## Blaming malaria rise on climate change is simplistic

WHO/TDR/S. Lindsay

Waste and run-off water can provide good breeding sites during the dry season for the mosquitos which transmit malaria.

The resurgence of *Plasmodium falciparum* malaria in four East African highland areas has *not* been caused by long-term climate change, according to an international team of researchers led by Oxford University epidemiologist Simon Hay (*Nature* 2002;415:905-9).

"The finding has important implications on the ground," says Hay. "If climate change is not responsible for the increase in malaria in these areas, government and public health officials should be focusing on the other possible causes, such as deteriorating public health systems and drug resistance."

For years, climate scientists have speculated that global warming, caused by the build-up of insulating "greenhouse gases" in the lower atmosphere, will trigger changes in the occurrence of various diseases worldwide, including vector-borne maladies such as malaria and dengue. Mathematical models suggest that shifts in temperature, rainfall and humidity will not only lengthen transmission seasons in some areas where malaria is endemic, but allow the *P. falciparum* parasite, and the *Anopheles* mosquitoes that carry it, to survive at higher altitudes and latitudes.

Hay and his colleagues set out to see if such global warming-related effects were already occurring in the East African highlands. There has been a surge in malaria cases in these areas since the 1970s. And the 2001 report on the Intergovernmental Panel on Climate Change (IPCC) noted a 0.7 °C warming over most of the African continent during the past century.

To see if the two phenomena were related, Hay's team analysed meteorological data from 1901 to 1995 for four highland sites where malaria cases are on the rise — Kericho in western Kenya, Kabale in south-western Uganda, Gikonko in southern Rwanda, and Muhanga in northern Burundi. For each month, the researchers determined the average temperature, as well as the average minimum and maximum temperature, rainfall and vapour pressure. They also noted months when average temperature was greater than 15 °C and rainfall exceeded 152mm — meteorological conditions suitable for *P. falciparum* transmission if they continued for two consecutive months.

After analysing the 95-years' worth of data, the team found no significant shifts in temperature or vapour pressure at any of the four sites. Rainfall had increased at only one, Muhanga. And Kabale was the only area in which the malaria season had got longer. None of these areas had had significant climate changes after 1970, when malaria was on the rise.

The findings came as a surprise. "We were expecting to find some evidence of significant trends," says Hay. "Our guess is that future climate changes may have an impact on malaria and other diseases, but the evidence just isn't there yet."

In addition to finding no evidence of long-term change, the researchers found that reconciling short-term climate fluctuations of the last century with malaria epidemics was also problematic. For example, they say that although in Kericho there is evidence of some slight warming and increased rainfall from 1971 to 1995, and it does coincide with the recent resurgence of malaria, historical data from the site show a series of very severe malaria epidemics in the 1940s — a decade that was significantly cooler and drier than average. Similar inconsistencies in attributing recent epidemiological changes to climate show up for the highlands of Uganda, the United Republic of Tanzania and Madagascar, the scientists say.

If the climate has not changed at the four study sites, other factors must have been responsible for the increases in malaria, the researchers say. Those conclusions are in line with other reports which also indicate that the IPCC's claimed 0.7 °C warming of Africa cannot be blamed for the continent's resurgence of malaria, says Pierre Guillet, a vector control expert at WHO. So what are the real causes? Possibilities include: resistance to chloroquine and other drugs; population growth rates that outpace health services; changes in land use; and short-term wobbles in weather such as those resulting from El Niño and La Niña events in the Pacific, as a paper in the *Journal of the American Mosquito Control Association* argued in 1998 (14:121-30).

However, the recent findings shed no light on the future. "Since [it] reports no evidence of climate trends at the sites studied," says epidemiologist Tony McMichael who co-edited the chapter on the health aspects of climate change in IPCC's 2001 report, "the study says nothing about the potential impact of any future climate change on malaria transmission."

Just how dramatically global warming will influence malaria will continue to be hotly debated. According to the IPCC, there are scenarios for the year

2080 which show malaria moving into some areas but out of others, so the net number of people living in malarial regions remains fairly stable. Other scenarios, however, are much more dire, with malarial zones vastly expanded, putting 260–320 million more people at risk. ■

Charlene Crabb, *Paris*

## China sets up Centres for Disease Control and Prevention

The public health system in China — which, according to Wang Huanzeng, director-general of the Ministry of Health personnel department is "outdated" — is to have a major facelift. Its new Beijing headquarters will be modelled closely on the US Centers for Disease Control in Atlanta, whose director, Jeffrey Koplan, is to be the first Senior Advisor to the new "China CDC".

Kurt Tong of the US Embassy in Beijing, who has been closely involved in providing advice to China, said he thought this could be the beginning of a rapid transformation of the old Academy of Health in Beijing. "There's a feeling here that the public health services could use some improvement" Tong told the *Bulletin*. To spearhead the change, the Academy is being expanded and converted from an academic research centre "where everyone was called 'professor'" into an institution more directly focused on public health, Tong said.

"There's been a lot of interest in China in how the US Centers for Disease Control operates, and at the same time the US CDC has shown itself very willing to help. So we'll be exchanging information on institutional organization and funding mechanisms, and even on physical architecture" Tong said.

While reporting to the Ministry of Health, China CDC will provide scientific evidence to underpin health policy, recommend prevention and control measures, and monitor and evaluate interventions. It will have twelve divisions covering an enormous range of issues and responsibilities, including infectious diseases, environmental health, rural water supply, nuclear safety, cancer, and maternal and child health. It will also affiliate 17 other existing professional health institutes in China.

*China Daily* reported health ministry director-general Wang Huanzeng as saying "China's disease-prevention system has not kept up with the development of various diseases and public health problems brought by industrialization, urbanization and the ageing of the population," and that the new CDC would help to tackle that problem.

A new campus for the organization is being built on the northern outskirts of Beijing, to house what are expected to be its rapidly growing staff and research facilities. ■

Robert Walgate, *Bulletin*

## Court orders South Africa to treat pregnant HIV-positive women with nevirapine

The South African government has received a court order to make the antiretroviral drug, nevirapine, available to all pregnant, HIV-positive women giving birth with public sector support. The government can, however, appeal against this order.

Nevirapine (and zidovudine) were included in the WHO Model List of Essential Drugs in 1999, for the prevention of mother-to-child transmission of HIV. Clinical trials have shown that short-course antiretroviral regimens using nevirapine alone, zidovudine alone, or a combination of zidovudine and lamivudine, substantially decrease the risk of HIV transmission to the child.

The order from the Pretoria High Court was the result of legal action launched by the Treatment Action Campaign (TAC), an AIDS activist organization. TAC's aim was to force the government to extend its prevention of mother-to-child HIV transmission (PMTCT) programme from its current 18 pilot sites.

TAC's two claims — that doctors in public service have the right to prescribe nevirapine to all their patients, and that the government has a duty to provide nevirapine to all public health facilities where the medicine is needed and can be properly used — were both upheld by the court last December.

The government is appealing against the decision on the grounds that the use of nevirapine is a policy matter and should be decided on by government, not the courts. In addition, the government argues that it needs more time to research the effectiveness of its PMTCT pilots, and that some of its health institutions lack the capacity to roll out the programme.

The court case has been a public relations nightmare for the South African government. Even its former liberation allies — most notably powerful religious organizations and the Congress of South African Trade Unions — took to the streets in support of TAC's court action. There is also widespread dissatisfaction within the ruling African National Congress (ANC) with government's AIDS policies.

Former president Nelson Mandela, a national executive committee member of the ANC, has been outspoken in his support for nevirapine to be made available to all pregnant HIV-positive women.

"If the government says 'Don't make any move until we have completed our research', young people and babies are going to die in scores every day," Mandela said shortly after the government had been granted leave to appeal. "The government must allow people, while it conducts its research, to go anywhere they want (to get nevirapine). If we do that, we will remove the perception that we don't care about our people who are dying."

A few days earlier Mandela had commented: "We can't afford to be conducting debates while people are dying. We have to ensure that our people are given the drugs which are going to help them. This is a war." He called for anti-retroviral drugs to be made available free for all AIDS sufferers, not just pregnant mothers, in public health facilities.

As this report went to press, the government had still not delivered nevirapine to all its clinics and hospitals. However, the country's top HIV/AIDS official, Dr Nono Simelela, said that it was time to "move away from pilots and go to scale" with initiatives to fight the disease. ■

Kerry Cullinan, *Durban*

Note: Experience in the field suggests that an oral tablet of nevirapine for the mother can be taken at home at the onset of labour. However, it is essential that the child should be brought to a health facility within 72 hours of birth for an oral dose of nevirapine in suspension.

## Could antibiotics cure river blindness?

WHO/TDR/Ward

An old man, blinded by onchocerciasis (river blindness).

River blindness, affecting 200 million people in rural Africa and to blame for hundreds of thousands of cases of preventable blindness, may be caused by a bacterium. If so, it could in principle be controlled by antibiotics — according to a recent paper in *Science* (2002;295: 1892-5).

This is something of a shock, because the textbook explanation of the disease is infection by filarial worms, *Onchocerca volvulus*, cured by annual treatment with ivermectin, a drug which kills the young microfilariae the adult worms produce in the body. But it's not the worms themselves, but the bacteria they carry, that cause the blindness in the disease, according to a team of researchers from the US, Germany and the UK.

*Onchocerca* worms are transmitted by blackflies which breed in fast-flowing rivers. After a person is bitten by an infected fly, the worms grow into adults, forming a nodule the size of a grape under the skin. There they live for over ten years, breeding and creating streams of young "microfilariae" or "little threads", which spread through the body, entering and irritating the patient's skin, where they are ready to be picked up by another blackfly to complete the cycle.

Blindness follows when the microfilariae migrate to the eyes. There, accumulating and dying over many years, they lead to the transparent cornea of the eye turning milky, eventually becoming opaque and causing complete blindness. But precisely how they made the cornea milky was not known — until now. It seems that a bacterium in the worm, *Wolbachia*, does most of the damage, rather than the worm itself.

Last year a team of scientists in Germany discovered that *Wolbachia* bacteria were an essential to the worms: without them the worms cannot produce microfilariae. *Wolbachia* also turned out to be essential for the filarial worms that cause lymphatic filariasis, *Brugia malayi* and *Wucheria bancrofti*.

Then the question arose: how important are the bacteria to blindness? To answer it, the German group, at the Hamburg School of Tropical Medicine, sent extracts of adult worms (which patients are pleased to get rid of, if a surgeon is available to cut off the nodules) to Eric Pearlman at Case Western Reserve University at Cleveland in the United States. In fact they sent two samples: one including the *Wolbachia* naturally present in the worms, and one without — after treatment with doxycycline, an antibiotic.

In Pearlman's laboratory, the extracts were injected into the corneas of mice, a model for river blindness. The corneas were affected by both extracts, but much more so when the *Wolbachia* were present. The researchers also showed how the corneas of certain mice, with a precise mutation that makes them insensitive to bacterial endotoxin, were not affected by either extract. So it seems that the endotoxin of the bacterium *Wolbachia* is causing more of the blindness of onchocerciasis than the worm *Onchocerca volvulus*.

So far, good science; but what about the impact on patients? The trouble is that a course of antibiotics would require a six-week, daily treatment. "Unfortunately it's completely impractical, unless the antibiotic regimens can be simplified" said Hans Remme of the Tropical Disease Research Programme at WHO. It has been a massive exercise to get single doses of ivermectin annually to the remote communities that need it, and six-week courses of anything would be far more difficult, he says.

"Even so, if antibiotics were the perfect intervention we would try to develop an appropriate distribution method" Remme says. "But there are risks of adverse reactions, and important exclusion criteria such as children below eight years old, and pregnant and lactating women. These prevent large-scale use and elimination of the parasite reservoir after the six weeks of intervention", says Remme.

One of the authors of the mouse paper, Mark Taylor of the Liverpool School of Tropical Medicine, argues, however, that "those ivermectin treatments will have to go on for more than 20 years, because the adult worms stay alive. Antibiotics could reduce this period by permanently sterilizing the adult worms, and at the same time remove the cause of the blindness. And we are planning trials to find the minimum period of antibiotic therapy, and to find out what effect antibiotics have on the other filariases."

Remme doesn't completely rule out antibiotics either. "We are thinking about using them to snuff out localized outbreaks, in areas that have previously been cleared", he adds. ■

Robert Walgate, *Bulletin*

## UN to help developing countries assess safety of GM crops

Agrochemical multinationals hail them as a panacea for everything from world hunger to pesticide pollution. Environmental organizations dismiss them as "Frankenfoods" which poison consumers and destroy the world's ecosystems. The Nairobi-based United Nations Environment Programme (UNEP) is attempting to help developing countries weigh up the pros and cons for themselves. The argument is about genetically modified (GM) crops.

In mid-January, UNEP kicked off a three-year project that will support up to 100 developing countries to prepare for the entry into force of the UN Cartagena Protocol on Biosafety (see Box 1). It will also help these countries put into practice the principles of risk assessment for GM foods announced in March by a task force of the Codex Alimentarius, a world reference body for food safety (see Box 2).

The environment "is different everywhere, and that's why GM crops have to be tested locally" says Sakiko Fukuda-Parr, the lead author of last year's Human Development Report, issued annually by the United Nations Development Programme (UNDP), which advocated a cautious application of biotechnology as a means to reduce world poverty. "But for local testing you need an increase in public sector investment in poverty-oriented agricul-

tural research. Unfortunately this has remained stagnant or even declined in recent years, especially in Africa," she adds.

The US$ 38 million UNEP project, financed mostly by the Global Environment Facility (GEF), should help. It is a joint venture between the UN and the World Bank which "aims at helping countries develop legal structures as well as administrative and scientific skills so that, at the end of the day, they can arrive at an informed, sovereign decision" on GM crops, says Charles Gbedemah, the project's regional coordinator for the African region.

Another goal, adds project manager Christopher Briggs, "is to establish regional and subregional networks that will share information such as data on risk assessments of GM crops" through a series of workshops and consultation meetings.

Advocates of biotechnology and development agencies tend to focus on the enormous potential of GM crops, especially for resource-poor farmers in the developing world, such as a reduced reliance on chemical pesticides. What's more, says Jorgen Schlundt, the coordinator of WHO's Food Safety Programme, by engineering staple crops to have increased nutritional value in, say, minerals or vitamins — such as Golden Rice producing vitamin A — GM crops "might even have a direct [positive] impact on human health."

While Briggs admits to the great potential of GM crops he is quick to point out that the UNEP project is far from being an endorsement of GM crop technology. "There are both potential benefits and potential risks, and it's important to look at both of them. If you think that I'd be either positive or negative about GM crops, then I'd be failing my job," he told the *Bulletin*.

Many development experts welcome the UNEP effort as something that is badly needed. Says UNDP's Fukuda-Parr: "For all new technologies, but especially for biotechnology, the risk aspects are extremely important. That's what makes the UNEP project a real priority."

Others, however, are less enthusiastic. "If the project leaves the agenda to the countries and offers expertise countries ask for it's OK. But if it is pushing someone else's agenda, then, of course, it's not," says Suman Sahai, the president of Gene Campaign, a New Delhi-based advocacy group.

And for Calestous Juma of the Science, Technology and Innovation Program at Harvard University, the project is bound to raise expectations that cannot be fulfilled. "Promoting the scheme as a capacity-building project creates the impression that it is going to help developing countries establish institutional capacities, scientific expertise and human resources. For this, the amount of money — US$ 400 000 per country — is utterly negligible because you need long-term professional training and not just a few workshops here and there," Juma says.

UNEP's Briggs concedes that the project is only a first step but thinks it should nonetheless enable all participating countries to draw up a draft biosafety framework "that could be developed into law in these countries pretty rapidly."

Meanwhile, the acreage of GM crops is increasing rapidly, especially in countries such as China, Argentina, Indonesia and South Africa. Last year, the global area of GM crops for the first time exceeded 50 million hectares (130 million acres), a whopping 19% increase compared to the previous year, according to estimates by the International Service for the Acquisition of Agri-biotech Applications.

More than a quarter of the global GM crop area was already grown in developing countries, and from the 5.5 million farmers who planted GM crops in 2001, more than three-quarters were in developing countries.

But not all developing countries are ready to move full steam ahead into the supposedly golden age of biotechnology. Brazil, an agricultural heavyweight and the world's second-ranking soy grower and exporter (after the US), still bans all GM crops. Thailand is planning to impose an import ban on 37 more GM crop varieties in addition to the 40 already prohibited.

India, another country relying heavily on agriculture to feed its growing population, is slowly warming to the idea of GM crops. After more than a year's experiments with GM cotton, the government will soon allow it to be grown commercially.

China, on the other hand, has relatively few inhibitions, and now accounts for half of the developing world's expenditure on plant biotechnology, according to a survey in *Science* in January. The biggest seller in China is the so-called Bt cotton, carrying a gene for a toxin that makes the plant resistant to insect pests. Around 2 million Chinese cotton farmers already grow Bt cotton on roughly 20% of the country's cotton fields. This yields several benefits, the *Science* survey shows: production costs have dropped by 28%, and the use of toxic pesticides by 80%. As a result, pesticide poisonings among farmers have declined more than fourfold.

And this is just the beginning, says Juma. "Most of what's grown in Argentina and China is similar to crops grown in North America. The next generation of GM crops will likely be crops specifically developed for tropical conditions. And those will be the most interesting ones for developing countries."

Given, however, that these varieties have been largely ignored by laboratories in industrialized countries, Juma calls for a stronger investment in research capacities in developing countries. "If you're concerned about the welfare of these countries you should create a balance between funding research facilities and funding biosafety frameworks" he says. "Only funding safety issues without funding the necessary research doesn't seem to make sense. If you ask people in the Sahara to regulate the use of water you'd better give them some," says Juma.

**Box 1. The Cartagena Protocol on Biosafety**

Adopted in January 2000 the Cartagena Protocol on Biosafety is the first international, legally binding environmental treaty. The Protocol seeks to protect biological diversity from the potential risks from genetically modified organisms (GMO) by regulating all transboundary movements of GMOs. The Protocol also establishes a so-called advance informed agreement procedure, which requires GMO-exporting countries to provide all pertinent information about the GMOs in question so that the importing countries can make an informed decision as to whether to accept the shipment or not. As one of its key elements the Protocol is to set up a biosafety clearing house, an Internet database containing all necessary information about any given GMO such as movements and transports of GMOs, release documents and risk assessments. So far more than 100 countries have signed the Protocol but only 11 have ratified it. As soon as 50 countries have ratified it, the Cartagena Protocol will enter into force worldwide.

MH

### Box 2. UN agrees principles for GM food risk analysis

After two years of deliberations, a UN task force on GM foods reached its final conclusions this March: a set of principles proposing that such foods be subjected to extensive pre-market safety assessments, combined with methods to overcome uncertainties in risk assessment, for example by monitoring potential effects after a product has been marketed.

Investigations should identify new or altered hazards relevant to human health, especially in relation to key nutrients and potential allergies, said the Intergovernmental Task Force on Foods Derived from Biotechnology in early March in Yokohama, Japan.

This Task Force of the FAO/WHO Codex Alimentarius Commission — a world reference body for food safety — says that their principles should be seen as providing an overall framework for evaluating the safety and nutritional aspects of GM foods in any country.

The principles also provide guidance on analytical methods and other tools to be used in risk management. FAO and WHO say that the task force "reached a very important new agreement concerning the tracing of GM products for the purpose of facilitating withdrawal from the market when a risk to human health has been identified."

The task force also adopted detailed requirements for assessing the safety of GM plants, including tests for allergenicity, and recommended that efforts be made to improve the capability of regulatory authorities — particularly in developing countries — to assess and manage GM foods. This is where the UNEP biosafety project will be helpful (see feature).

RW

Fukuda-Parr likewise calls for a balanced view: "Biotechnology is a promising avenue for global poverty reduction. To throw out a tremendously promising technology is doing the world a disservice. At the same time ignoring its dangers is equally irresponsible," she says.

WHO's Schlundt agrees. He thinks one great goal is to increase the nutritional value of crops to alleviate micronutrient malnutrition. "I think this is going to be the big thing in the future," he says.

A case in point is the Golden Rice that had been developed by scientists in Switzerland and Germany to combat the Vitamin A deficiency that afflicts more than 25 countries in Asia, Africa and Latin America. This rice is offered to farmers in developing countries free of charge, unlike other GM products, which are mostly unaffordable for the poor because of patent fees. Neither the Cartagena Protocol nor the UNEP biosafety project tackle the problem of patenting.

At the moment the transgenic rice plants are cross-bred with local varieties in Viet Nam and the Philippines, to transfer the new genetic traits to the desired strain of plants; other countries like China and India will start soon, says Ingo Potrykus, one of the co-inventors of the Golden Rice from the Swiss Federal Institute of Technology in Zurich. "The interest from developing countries was enormous. We even had to turn down some requests from countries like Pakistan, Bangladesh, Myanmar or North Korea, because these countries did not have legal or administrative structures in place to handle GM crops. That's where the UNEP project fits in nicely."

With all these prospects coming into view, Fukuda-Parr thinks it is a pity that "much of the public discussion has been hijacked by extremist views. We need a much more objective debate." To get the discussion on GM crops out of its ideological gridlock, Schlundt advocates a "more holistic view of biotechnology" that would take into consideration potential benefits, environmental and health concerns but also socioeconomic and ethical factors. To that end, he says, "WHO has just initiated a one-year project to review all the data on GM crops that is out there." If everything goes as planned a report should be issued by the end of the year. ■

Michael Hagmann, *Zurich*

## Global Fund: the gap to fill

The new Global Fund to Fight AIDS, TB and Malaria has a lot of money to spend, and should announce its first grants this month (see our interview with the interim director last month). But in 2002 even these large sums are only 11% of the practical needs of established intervention programmes against the three diseases. The graphic below takes into account the fact that those practical needs could also grow rapidly, by 20% a year. For example, more and more people may be placed on antiretroviral therapy, all requiring drug supplies indefinitely. Assuming as a hypothesis that the Fund will never meet more than 11% of those practical needs, the white bars show the corresponding growing spending requirement from the Fund. The coloured bars show the present major donor commitments to the Fund. The gap is what has to be filled by new donations, and they are expected to follow only if the first funded programmes are well-managed. The figure is derived from the opening statements by the Director-General of WHO and the Executive Director of UNAIDS to the first Board Meeting of the Global Fund on 27 January 2002.

More detailed estimates of the practical needs of AIDS programmes can be found in *Science*, Vol. 292, Issue 5526, 2434-6, June 29, 2001. ■

Robert Walgate, *Bulletin*

**Current Global Fund to Fight AIDS, Tuberculosis and Malaria pledges by year 2002–06**