

SARS outbreak over, but concerns for lab safety remain

The recent outbreak of Severe Acute Respiratory Syndrome (SARS) in China which infected nine people and killed one of them is now over said WHO on 19 May. The outbreak, which began in April at a laboratory in Beijing, has raised questions about storing and handling the killer virus in laboratories.

The recent outbreak was the third of four SARS outbreaks associated with a laboratory since 5 July 2003 — when the virus was declared to be under control following a major epidemic which left nearly 800 people dead.

The outbreak in April began after two graduate students working at a laboratory at the National Institute of Virology in Beijing, where experiments using the live SARS coronavirus were conducted in February and March, became infected with the virus. WHO experts are helping the Chinese authorities investigate the source or sources of infection.

Dr Angela Merianos, the SARS focal person at WHO's Global Alert and Response unit, noted that the virus can be transmitted by droplets, through contact with contaminated objects as well as by touching the eyes, mouth or nose with contaminated hands but said it

was still unclear how the lethal virus had escaped at the Chinese institute. WHO is working closely with China's Ministry of Health and provincial health authorities to ensure biosafety procedures at the Institute of Virology are correct. Chinese health authorities are reviewing biosafety standards in other facilities undertaking research on the SARS virus.

"The investigation conducted to date has yet to identify a single source of infection or single procedural error at the institute. Consequently the route or routes of transmission are not known at this time," said Merianos, who visited China in May. It also remained unclear how two researchers at the institute became infected since they were not even working with the SARS virus. All those who became infected in the latest outbreak were people working at the institute and people who came into contact with them.

One of the nine SARS patients, a 53-year-old physician in China's Anhui province died on 19 April after being infected by her daughter, a 26-year-old postgraduate medical student who had been doing research at the Beijing institute. Her daughter and the seven other patients were treated in isolation at Ditan Hospital in Beijing. At the time of writing, seven patients have recovered whilst one remains in critical condition.

"The big question is: is it safe to handle SARS?" said Dr Cathy Roth from the Dangerous and New Pathogens team at WHO's Global Alert and Response unit, adding: "Countries need to identify all the laboratories holding the virus and to ensure that all correct biosecurity measures in those labs are in place." Roth said it was impossible to know how many laboratories across the world were storing SARS virus stocks.

She noted that WHO had issued recommendations in April, October and December last year on handling and storing SARS specimens and cultures in laboratories. Since the latest outbreak WHO has called on the Chinese Government to ensure that all research work on the live SARS virus should be conducted at least to standards that correspond to WHO biosafety level 3 guidelines to achieve maximum containment. Dr Merianos, who recently visited the Institute for Virology in Beijing, could not say whether laboratories here or in other Chinese research facilities adhered to biosafety level 3. "There is evidence that work practices in the lower level labs have room for improvement," Dr Merianos said, referring to the Beijing institute.

The third highest of four risk groups which are set out in the second edition of the WHO Laboratory biosafety manual related to handling infectious agents that pose a high risk to individuals, but a low risk to the population in general.

The Beijing institute was closed on 23 April to allow most of its staff to be quarantined for medical observation, while a handful of staff stayed on to continue essential experiments and care for laboratory animals. ■

Fiona Fleck, *Geneva*



Reuters/China Photos

Supplies arrive for staff under quarantine at the National Institute of Virology in Beijing, China, 30 April 2004. A laboratory at the institute is thought to be the source of the recent SARS outbreak.

Cardiovascular disease — a global health time bomb

Cardiovascular diseases such as heart disease, stroke and diabetes — usually associated with wealthy, developed countries — have become far more prevalent in poorer, less developed countries than previously thought, according to a new report published by Columbia University's Earth Institute in New York on 26 April.

The report, *A Race against Time: The Challenge of Cardiovascular Disease in Developing Economies*, concluded that cardiovascular diseases could become a public health time bomb in developing countries if too little is done to reverse the trend.

Dr Shanthi Mendis, Coordinator of WHO's Cardiovascular Diseases unit described the report as "a compelling and cogent argument to convince policy-makers and politicians of the need for commitment, development and implementation of policies for prevention and control of the cardiovascular diseases epidemic."

The researchers, led by Australian epidemiologist Stephen Leeder, analysed mortality and disease data from four middle-income countries: Brazil, China, South Africa and the Russian Republic of Tatarstan, and one low-income country, India.

They found that even if nothing changes in the next 30 years, population growth alone will lead to major increases in cardiovascular disease in developing countries which could severely curb workforce productivity and economic progress. According to the report, the problem is often neglected by developed countries, whose chief health-care priority is infectious diseases such as AIDS, malaria and tuberculosis.

Cardiovascular mortality rates among people of working age in India, South Africa and Brazil were one-and-a-half to two times higher than those in the US, said the report. In South Africa, despite the predominance of AIDS, 12% of men aged between 35 and 44 died from cardiovascular disease while the figure for women was 17.2%. In India, 28% of the five million people who die of cardiovascular diseases every year are under 65. The authors said this was even higher than the equivalent figure for the US 50 years ago, before treatment for cardiovascular diseases became a public health priority.

Recommendations included a reduction in tobacco production and consumption, campaigns aimed at improving nutrition, including school programmes on healthy diet and physical exercise. These recommendations are also part of a global plan to prevent chronic disease through healthy diet and physical exercise to be adopted by WHO's 192 Member States during the Fifty-seventh World Health Assembly in Geneva, 17–22 May.

Professor Shah Ebrahim, a cardiovascular diseases expert at Bristol University in England, said the projections were reasonable and should be enough to make policy makers take notice. He also said that cardiovascular diseases were also often neglected because of a lack of data and training.

The report is available at: http://www.earth.columbia.edu/news/2004/images/raceagainsttime_FINAL_051104.pdf ■

Fiona Fleck, *Geneva*

Brazilian genomics breakthrough offers hope for leptospirosis control

A team of Brazilian researchers has sequenced the genome of a bacterium which causes leptospirosis, a disease which infects over 100 000 people and causes 1000 deaths worldwide every year. The breakthrough has been hailed as a first step towards creating a vaccine against one of the world's most widespread zoonoses (diseases affecting both humans and animals).

"The research is important since ... it will open new opportunities for developing quicker and more precise diagnostic tests and vaccines for preventing leptospirosis," said Dr Carlos Morel from the Oswaldo Cruz Foundation, a biomedical research centre linked to Brazil's Ministry of Health.

The researchers, whose findings were published in the *Brazilian Journal of Medical and Biological Research* (2004;37:459-77), analysed the 4.6-million-base-pair genome of the strain of bacteria mainly responsible for the disease in Brazil, *Leptospira interrogans* serovar *Copenhageni*. The results of their research have pointed to the identification of candidate proteins for this purpose. Although leptospirosis can be treated with antibiotics, when left untreated it can lead to kidney damage, liver failure and, in extreme cases, death.

"We have already isolated 23 proteins ... that we consider potentially important for the development of a vaccine against leptospirosis," said Ana Lucia Tabet Oller do Nascimento, a researcher from Butantan Institute in São Paulo and lead author of the study. The 23 proteins were selected because of their ability to induce the production of antibodies in humans, explained Nascimento. "However, we

need now to test if such antibodies are in fact protective against the disease," she added. The researchers are now analysing another 200 proteins.

Despite the success of their research, Nascimento estimated it would take around ten years to develop a vaccine or any other product offering protection against the disease.

"Nothing is done in the short term when we are talking about developing a vaccine, which includes several steps between the sequencing and the final product. To believe that genomics can shorten such a period of time is to believe in magic or miracles," said Morel who views genomics research as a potentially powerful tool for controlling developing country diseases.

Leptospirosis occurs worldwide in urban and rural areas and in both tropical and temperate regions, mostly in developing countries. It is contracted by humans through direct contact with the urine of infected animals or by contact with a urine-contaminated environment. The disease has been found in both wild and domestic animals including rodents, insectivores, dogs, cattle, pigs and horses. It is therefore an occupational hazard for those who work outdoors or with animals and a recreational hazard for those who swim or wade in contaminated waters.

The number of human cases worldwide is not well-documented. According to WHO, it probably ranges from 0.1 to 1 per 100 000 per year in temperate climates to 10 or more per 100 000 per year in the humid tropics. During outbreaks and in high-risk groups, 100 or more per 100 000 may be infected. In Brazil 4128 cases were recorded in 2000, according to the National Foundation of Health.

The science of genomics — the branch of genetics that studies organisms in terms of their full DNA sequences (or genomes) — has been accelerating in recent years with very positive implications for combating diseases afflicting developing countries, says the report *Genomics and world health*, published by WHO in 2002. However, according to the report, 80% of DNA patents in genomics between 1980 and 1993 are held in the US. Of the 1233 new drugs marketed between 1975 and 1999, only 13 were approved specifically for tropical diseases.

"In this regard, steps need to be taken to avoid the creation of a 'genomics divide,' to ensure that the benefits of the

genomics revolution also accrue to developing countries and that ethical, legal and social implications are taken into account," said Dr Tikki Pang, Director of WHO's Research Policy and Cooperation department.

A resolution on genomics and world health adopted during the Fifty-seventh World Health Assembly, 17–22 May 2004, called upon WHO Member States to facilitate greater collaboration among the private sector, the scientific community, civil society, and other relevant stakeholders, particularly within the United Nations, in order to mobilize "more resources for genomics research targeted at the health needs of developing countries." ■

Luisa Massarani, *Rio de Janeiro*

Rwandan genocide survivors in need of HIV treatment

Thousands of women who were sexually assaulted and infected with HIV during the 1994 genocide in Rwanda do not have access to treatment, said the Survivors' Fund (SURF), a UK-based non-profit organization which launched a campaign on 20 April calling for the provision of affordable antiretroviral treatment for women infected with HIV during the conflict which claimed at least 800 000 lives.

"These women were left impoverished after their husbands, fathers and brothers were murdered," said Mary Kayetisi Bluitt, Director of SURF, a non-profit group based in London, aiming to address the needs of women and children who survived the Rwandan massacre. "They are still suffering from trauma and have few resources, and only a handful can afford the anti-retroviral drugs that could improve and prolong their lives," said Bluitt, who lost 50 members of her family during the massacres.

"It [the genocide] is still claiming victims who contracted HIV as a result of sexual violence," said Colette Delhot, Regional Adviser for Gender and Women's Health at WHO's Regional Office for Africa in Brazzaville, Congo. No one knows precisely how many women became infected during the assault, which was marked by a rash of gang rapes.

Only one organization, the Rwandan Association of Genocide Widows (AVEGA-AGAHOZO), based in the

Remera area of Kigala, has published survey results. The non-profit group, which consists of 25 000 widows, estimates two-thirds of its members are now HIV-positive as a result of being raped during the 1994 conflict. "There is little doubt the numbers are actually higher, however, because many women hesitate to come forward. They ask themselves, 'Why should I get tested and find out I carry the disease? I can't get treatment anyway,'" said Bluitt. The group also estimates that of five million women living in Rwanda, half are widows who lost their families during the 1994 conflict.

According to non-profit groups like the Rwandan Association of Genocide Widows (AVEGA-AGAHOZO) and SURE, international groups and charities working in Rwanda have failed to devote sufficient attention to the genocide widows.

Delhot agrees that the Rwandan women deserve special treatment. "These women lost everything because of the genocide and are struggling to survive. We have to fight to get them access to basic health care. It is a human rights and war reparations issue, not just a health issue," she said.

The UK's Department for International Development announced in mid-April a donation of GBP 200 000 towards the cost of providing antiretroviral treatment for witnesses of the genocide suffering from AIDS.

The International Criminal Tribunal for Rwanda, currently under way in Arusha, United Republic of Tanzania, is prosecuting some five dozen cases against the alleged ringleaders of the slaughter, which targeted the country's minority Tutsis and politically moderate Hutus. The 100 day-long assault, executed by Hutu extremists in April 2004, followed the death of Rwanda's Hutu President Juvenal Habyarimana after his aeroplane was hit by a missile. ■

Judith Mandelbaum-Schmid, *Zurich*

New international convention allows use of DDT for malaria control

Malaria-endemic countries can continue using dichlorodiphenyltrichloroethane (DDT) to help control malaria due to an exemption clause in a convention banning the controversial substance. The Stockholm Convention on Persis-

tent Organic Pollutants which came into force on 17 May, following its ratification by 50 states, outlawed the use of 12 industrial chemicals — dubbed the "Dirty Dozen," — including DDT.

The exemption clause allows malaria-endemic nations to use DDT strictly for indoor residual wall spraying (IRS): a measure which contributed to slashing the number of malaria cases in South Africa from 64 622 in 2000 to 8016 last year.

"Malaria is now at its lowest level in ten years," said Rajendra Maharaj, a specialist scientist working with South Africa's national malaria control programme. "We attribute that to DDT."

Under pressure from environmentalists, South Africa suspended DDT for IRS in 1996 after five decades of use and switched to another class of insecticide known as pyrethroids. But the 1999–2000 malaria epidemic in KwaZulu-Natal and neighbouring provinces prompted the government to revert to DDT for prevention and to introduce artemisinin-based combination therapy for treatment.

Other African nations, such as Eritrea, Ethiopia and Swaziland have continually used DDT for IRS in certain areas. China and India — the main supplier of the insecticide — are two other countries currently using DDT focally. Some other countries in eastern and southern Africa are considering the introduction of DDT as part of their malaria control operations in epidemic-prone areas. The United Nations Environment Programme estimates that about 25 countries will use DDT under exemptions from the DDT pesticide ban.

Recognizing the role of DDT in disease vector control, WHO helped lobby for the exemption provisions during negotiations on the content of the Stockholm convention in 2000. Allan Schapira of WHO's Roll Back Malaria department said that IRS is often more rapidly effective in controlling epidemics than insecticide-treated bed nets. However, "insecticide-treated bednets remain the recommended method in settings of intense, ongoing transmission where it is at least as effective and usually much more acceptable by the populations," said Schapira.

Junaid M. Seedat, Managing Director of the international non-profit organization, Massive Effort Campaign, which campaigns to raise awareness of developing country diseases, said WHO

should be more active in promoting DDT for IRS rather than relying on insecticide-treated bed nets alone as a preventative tool.

However, Dr Kabir Cham, Senior Adviser with WHO's Malaria Policy and Strategy Team, said that insecticide-treated bed nets and IRS each have their specific roles in malaria control. "DDT is one of 12 insecticides approved by WHO for IRS, and like all of them it has certain advantages and disadvantages, which should be analysed in the local context to make the best choice," said Cham.

In 1935 DDT was discovered to be a highly effective insecticide which led to its widespread use as a general pesticide in agriculture. Its use for disease control began during the Second World War and became the main product used in global efforts, supported by WHO, to eradicate malaria in the 1950s and 1960s. According to WHO's booklet, "Frequently asked questions on DDT use for disease vector control," this campaign resulted in a significant reduction in malaria transmission in many parts of the world and was probably instrumental in eradicating the disease from Europe and North America.

However, following widespread concern over the environmental and health risks posed by the chemical's persistence in the environment long after its initial application, DDT was banned in the US in 1972 and later in other countries. According to WHO, although there is no direct link between DDT and any negative human health effect, there is growing evidence that it may disrupt reproductive and endocrine function.

The WHO booklet "Frequently Asked questions on DDT use for disease vector control," is available at: <http://mosquito.who.int/docs/FAQonDDT.pdf> ■

Clare Kapp, *Johannesburg*

In brief

Young motherhood biggest killer of girls in developing world

Pregnancy and childbirth are the leading causes of death among girls and young women aged 15 to 19 in the developing world, according to a new

report released by the US-based non-profit organization, Save the Children.

The *State of the World's Mothers 2004*, released on 4 May, argues that providing girls with better educational opportunities and access to improved health care is key to preventing pregnancy in teenage women.

"For too many young girls around the world, motherhood is a disabling tragedy, or worse yet, a death sentence," said Mary Beth Powers, the group's reproductive health adviser.

Around 70 000 teenagers die annually because of complications from pregnancy and childbirth, according to Powers. The girls who do survive often struggle to overcome poor health, education and poverty, she added.

The prospects for the children of these young mothers are little better. According to the report, the offspring of teenaged mothers are 50% more likely to die than those born to older women. An estimated 1 million infants born to teenaged mothers die before their first birthday.

The report is available at: http://www.savethechildren.org/mothers/report_2004/index.asp ■

"Kill or Cure?": BBC broadcasts series on developing-country diseases

"Malaria" was the first subject of a new BBC television documentary series about the diseases which take a heavy toll on populations in developing countries but have been traditionally neglected by the pharmaceutical industry because of lack of profit potential. The first programme in the series was aired worldwide on 14 May on BBC World — a network with an audience reach of approximately 250 million viewers.

The programme on "Malaria" is to be followed by "Kalar Azar" (leishmaniasis) from 21 May, "Lymphatic Filariasis," from 28 May, "TB" (tuberculosis) from 4 June, "Hep B," from 11 June, "Diarhoea" from 18 June, "Bilharzia" from 25 June and "Polio" from 2 July.

"For too long these diseases have been ignored," says Professor David Molyneux of the Liverpool School of Tropical Hygiene. "The BBC is to be praised for running a series that vividly portrays the reality of life for tens of millions of people around the world."

Malaria — time to ACT

Lack of funding, political will and long lead times were cited as some of the major barriers to the implementation of artemisinin combination therapy (ACT) for malaria treatment during an international conference, held at Columbia University, US, 29–30 April.

The International Symposium on Malaria, cosponsored by WHO, UNICEF, Médecins Sans Frontières and Columbia University's Mailman School of Public Health, brought together technical experts, policy-makers, economists, service providers, pharmaceutical and diagnostics manufacturers, and donors to find ways to overcome remaining barriers to the implementation of ACT for effective malaria treatment.

"Urgent solutions need to be found to support changes in national protocols in endemic countries, to fund effective treatment and to ramp up the production of ACTs," said meeting organizers in a joint statement.

The call to action follows the increasing resistance exhibited by malarial parasites to conventional antimalarial drugs. Despite evidence which suggests that drugs derived from *Artemisia* plants hold enormous potential for combating the global malaria epidemic, progress in getting these new drugs to patients has been slow. (See related article, "WHO refutes malaria malpractice allegations": *Bulletin* 2004;82:237.) ■

India bans smoking

India, home to 250 million smokers, has banned smoking in public places as well as the advertising of all tobacco products and the sale of tobacco to minors.

Like Ireland's recent ban, its Indian counterpart, instituted on 1 May, applies to enclosed areas such as restaurants, offices, airports and buses. India, the world's second largest tobacco consumer after China, accounted for one-fifth of the 4 million deaths resulting from tobacco-related illnesses in 2000. ■