News

Gates Foundation picks 14 grand challenges for global disease research

The Bill and Melinda Gates Foundation announced the first 14 targets of a US$ 200 million programme on global disease research, on 17 October. The "Grand Challenges in Global Health" initiative, launched by Bill Gates at the World Economic Forum in Davos, Switzerland, in January 2003, is intended to encourage innovations in science and technology in order to remove some of the obstacles to more rapid progress against the burden of disease carried by the developing world.

The mostly biomedical list was created with advice from 1048 scientists in 75 countries and following the deliberations of a 20-member, 13-country Scientific Board. Ten of the 14 challenges concern infectious diseases, including six — nearly half the total — relating to vaccines.

"Our goal was twofold," said Richard Klausner, Executive Director of the Global Health Program of the Gates Foundation. "Firstly, to use the whole concept of grand challenges to force ourselves to articulate the world's health problems and to stimulate excitement to work on problems that will have an impact on the world's poor. Secondly, to solve those problems and fund those solutions."

He also explained that "grand challenges are not the same as grand problems. We need to distinguish between the two. AIDS is a problem but it is not a grand challenge. Finding an AIDS vaccine is not even a grand challenge. But solving the bottleneck that prevents the creation of an AIDS vaccination *is* a grand challenge. It's about finding critical pathways through the problems. Many proposed problems did not make it onto the Grand Challenges list because they could not be turned into critical pathways."

Board member, Professor Roy Anderson, an epidemiologist at Imperial College, London, welcomed the focus on vaccines. "The lack of vaccines is the stumbling block for most major international health problems. And the paucity of our immunological understanding is really quite gross in some areas, especially for the antigenically varying organisms."

The list also includes two substantial health assessment issues: to "develop technologies that permit quantitative assessment of population health status" and to "develop technologies that allow assessment of individuals for multiple conditions or pathogens at point-of-care."

One of the key problems for governments is to know what their populations are suffering from, so that they can rank diseases for intervention, said Anderson. "Only a quarter of the world has effective disease surveillance and recording systems. In China, India, Indonesia and much of sub-Saharan Africa we have very limited knowledge of what's going on. We must try to improve that information base."

However, some experts believe health systems research should have had higher priority among the Grand Challenges. Dr André de Francisco, a Geneva-based public health specialist, said that "health systems research is fundamental … we need it to complement any useful tools that may arise."

According to Anderson, however, health research has already been addressed in the other areas of the Gates Foundation's activities. For example Gates' malaria, TB, filariasis and schistosomiasis programmes "are much more oriented towards implementation — in other words — how to deliver to poor regions of the world what we already know how to do well," he said.

Francisco also raised concerns that only two of the Grand Challenges relate to chronic ailments. "Infectious diseases are a major part of the public health burden but there's a lot to understand about cardiovascular disease, mental disorders, and cancer, some of which can be detected early and prevented. As countries are developing, these are increasing, including obesity," he said.

However, in an article in *Science* (2003;302:398-9) members of the Board said that "the Scientific Board recognizes and discussed at length the problems increasingly posed by chronic noncommunicable disorders and the importance of underlying living conditions, particularly access to clean water and adequate food, in large parts

The 14 Grand Challenges in Global Health:

Improve childhood vaccines:

1. Create effective single-dose vaccines that can be used soon after birth.
2. Prepare vaccines that do not require refrigeration.
3. Develop needle-free delivery systems for vaccines.

Create new vaccines:

4. Devise reliable tests in model systems to evaluate live attenuated vaccines.
5. Solve how to design antigens for effective, protective immunity.
6. Learn which immunological responses provide protective immunity.

Control insects that transmit agents of disease:

7. Develop a genetic strategy to deplete or incapacitate a disease-transmitting insect population.
8. Develop a chemical strategy to deplete or incapacitate a disease-transmitting insect population.

Improve nutrition to promote health:

9. Create a full range of optimal, bioavailable nutrients in a single staple plant species.

Improve drug treatment of infectious diseases:

10. Discover drugs and delivery systems that minimize the likelihood of drug resistant micro-organisms.

Cure latent and chronic infections:

11. Create therapies that can cure latent infections.
12. Create immunological methods that can cure chronic infections.

Measure disease and health status accurately and economically in developing countries:

13. Develop technologies that permit quantitative assessment of population health status.
14. Develop technologies that allow assessment of individuals for multiple conditions or pathogens at point-of-care.

of the developing world. The board intends to pursue these issues by convening workshops on such topics and considering additional grand challenges in subsequent years."

The US$ 200 million fund will be managed and administrated by the Foundation for the National Institutes of Health (FNIH). Final decisions on which proposals are selected for grants will be made by the independent Scientific Board operating according to its own separate peer review and scientific process.

The Gates Foundation has just raised its original donation to US$ 250 million. This extra US$ 50 million will not be given to the Foundation for the National Institutes of Health but will directly fund or partly fund proposals selected from those already approved by the Board. "This is to act as a model for other potential funders who can chose to fund specific projects directly rather than donate money to FNIH," explained Klausner.

Requests for proposals for research costing up to US$ 20 million over five years have been issued globally, and individual researchers, research institutions, networks of institutions — and even whole countries — can apply. Potential researchers must first submit a letter of intent, the deadline for which is 9 January 2004. The first awards are expected in October 2004. ■

Robert Walgate, *London*

UN calls for international debate on road safety crisis

A UN General Assembly resolution adopted on 5 November has called for a debate among governments, UN agencies, WHO and the World Bank, on the global road safety crisis. A plenary meeting of the 191-member Assembly devoted solely to road safety, planned for April 2004, will coincide with World Health Day and the launch of the first ever World Report on Road Traffic Injury Prevention.

The meeting next April is intended to increase awareness at a high level of the magnitude of the road traffic injury problem. The UN's involvement in the problem in such a major way began earlier in the year with the first ever General Assembly resolution on road safety. Adopted in May and sponsored by 56 countries, it called for a report on the crisis by the UN Secretary-General, Kofi Annan.

Annan's report, presented in August, drew attention to the seriousness of the problem which sees over 1.2 million deaths annually resulting from road traffic crashes — the vast majority of which occur in low- and middle-income countries — and called for urgent action. "To date, road safety has received insufficient attention at the international and national levels," Annan told the Assembly. "This has resulted in part from a lack of information on the magnitude of the problem and its preventability, a fatalistic approach to road crashes and a lack of political responsibility."

Annan's message and the involvement of the UN in road safety has received strong international support. The European Union, addressing a plenary meeting of the 58th General Assembly on 22 October, said that it "believes that saving human lives through an effective road safety policy is a difficult challenge but also a moral obligation for all member states." In the European Union alone, more than 50 000 people are killed each year and more than 150 000 are disabled for life.

WHO/P.Virot

A cyclist takes his life into his own hands on this busy road in Ghana. In low- and middle-income countries, which account for 90% of global mortality resulting from road traffic injuries, most victims are cyclists and pedestrians.

In response to the UN Secretary-General's report, the latest resolution calls for a plenary meeting of the Assembly on 14 April and also invites governments, the President of the General Assembly, the UN Secretary-General, the Director-General of WHO, the President of the World Bank, the Executive Director of the UN Children's Fund and the Administrator of the UN Development Programme to address the Assembly on the issue. The only other health topics to have been discussed in the General Assembly plenary are HIV/AIDS and malaria.

"The plenary discussion called for in this latest General Assembly resolution will be a historical event," said Dr Etienne Krug, Director of WHO's Department of Injuries and Violence. "It offers a unique opportunity to create the political will needed to address this major public health crisis at a global level."

The discussion has been planned in connection both with World Health Day on 7 April 2004, whose theme is road safety, and with the release of the World Report on Road Traffic Injury Prevention. The report, a joint project of WHO and the World Bank, is expected to be launched in Paris on World Health Day. It aims to raise awareness about the health and societal impact of a problem which costs developing countries US$ 100 billion a year — twice the annual amount of development assistance received by those countries. The report will present comprehensive documentation of what is known about the magnitude and determinants of road traffic injuries and offer evidence-based solutions to address the problem.

The resolution also asks the UN to make recommendations for traffic safety and requests Annan to submit a second report in time for the 2005 General Assembly session. In addition, it calls for the UN Department of Public Information to organize a meeting of experts, the private sector, relevant nongovernmental organizations and other interested parties on 15 April 2004 to raise awareness and exchange information.

WHO predicts that road traffic injuries will join the top 3 causes of worldwide mortality and disability, ahead of tuberculosis, HIV/AIDS and malaria. Whilst it is a global problem affecting all sectors of society, 90% of global mortality resulting from road traffic injuries is carried by low- and middle-income countries.

"Most high-income countries have seen dramatic reductions in road traffic fatality rates whilst most low-and middle-income countries have witnessed the opposite," said Krug. According to WHO, the US has seen the numbers of deaths due to road traffic crashes fall from 26 per 100 000 in 1996 to 15 per 100 000 in 2000. In Finland, the number of fatalities has been halved in the last 30 years despite a tripling in the volume of road traffic. This has been mainly due to effective government road safety policies.

The story in the developing world is very different. India, for example, has witnessed a mortality rate of 30 per 100 000 in the early 1970s rocket to more than 50. "This is a typical trend in most developing countries," said Krug. He also said that in developing countries it is often cyclists and pedestrians who are dying, whereas in developed countries most victims are in the car.

A new World Health Assembly resolution on road safety is also likely to be adopted in 2004. This will replace the previous resolution adopted in 1974. Currently under preparation by experts at WHO, it is expected to support Annan's call for a "systems approach" in order to identify all the risk factors that contribute to road crashes before trying to reduce their consequences. Pending approval by WHO's Executive Board in January, the final version is expected to be presented in May 2004. ■

Sarah Jane Marshall, *Bulletin*

Conference warns of danger of re-emergence of smallpox as weapon of bioterror

Epidemiologists and biological warfare defence experts joined forces at a Geneva conference in October to warn governments that smallpox, a killer disease that was eradicated globally two decades ago, could re-surface as a weapon of terrorism.

When smallpox was eradicated worldwide in 1979 it was hailed as the greatest public health achievement of the 20th century. But since the 11 September attacks, there have been growing fears that rogue states or terrorists may have procured illegal smallpox stocks to launch a major bioterror attack.

Experts told the conference that the chances of such an attack were very small, but warned that it should not be underestimated because an outbreak could be even more devastating than 20 years ago due to reduced immunity in the population.

"It's a new type of terrorism, when you're in a state of anxiety every day. It's not spectacular, there is no explosion but every day for weeks you hear about people who died," said leading biosecurity expert, Ken Alibek, who once headed the former Soviet Union's secret bio-weapons programme and defected to the US in 1992. "This creates wide-spread panic, people stop going out and the whole society and economy collapses."

Since 11 September, the United States has stepped up its biodefence programme, aiming to vaccinate half a million military personnel and 38 000 civilian health workers against smallpox. Other governments, in countries such as Britain, Belgium, France and Germany, have carried out more limited "ring" or selective vaccinations of key personnel for smallpox.

Washington has established emergency networks for rapid response to such an attack and is promoting research in the quest for safe vaccine with fewer side effects as well as new vaccines that can be used for people with weakened immune systems. Meanwhile, it has boosted vaccine stockpiles and is promoting modern therapeutic treatment for smallpox, a disease which was last reported in Somalia in 1977.

Speakers said, if used as a biological weapon by terrorists, smallpox had the greatest potential to cause widespread damage, followed by plague, anthrax and finally botulism. The four bioagents were ranked according to their infectiousness, potential to kill and ability to survive storage in aerosol or other containers for long periods of time.

"The attack on the World Trade Centre took a huge toll with thousands of deaths, but the economic damage as a result of anthrax could be as much or greater and it only involved 3, 4 or 5 grams of anthrax," Alibek said, adding: "That's the reality and we have to understand this because the terrorist groups understand this perfectly well."

Scientists told the conference however that it would be wrong to rely solely on vaccines to protect populations today because sophisticated terrorists could commission scientists to genetically engineer new, even more virulent, virus strains capable of shutting down the whole immune system. Such new strains would render vaccines useless.

Mark Buller, Professor of Microbiology and Immunology from St Louis University in the United States, described experiments in which scientists had genetically altered the mousepox virus, ectromelia, to express a protein IL4. When infected with this new mousepox strain, mice vaccinated for the original mousepox virus had no protection.

"There are cook books on the internet on how to do this, the equipment is in most labs and expertise is minimal, a PhD scientist with knowledge of pox viruses could do it," Professor Buller told the conference entitled: Smallpox Bio-Security: Thinking the Unthinkable which was held in Geneva on 21 and 22 October. ■

Fiona Fleck, *Geneva*

Islamic states renew commitment to eradicate polio

The Organization of the Islamic Conference (OIC) adopted a new resolution on 20 October 2003 urging Member States which are still polio-endemic to accelerate their efforts to drive out the disease. The resolution has come at a critical time for the Global Polio Eradication Initiative. Six of the world's seven remaining countries that are still polio-endemic are OIC Member States — Afghanistan, Egypt, Niger, Nigeria, Pakistan, and Somalia.

Adopted by the 57 OIC member countries during the 10th Session of the Islamic Conference in the Malaysian city of Putrajaya, the resolution also called on the international community — including OIC Member States — to urgently come up with the necessary funds to stop transmission completely by the end of 2004.

This landmark resolution has been welcomed by the Global Polio Eradication Initiative, a partnership spearheaded by WHO, Rotary International, US Centers for Disease Control and Prevention (CDC) and the United Nations Children's Fund (UNICEF). Since 1988, when the Global Polio Eradication Initiative was launched, significant progress has been made and today, only seven countries in the world remain polio-endemic: Afghanistan, Egypt, India, Niger, Nigeria, Pakistan, and Somalia. The number of polio cases has been reduced from greater than 350 000 in 1988 to 520 reported cases in 2003 (as of 12 November 2003), representing a greater than 99% reduction.

"This statement by the OIC is extremely important at this stage of the eradication effort," said Dr Hussein A. Gezairy, Regional Director of WHO's Eastern Mediterranean Region. "This commitment is vital to wiping out this terrible disease in the remaining endemic OIC countries."

The resolution follows concerns raised at the World Health Assembly in May 2003 by many OIC countries about the risk ongoing transmission anywhere poses to polio-free countries. Their concerns turned out to be well founded: the OIC resolution coincided with the onset of a new polio outbreak which has spread from Nigeria to neighbouring countries putting 15 million children at risk. Eleven children have been recently paralyzed with wild poliovirus in countries which have been polio-free for several years including Burkina Faso (1), Chad (3), Ghana (6), and Togo (1) and in each case, the origins of the wild poliovirus were genetically traced to northern Nigeria.

"Nigeria is now the country with the greatest number of polio cases in the world," said Dr David Heymann, Representative of the Director-General for Polio Eradication at WHO. "Polio and other infectious diseases know no national boundaries. We face a grave public health threat, and our collective goal of a polio-free world is in jeopardy."

In response to the outbreaks in West Africa, WHO launched a US$ 10 million immunization campaign across five countries in west and central Africa. Beginning on 22 October, hundreds of thousands of volunteers and health workers in Benin, Burkina Faso, Ghana, Niger and Togo worked to ensure that every child at risk in these key countries was reached with polio vaccine. A similar campaign also took place in Chad in mid-November.

Monitoring data from these campaigns suggest that insufficient numbers of children may have been reached to interrupt transmission of these imported viruses. It will be critical that every child is reached during the upcoming rounds of supplementary immunization activities.

On 15 January 2004, the Global Polio Eradication Initiative will launch a countdown to stopping transmission by end-2004. ■

Sarah Jane Marshall, *Bulletin*

Study confirms effectiveness of antiretroviral drugs for HIV patients

An international team of researchers looking at more than 7700 HIV patients undergoing combination therapy with antiretroviral (ARV) drugs has reported an increase in survival rates and a significantly reduced risk of progression to full-blown AIDS.

"Predicted survival for people with HIV-1 has continued to increase, since the introduction of HAART [highly active antiretroviral therapy]," say the authors — a collaborative team funded largely through a grant from the European Union. The study found that compared with pre-1997 data — when ARVs were first introduced to curb viral replication — the hazard ratio for death fell sharply to 0.47 (95% confidence interval (CI) = 0.39–0.56) in 1997, dropping further to 0.16 (CI = 0.12–0.22) in 2001. The authors also said that, compared with pre-1997 data, the hazard ratio of disease progression was 0.46 (CI = 0.38–0.55) in 1997, falling to 0.13 (CI = 0.09–0.21) by 2001.

"The study shows that ARVs are among the most effective health care interventions. When you compare them, for instance, to anticancer drugs or to anti-hypertensives, ARVs are orders of magnitude better," said Dr Jos Perriëns of the World Health Organization's HIV/AIDS department. The study, published in the *Lancet*, (2003;362:1267-74), compared disease progression and death rates in the period prior to 1997 to the period between 1999 and 2001, when ARVs were widely available to most, if not all, HIV patients in high-income countries.

The study's results, based soley on HIV-positive cohorts in Europe, Australia and Canada, show that ARVs prolong the lives of HIV patients in industrialized countries where hospitals are well equipped with state-of-the-art laboratory facilities. However, numerous small-scale pilot projects run by UNAIDS, a French initiative called the International Therapeutic Solidarity Fund (FSTI) and nongovernmental organizations such as Médecins Sans Frontières — as well as the Brazilian national AIDS programme — have since demonstrated the feasibility of ARV treatment even in resource-poor settings.

"In terms of patient compliance and survival rates, ARVs do indeed work extremely well in developing countries – even when compared to best practise in the industrialized world," said Peter Graaff of WHO's Essential Drugs and Medicines Policy (EDM) who also added that their therapeutic effectiveness was the reason for EDM's move to include ARVs on WHO's model list of essential drugs last April.

"You don't need sophisticated lab infrastructure to initiate successful first-line treatment," confirmed Perriëns who added that in Malawi and South Africa, for example, AIDS-related mortality rates have dropped from more than 50 per cent to around 10 per cent per year. "Treatment adherence in programmes in Malawi, Uganda and South Africa was at least as good – if not better – than in the US and other industrialized countries."

According to WHO, successful application of ARV therapy in developing countries depends on keeping the drug regimen as simple as possible by limiting the choice of drugs for first-line treatment. "Therefore, health workers delivering the ARVs need to know the side effects of only three instead of fifteen drugs. This makes it a lot easier to screen many more people," said Perriëns.

Of the estimated 42 million people infected with HIV, only about 1.5 million live in high-income countries and most of these are already receiving ARV treatment. In developing countries, however, only 300 000 patients — most of them in Brazil — currently benefit from ARVs. At the current rate of delivery, less than one million people will have access to ARVs by the end of 2005. The failure to deliver ARVs to developing countries was declared a global health emergency in the September by WHO and prompted the launch of WHO's 3-by-5 strategy which aims to have 3 million people in the developing world on ARV treatment by 2005.

In developing countries, the price of ARV treatment has now fallen from US$ 10 000 per patient per year to less than US$ 300. In late October, the William J. Clinton Foundation struck a deal with four generic manufacturers to supply several African and Caribbean countries with first-line ARVs for US$ 132 per patient per year. "Whilst this is a welcome development," said Perriëns, "in many countries people live on only US$ 1 a day; so even US$ 100 per year would still be out of their reach. This signals the need for strong commitment from the international community to the HIV treatment agenda." ■

Michael Hagmann, *Zurich*

UNICEF report has grave implications for child health in developing countries

More than one billion children — or over half the youngsters growing up in developing countries — suffer from severe deprivation of basic human needs, and 674 million of them live in absolute poverty, according to a study sponsored by the United Nations Children's Fund (UNICEF). Authors of the "Child Poverty in the Developing World" report note that the dismal living conditions have serious adverse consequences for the health, well-being and development of children.

"Many of the 10 to 11 million children who die each year, mainly in the developing world, die because of the living conditions recorded in this study," says Professor David Gordon, Director of the Townsend Centre for International Poverty Research at the University of Bristol, who led the research. "In particular, poor sanitation, inadequate clean water and overcrowded dwellings contribute greatly to diarrhoeal and respiratory diseases — the major killers."

Commenting on the report, Dr Hans Troedsson, Director of Children and Adolescent Health and Development at the World Health Organization, called the figures it contains "shocking but not surprising." "It's confirming the fears we have of how bad the situation actually is," he added.

For the analysis, Gordon and colleagues at the Townsend Centre along with researchers at the London School of Economics and Political Science pored over details of the lives of nearly 1.2 million children. The information was collected, mainly during the late 1990s, from the Demographic and Health Surveys of 45 countries and, for China, the China Health and Nutrition Survey. Using the survey data, the researchers charted the availability of seven essentials: food, water, sanitation, health, shelter, education and access to information.

The 36-page report, which was released in October, paints a bleak picture. Those living in "severe deprivation" included 91 million severely malnourished children younger than 5 years, nearly 376 million children who use unsafe water, more than 5 billion children who have no kind of toilet facility, and 265 million children who have never received *any* immunizations or have chronic diarrhoea. Furthermore, the 674 million children living in "absolute poverty" suffer from two or more severe deprivations of basic human needs.

The researchers themselves describe the findings as shocking, but they also point out that the figures may be minimum estimations since the report focuses on particularly severe living conditions. "We used far harsher definitions of deprivations, such as having no toilet facility whatsoever, than those used by most international organizations," Gordon says. "And we still came up with these enormous numbers of children. That's what is shocking."

The report concludes that helping the world's poorest children needs to include improving infrastructure. Otherwise, the lack of adequate housing, water treatment and sanitation facilities could undermine efforts aimed at health, nutrition and education. "Building schools without tackling the causes of what makes children sick," Gordon says, "won't necessarily improve the education of children living in these circumstances." ■

Charlene Crabb, *Paris*