for download at: www.who.int/tdr/svc/publications/training-guideline-publications/good-laboratory-practice-handbook

**Good laboratory practice training manual: Trainer (2nd edition)**
A tool for training and promoting good laboratory practice (GLP) concepts in disease-endemic countries

268 pp., 2008 (ISBN 978 92 4 154756 7)
DOI 10.2471/TDR.09. 978-924-1547567

This manual is aimed at trainers of good laboratory practice (GLP) and is a companion manual to the GLP trainee manual. Distribution of hard copies, complete with CD-ROM, is strictly limited to those who have undertaken the TDR-GLP training of trainers workshop or who are already GLP experts.

Now available in hard copy, or for download at: www.who.int/tdr/svc/publications/training-guideline-publications/good-laboratory-practice-manual-trainer

**Operational research in support of anti-retroviral therapy scale-up: Lessons learned workshop and product development team meeting**

44 pp., 2009 (ISBN 978 92 4 159876 7)
DOI: 10.2471/TDR.09.978-924-1598767

Scale-up of ART treatment is a major goal of African health services. However, fears of social stigmatization, as well as other factors, may inhibit access to available testing, treatment and follow-up counseling. This report summarizes the studies and findings of operational research projects undertaken in Uganda, Malawi, Burkina Faso, Zambia and the United Republic of Tanzania to support anti-retroviral therapy (ART) scale-up. It reviews lessons learned and reflects on how to take operational research forward in the area of ART scale-up, and more generally.

Available for download at: www.who.int/tdr/svc/publications/tdr-research-publications/op-research-hiv
In cooperation with others

Pathways to better diagnostics for tuberculosis: a blueprint for development

125 pp., 2009 (ISBN 978 92 4 159881 1)

This publication offers a structure to guide researchers through the different phases of tuberculosis (TB) diagnostic development – from the discovery of new techniques and tools to their delivery in neglected markets. Described here are TB diagnostic approaches and tools available today, and in the pipeline. The publication can help TB diagnostics researchers work more effectively with health services as well as academics and industry professionals.

Available for download at: www.who.int/tdr/svc/publications/tdr-research-publications/tb-blueprint

Available through others

Global health risks, mortality and burden of diseases attributable to selected major risks

125 pp., 2009 (ISBN 978 92 4 156387 1)

A response to the need for comprehensive, consistent and comparable information on health risks at global and regional level. Global health risks provides detailed global and regional estimates of premature mortality, disability and loss of health attributable to 24 global risk factors, ranging from environmental factors such as unsafe water and sanitation to behavioural factors such as smoking and sedentary lifestyles. Many diseases and injuries are caused by more than one risk factor. For example, the infectious agent, Mycobacterium tuberculosis, is the direct cause of tuberculosis. However, crowded housing and poor nutrition also increase the risk. In turn, most risk factors are associated with more than one disease, and targeting those factors can reduce multiple causes of disease. For example, reducing smoking will result in fewer deaths and less disease from lung cancer, heart disease, stroke, chronic respiratory disease and other conditions. By quantifying the impact of risk factors on diseases, evidence-based choices can be made about the most effective interventions to improve global health.

Available for order or download at: www.who.int/healthinfo/global_burden_disease/global_health_risks/en/

Dengue: guidelines for diagnosis, treatment, prevention and control

160 pp., 2009 (ISBN 978 92 4 154787 1)

Since the second edition of Dengue haemorrhagic fever: diagnosis, treatment, prevention and control was published by the World Health Organization in 1997, the magnitude of the dengue problem has increased dramatically and has extended geographically to many previously unaffected areas.

This new edition represents a concise source of information of worldwide relevance on dengue for health practitioners, laboratory personnel, vector control officers and other public health officials. The guidelines provide updated information on clinical management, vector management, diagnostic tests, surveillance, emergency preparedness and response. New and promising avenues of research and guidance on specialist areas related to dengue also are discussed.

Available for order (CHF 48.–/24.– for developing countries) or download at: www.who.int/neglected_diseases/en/

Treatment Action Group 2009 pipeline report

70 pp., 2009 (ISBN 978 0 9819863 2 6)

Treatment Action Group (TAG) is an independent research and policy think tank focusing on antiretroviral treatments, HIV basic science and immunology, vaccines and prevention technologies, hepatitis and tuberculosis.

This year’s TAG pipeline report shows, in brief, a lull in anti-HIV drug development, an alarming stasis in hepatitis B treatment research, renewed activity (after a gap of almost 40 years) in TB drug development, agonizingly slow and incremental progress in TB diagnostics research, very preliminary human studies of several new TB vaccine candidates, a back-to-basics mood in the HIV vaccine research community, renewed hopes for efficacy in microbicide and pre-exposure prophylaxis, and no dramatic developments in immune-based therapies or therapeutic vaccines for HIV.

Download or order hard copies from: www.treatmentactiongroup.org/publication.aspx?id=3212
TDR in the scientific press

TDR-supported research leads to the publication of hundreds of articles in the peer-reviewed press every year. In 2008, 212 articles were published with TDR support. Of those, 149 were by first authors from disease-endemic countries. A complete listing is posted on the TDR web site at the end of each year (see the 2008 list at: www.who.int/tdr/svc/publications/peer-reviewed-articles).

During the year, peer-reviewed publications in each TDR area of work also are posted on the TDR web site as they are identified. Examples of recent 2009 publications are noted below with links to more recent peer-reviewed publications by area of work. If you are a TDR-supported researcher who has published an article in a peer-reviewed journal and we do not know about it yet, you are welcome to send a link or PDF of the article to: tdr@who.int.

Drug discovery


For other drug discovery articles, see: www.who.int/tdr/svc/research/lead-discovery-drugs/publications-resources

Innovative vector control


For other vector control articles, see: www.who.int/tdr/svc/research/vector-control-interventions/publications-resources

Antimalarial policy


For other articles on antimalarial policy, see: www.who.int/tdr/svc/research/antimalarial-policy-access/publications-resources#_Peer-reviewed_articles

Diagnos tics


For other diagnostics articles, see: www.who.int/tdr/svc/research/quality-assured-diagnostics/publications-resources

Drug development for helminths and neglected tropical diseases


For other drug development articles, see: www.who.int/tdr/svc/research/drug-development-helminths-ntds/publications-resources#_Peer-reviewed_articles

Visceral leishmaniasis (VL) elimination


For other articles on VL research, see: www.who.int/tdr/svc/research/visceral-leishmaniasis-elimination/publications-resources

Community-based interventions (CBI)


For other articles on CBI, see: www.who.int/tdr/svc/research/community-based-interventions/publications-resources
Celebrate the discovery, combat the disease

“Carlos Chagas’ 1909 discovery was a unique achievement in biomedical science and showed that this brilliant scientist was more than a ‘microbe hunter’. The description of Trypanosoma cruzi, its life cycle, vectors, domestic and sylvatic reservoirs and corresponding human disease, was both remarkable scientifically and in terms of its relevance to human health and well being. However, decades were required for international recognition of the profound impacts of Chagas disease in Latin America – and beyond. Today, a hundred years later, approximately 12-14 million people remain infected in 18 Latin American countries and an unknown number throughout the world. This silent ‘neglected disease’ progressively ruins lives. On the centennial of Chagas’ discovery, we call for a renewed effort to sustain and expand policies for continuous transmission control. We call for research into new and more effective means of preventing and eliminating Chagas as well as better treatments for already-infected individuals, who lack adequate therapies and diagnosis.”

– Joseli Lannes-Vieira, Maria de Nazaré Correia Soeiro, Tania C. de Araujo-Jorge, Paulo Gadelha, and Rodrigo Corrêa-Oliveira - Coordinators of the Fiocruz Program for Research and Technological Development on Chagas Disease (PIDC) and organizers of the International Symposium on the Centennial of the Discovery of Chagas Disease, 8-9 July 2009, Oswaldo Cruz Foundation (Fiocruz), Rio de Janeiro, Brazil.

For more on the FiOCRUZ Centennial, see: www.fiocruz.br/chagas100

TDR grant awards in 2009

In 2009 TDR awarded 104 grants to promote the vision of fostering research on infectious disease of poverty in which disease-endemic countries play a leading role.

Empowerment grants include grants to developing-country scientists and institutions for leadership training, programme and career development and skills-building, as well as grants for post-graduate and research training.

Research grants include grants to institutions and individuals in developed and developing countries on TDR priorities. These also may involve collaborations with governments, industry and networks for clinical trials and drug R&D.

The 104 grant awards approved by TDR scientific committees in 2009 were disbursed to recipients in 45 countries across all WHO regions – with Africa and the Americas being the most heavily represented, followed by South-East Asia, the Western Pacific, the Eastern Mediterranean and European regions.

The awards ranged from small field studies to high-tech collaborations on drug discovery.

Grant awards are only one component of TDR’s work. Areas of funding are determined on the basis of TDR stewardship and priority-setting exercises. Research projects are accompanied by TDR coordination, monitoring & evaluation, as well as communications. For details on TDR’s 2009 grant awards, see: www.who.int/tdr/svc/grants/grants-awarded

For information on calls for grant applications please see: www.who.int/tdr/svc/grants