News

Mixed reaction to US pledge of US$ 15 billion to fight AIDS

AIDS campaigners are ambivalent about the five-year US$ 15 billion package promised by US President George W. Bush to fight AIDS in sub-Saharan Africa and the Caribbean.

While welcoming the increased commitment to spending on AIDS in Africa, activists are upset that Bush has set aside only US$ 200 million a year for the Global Fund to Fight AIDS, Tuberculosis and Malaria. The Global Fund was set up two years ago to coordinate and deliver resources to projects around the world quickly and with a minimum of bureaucratic red tape. Next year the Fund faces a US$ 4 billion shortfall.

Sharon Ekambaram, spokesperson for the AIDS Consortium, a South African-based advocacy and lobbying organization, told the *Bulletin*: "What is the US agenda in setting up a separate funding mechanism instead of using existing structures like the Global Fund? The US obviously wants its own funding which it can control."

Nathan Geffen, spokesperson for the Treatment Action Campaign, agreed: "The Global Fund has requested $2.5 billion this year from the Bush administration and $3.5 billion in 2004. We call on this commitment to be made to the Global Fund, which has the independence and integrity to ensure that the money is properly allocated and accounted for."

The US$ 15 billion programme was first announced in the President's State of the Union address on 28 January. President Bush described it then as "a work of mercy", in which the United States "can lead the world in sparing innocent people from a plague of nature". The response at that time of Stephen Lewis, the United Nations special envoy for HIV/AIDS in Africa, was: "It opens the floodgates of hope."

The programme of funding was signed into law at the end of May. It will more than double US contributions to the worldwide fight against AIDS. The United States this year is spending about US$ 1.2 billion on international AIDS efforts.

Ms Ekambaram said: "It is an important gesture but in many ways seems to be a public relations act. It seems to be a lot of money but not when you look at it in the context of how much money has already been spent on SARS in a short time, or on the Iraq war."

She added: "There are a number of questions over whether the money comes with strings attached, for example over the use of generic drugs. At the end of the day it is the US deciding how the money gets spent without caring about the priorities of developing countries."

The US House of Representatives passed the US$ 15 billion bill only after the President's conservative allies insisted that abstinence from sexual activity should get a prominent role in the AIDS effort. The House approved, by 220 votes to 197, an amendment requiring that one-third of funds spent on prevention go to abstinence programmes. The new package recommends that 55% of direct aid should go to treatment programmes, 20% to prevention, 15% to care for those dying of AIDS, and 10% to children orphaned by the disease.

Nathan Geffen told the *Bulletin*: "We are worried that there are moves afoot to ensure that this money is going to go to organizations with a pro-life agenda which promote abstinence at the expense of condoms. This may result in the money being put to detrimental use and it is important that this issue gets rectified and clarified."

At the G8 Summit in Evian (1–3 June) European countries agreed to try and match the US funding. However, activists are disappointed that the leaders of the world's richest countries failed to make progress on new trade rules to allow poor countries to buy cheap, generic versions of new medicines, including antiretrovirals. ■

Jacqui Wise, *Cape Town*

Nepalis question the law against selling human organs

Hari Narayan Lama, who made a living from finding donors for patients with kidney failure, was taken into police custody on 4 May. He is charged with selling human organs for transplant, a crime according a Nepali law enacted in 1998. If found guilty, he will face up to five years in prison and a fine of up to half a million Nepali rupees (US$ 6667).

A kidney donor himself, Narayan confessed to police that he had persuaded more than 50 people to sell one of their own kidneys for transplant. A recipient pays the broker between US$ 2000 and US$ 3500, but the donor, being poor, is often satisfied with much less than this, so an able broker can get rich. Narayan, having been a donor himself and in good health, could easily persuade others to part with a kidney without fear of disablement.

One of his clients is Dr Sunil Chakradhar, a Nepali physician whose transplant was carried out in India. Chakradhar says there are 50 hospitals in India that are equipped for transplant surgery, and they compete for patients to cover their operating costs, offering commissions to brokers to find patients. This in turn encourages "transplant tourism", as the operation is more readily available and cheaper in India than in many other countries. In India too, however, it is a punishable offence to buy or sell human organs, and so the arrangements are made to a large extent unofficially except where the donor is a close relative.

No Nepali hospital is equipped for organ transplantation, but dialysis is available in some, including the National Kidney Centre. As dialysis costs nearly US$ 7000 a year, the Centre urges patients to arrange for a transplant in India as soon as they can. The Director of the Centre is Dr Rishi Kumar Kafle, who is Nepal's top kidney specialist. Thanks to a German donation, his centre has recently increased its number of dialysis machines from five to fifteen.

He believes the current law on transplants is too harsh, and puts transplant surgeons in danger of being criminalized for saving lives. Chakhradar is also against this law, arguing that he is still young, and if it had been enforced he would probably have been dead some time ago. His solution would be to provide more protection to donors against grasping middlemen.

The trial of Hari Narayan Lama will be a test of official and public opinion in Nepal. On the one hand organizing organ donations can save lives and perhaps solve a personal financial problem; on the other it puts pressure on the poor to sell their own living flesh to the rich. ■

Prakash Khanal, *Kathmandu*

Coming soon: a European Centre for Disease Control — of some kind

On 2 June, European health ministers "welcomed in principle" the idea of setting up a Centre for Disease Prevention and Control for the European Community by 2005. The European Commission should make a decision on the proposal on 18 July, but what such a centre should amount to in practice has not yet been agreed.

The European Health Commissioner, David Byrne, has proposed a surveillance structure similar to the Institut national de veille sanitaire for France (http://www.eurosurveillance.org/ew/2002/021003.asp). At the European Council meeting that endorsed the idea, Commissioner Byrne said: "The Centre should analyse and assess risks to human health from communicable diseases and other health threats. It should provide expert advice to EU policy makers on matters concerning their management, and enhance the capacity of the European Union and its Member States to protect human health through prevention and control measures." The components he lists as examples include "increased joint investigative capacity", "reinforced laboratory networking", and "better communication with the public", all of which could be done in cyberspace.

Michel Tibayrenc, who made his case in the *Bulletin* for such a centre 18 months ago (2001;79:1094), thinks there also needs to be a building, with a staff, like at the CDC in Atlanta, USA. "It is the only way the Europeans can reach the critical sizes the Americans can afford for certain kinds of essential research," he told the *Bulletin*. "This is beyond the resources of any single European country working nationally."

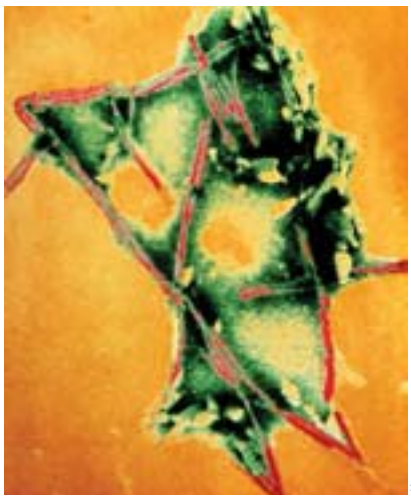
The centre according to Tibayrenc's proposals consists of a centralized structure, "with walls", and with a staff of about 500, and a threefold mission: advanced research; control and surveillance; and professional training. The research function should avoid duplication with national activities, and could go in two complementary directions: first, large-scale technologies that require cost-sharing at the European level; second, protecting vanishing competences such as medical entomology, which are essential for disease control but avoided by young researchers because they do not generate high impact factors. Control and surveillance activities should set clear limits for national sovereignties in the field of communicable diseases, as was illustrated by the SARS epidemics. International treaties are also urgently needed for this, Tibayrenc says. Professional training should also include a component involving developing countries.

As this issue of the *Bulletin* goes to press, the Federation of European Societies of Microbiology is debating the specifics of the proposed centre at its Congress in Ljubljana (29 June–3 July), which both Tibayrenc and Commissioner Byrne will attend. ■

Desmond Avery, *Bulletin*

Canadians find marker for prion diseases

Researchers led by neurologist Neil Cashman at the University of Toronto have found a distinctive marker on the misfolded proteins responsible for bovine spongiform encephalopathy (BSE or mad cow disease), and other prion diseases in animals and humans. The discovery, reported on 1 June in *Nature Medicine* (online) could lead to better diagnostic tests and, possibly, vaccines or immunotherapies for the fatal, brain-destroying diseases.



Keystone

Computer model of molecules of the prion protein responsible for causing bovine spongiform encephalopathy in cows and Creutzfeldt–Jakob disease in humans.

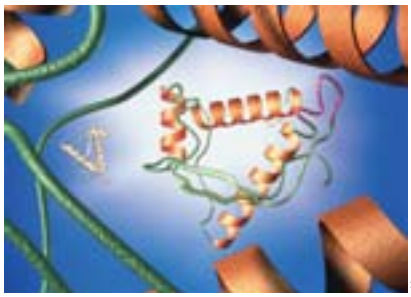
The announcement of this finding came just 14 days after Canadian food inspection officials launched a massive programme to quarantine, test and cull beef cattle in three western provinces after a cow in Alberta tested positive for BSE. It is only the second case of BSE that has ever occurred in Canada. The first, in a bullock that had been imported from Britain in 1987, occurred in 1993. In the current case, some 1700 head of cattle have been slaughtered. Many of the carcasses were used to test for BSE in herds that may have had contact with the infected animal or contained its offspring. So far, no other diseased cows have been found.

If scientists succeed in developing a diagnostic test based on the recently discovered marker, the need to sacrifice animals to obtain brain tissue for testing will be eliminated. Instead, the misshapen prions could be fished out of a blood sample.

Prion protein is normally found in animals. Like all proteins, it is made up of a chain of amino acids that folds itself into a specific shape, which gives the molecule stability as well as a unique function. The function of prion proteins, which are found most abundantly in the brain, remains a mystery. When misfolded, however, they wreak havoc in the brain, causing cells to die, abnormal amyloid protein to build up, and other anomalies to occur.

Moreover, scientists think that misshapen prion protein acquires the ability to transform any normal prion protein that it contacts into the pathogenic version. "So prion infection is more like a crystallization process than biological replication," says Cashman. "But the end result is that normal protein in the brain is gradually and disastrously turned into the abnormal shape."

Cashman and his team reasoned that stretches of the amino acid chain buried within the nooks and crannies of a normal prion protein might be thrust to the surface once it refolded into the abnormal shape. If so, the exposed sections might contain unique combinations of amino acids that could be used to distinguish disease-causing prion protein from its normal counterpart.



Keystone

Coloured transmission electron micrograph of prion fibrils in the brain of a cow infected with bovine spongiform encephalopathy. The elongated fibrils (green) are believed to be aggregations of the protein that makes up the infectious prion.

And that is just what the researchers found. A trio of amino acids consisting of two tyrosine molecules and an arginine showed up on synthetic or recombinant prion proteins that the scientists had deliberately misfolded in the laboratory. The team also demonstrated that antibodies that target the tyrosine-tyrosine-arginine trio, or epitope, bind to the misfolded prion proteins in the brains of prion-diseased cattle, sheep, elk, mouse and hamster models, and humans. But, the antibodies do not latch on to normal prion proteins in healthy brain tissue.

So far, antibodies have failed to detect misshapen prion proteins in blood, but the preparation of a diagnostic blood test based on the tyrosine-tyrosine-arginine epitope is under way. The Johnson & Johnson corporation has bought the rights to develop such a test for human prion diseases, which include variant Creutzfeldt–Jakob disease, the disease thought to result from eating BSE-tainted beef products. Similarly, IDEXX Laboratories, Inc., is working on a diagnostic blood test for prion diseases in animals.

Meanwhile, Cashman and his team are doing groundwork that could lead to vaccines or immunotherapies. In theory, the antibodies would bind to the three amino acids and thereby prevent the pathogenic protein from deforming the rest. In research funded in part by the hamburger giant, McDonald's Corporation, the scientists have immunized mice with the tyrosine-tyrosine-arginine molecule. Over the next few months, the rodents will be inoculated with misfolded prions. If the mice are protected from disease, it will open the door for testing the technique in larger animals and, possibly, humans. "It could be the royal road to containing and extinguishing prion epidemics including BSE, chronic wasting disease in elk and even sheep scrapie," says Cashman. ■

Charlene Crabb, *Paris*

EU launches measures to stop diversion of cut-price drugs

The European Union has launched new measures to prevent unscrupulous middlemen from diverting low-cost life-saving drugs intended for poor countries and selling them on the black market in rich ones. The re-importation ban aims to encourage companies to increase the supply of cut-price drugs, known as "tiered-price products", to treat HIV/AIDS, malaria, and tuberculosis in some of the world's poorest countries.

Access-to-medicines activists welcomed the move as a safeguard for the pharmaceuticals industry, and were confident that EU customs were tough enough to implement the new rules effectively, but drug industry groups were sceptical. Under the new EU regulation, which came into effect on 4 June, pharmaceutical companies may register their products sold at a discount of 75% or more on European prices, or those with a mark-up of 15% or more on production costs, on a voluntary basis.

These patented and generic medicines, destined for 76 poor countries that are unable to produce locally the drugs they need, will then be placed on a list administered by the European Commission. Drugs companies will be required to stamp these products with a special logo that can be easily identified by customs authorities. The regulation has made it a criminal offence to import any of these products into the EU "for free circulation, re-exportation, warehousing or trans-shipment".

Lena Sund, who drafted the regulation for the European Commission, said the re-importation ban was one part of the jigsaw, adding that drug distribution in developing countries needed to be improved, and more funding had to be found for research into "neglected" poverty-related diseases seen as unprofitable by the drug industry.

"Price discounting is an important step towards solving the problem, but we shouldn't only focus on a solution to trade diversion," Sund said. She added that some companies said they would be ready to register their products within the next few weeks, but others had been reluctant to join the system, complaining that it would be costly to re-label and re-package products. It would also be time-consuming in cases where they need new permission to import these re-packaged medicines, in the event, for instance, of distribution problems.

German Velasquez, coordinator of the WHO drug action programme, said he believed the ban was an effective tool to stem drug smuggling and he hoped it would spur other wealthy nations to follow suit. He added, however, that he thought the problem of diversion was "partly artificial" because the chance of drugs being diverted back to Europe was so slight. "What chemist in Europe would buy black-market drugs from Africa?" he asked.

Harvey Bale, Director-General of the International Federation of Pharmaceutical Manufacturers Associations based in Geneva, said the EU ban on re-importation of discounted drugs was "on the whole the right idea" but doubted whether it could be implemented properly. "They [EU states] will have to beef up vigilance and oversight in customs controls," he said, since not all EU customs controls were effective, for instance under the open-borders Schengen agreement within some EU states. He also he argued that drugs smugglers could use diplomatic pouches to circumvent customs.

A spokesman for the European pharmaceuticals industry was scathing about the EU re-importation ban. Christophe de Callatay of the European Federation of Pharmaceutical Industries and Associations in Brussels said the EU was taking the wrong approach. "The trouble is in the delivery [of drugs] because there's no public health infrastructure in many of these countries, no hospitals, no needles and no beds," he said, adding: "EU customs may be effective, but action must be taken at African borders too". ■

Fiona Fleck, *Geneva*