News

Medicines for all, not just the rich

March brought bad news for the HIV virus, but good news for HIV/AIDS patients, particularly those in poor countries. In the second week of the month, Merck and Co., a leading US pharmaceutical manufacturer, announced it would slash the prices of two of its antiretroviral drugs, indivar (Crixivan) and efavirenz (Stocrin), by 90% to US$ 600 and US$ 500, respectively, per patient per year. The price cuts would be extended, Merck said, to all developing countries provided they could guarantee that the low-cost drugs wouldn't be re-exported.

At about the same time, another drug firm, GlaxoSmithKline, which produces 40% of the world's anti-AIDS drugs, said it would make cut-price AIDS drugs available to any not-for-profit organizations with the capacity to deliver them in developing countries. And the ball kept rolling: yet another US pharmaceutical manufacturer, Pfizer, announced it would distribute the antifungal drug fluconazole (Diflucan) — used to treat AIDS-related meningitis and fungal infections — free of charge in South Africa up till December 2002.

Then on 15 March came an offer by the New York-based pharmaceutical company Bristol-Myers Squibb to reduce the prices of two of its antiretroviral drugs, stavudine (Zerit) and didianosine (Videx), to a combined price of US $1 per day and to relax its patent protection over Zerit in South Africa. The offer would allow South African-based drug companies to produce and market the drug at low cost. The surprise announcement followed protests from students at Yale University in the United States where stavudine was developed. The university holds the patent for this drug and allows Bristol-Myers Squibb to produce it on licence.

What triggered this price avalanche? Certainly, the curtain was raised on this new scenario by the dramatic February offer of the Indian drug company Cipla to sell governments a cocktail of three antiretroviral drugs for US$ 600 a year — a fraction of the US$ 10 000–15 000 price tag for this triple therapy in the United States and other countries in the west. Certainly, Cipla's offer turned the focus from country-by-country negotiations to across-the-board price reductions aimed at the poorest countries. And for sure, these reductions are part of a broader process which combines pressure from nongovernmental organizations, political will, market forces and close collaboration between the pharmaceutical industry and international organizations to make wider access to AIDS medicines a reality. Meanwhile, another Indian manufacturer of generic drugs is reportedly offering triple antiretroviral therapy for US$ 350 a year.

"This is not about profits and patents. It's about poverty and a devastating disease," said Mr John L. McGoldrick, executive vice president, Bristol-Myers Squibb. "We hope our initiatives can be of some help to African AIDS sufferers and may help energize and accelerate world understanding and action."

Cipla's offer catapulted it into the centre of an international squall over the production of low-cost copies of expensive AIDS drugs, since it is far from clear which countries can import and sell generic drugs without breaking existing trade agreements granting exclusive rights to patent-holding companies.

The squall is fuelled, among other things, by mounting international concern over the high price of many essential drugs — but especially antiretroviral drugs for the treatment of HIV/AIDS — which puts them beyond the reach of the poorest countries where they are needed most. Of the over 36 million people living with HIV/AIDS, less than 10% have access to lifesaving drugs. Of the 25 million Africans living with HIV, only around 10 000 currently receive proper medical care.

Under an international trade agreement known as TRIPS — an acronym for Trade Related Aspects of Intellectual Property Rights — new drugs can be patented for up to 20 years. This gives manufacturers exclusive marketing rights throughout that period at a price set by them. However, under exceptional circumstances — in the event of a national emergency, for example — TRIPS allows signatory states to pass national laws enabling them to bypass patents and to produce or import cheaper versions of a patented drug.

Taking advantage of this possibility, the South African government passed a law in 1997 that enables it to import cheaper versions of AIDS drugs for the 4.7 million South Africans now living with HIV/AIDS. The law has never been enacted because in the following year the pharmaceutical industry initiated legal action to overturn it on the grounds that it is too broad and contravenes international trade agreements. The action has culminated in a high-profile court case due to start in April in the South African capital, Pretoria, with 39 international pharmaceutical companies challenging the South African government.

In a press statement, the International Federation of Pharmaceutical Manufacturers' Associations (IFPMA) warned that any loss of patent protection would threaten research and that price reductions would do little to improve access to AIDS drugs unless national governments and donors increased funding. The IFPMA's director general Dr Harvey Bale Jr said: "The international pharmaceutical industry firmly believes that the weakening or infringement of intellectual property rights as reflected in the international trade agreements amounts to a disincentive for investment and research and development, and that factors other than intellectual property rights are at the root of the problems of access to medicines."

The Geneva-based World Trade Organization agrees that ways must be found to improve access to essential drugs in low-income countries but maintains that drug companies must be given incentives to develop new drugs, which can each cost as much as US$ 500 million to produce. "Were it not for a patent system that rewards companies for risking millions on research," Mr Mike Moore, director-general of the World Trade Organization, wrote in a recent editorial in the *International Herald Tribune,* "anti-AIDS drugs would not exist."

The British charity Oxfam is campaigning for a change in world trade rules to drastically widen access to essential drugs. Mr Kevin Watkins, Oxfam's senior policy adviser, maintains that differential pricing by the pharmaceutical companies on a product-by-product and country-by-country basis is too limited and not the answer. "What is needed," he told the *Bulletin,* "is a system of differentiated patents, with improved safeguards built in to ensure that the public interest comes first and corporate interest second."

Oxfam argues that public investment and international cooperation — not extended patents — should be used to finance research. The charity is calling for a US$ 5 billion international fund to be established, under the auspices of WHO, to support a global network of public research institutions dedicated to developing new

medicines and vaccines. Oxfam also wants to see an international fund established to subsidize drug purchases and delivery systems in the poorest countries.

In Norway this month (April) about 50 experts from around the world are meeting at a workshop organized by WHO and the WTO to discuss differential pricing as a means to ensure that the poor have access to essential drugs without undermining the international patents system — a system that gives pharmaceutical manufacturers an incentive to develop new drugs.

However, even at heavily discounted prices, many drugs still remain way beyond the means of low-income countries. WHO's director-general, Dr Gro Harlem Brundtland, says that no matter how low prices go, additional funding — in the form of development assistance and debt relief — will be needed to meet the costs of care for the poorest: "The private sector is showing it is willing to do its part to fight the HIV/AIDS epidemic. The onus is now on governments and international organizations to make sure the funds to pay for these drugs are made available and that health systems are strengthened so that they are able to provide the care needed. We are talking about a 500-fold increase in care that could translate to as much as US$ 10 billion per year. This is a great challenge for all of us." ■

Sheila Davey, *Geneva, Switzerland*

Lifestyle and Alzheimer disease — study strengthens link

African-Americans living in an industrialized US city are more than twice as likely to develop Alzheimer disease and other dementias than are Africans living in Nigeria, according to a study published in the 14 February *Journal of the American Medical Association.*

The ten-year study, a collaborative effort of researchers from both countries, compared the incidence rates of Alzheimer disease (AD) and other dementias in people over age 65 in Indianapolis, Indiana, in the US, and in Ibadan, Nigeria. A baseline survey identified 2147 African-Americans in Indianapolis and 2459 Yoruba residents of Ibadan who did not have dementia. Follow-up studies at 2 and 5 years found that 2.52% of the African-Americans eventually developed AD, compared to only 1.15% of the Yoruba; overall, 3.24% of the African-Americans developed any form of dementia (including AD), compared to 1.35% of the Yoruba. The rates found among the African-Americans are in the "higher range of previously published" rates, while the rates found in the Yoruba are among the lowest, reported the study's principal investigators, Dr Hugh C. Hendrie of the University of Indiana School of Medicine in the US and Dr Adesola Ogunniyi of the University of Ibadan.

The researchers did not draw conclusions as to why the disease rates varied, but postulated two factors: genetics and lifestyle. They found that a gene (apolipoprotein E), known to raise the risk of Alzheimer disease, occurred with equal frequency in the two groups. However, "in the African-Americans the gene is definitely increasing the risk for Alzheimer disease, while in the Nigerian group it doesn't seem to have an effect," Dr Frederick W. Unverzagt, a co-author of the study, told the *Bulletin*. As for possible lifestyle influences, the study found that the Yoruba have a "much lower prevalence" of vascular risk factors — lower cholesterol levels and fewer cases of diabetes and hypertension — than the African-Americans.

"Maybe the incidence numbers can be explained by a gene–environment interaction," says Unverzagt. "It could be that the ApoE gene is just not activated in certain environments." Follow-up studies, he says, will examine diet, activity levels, and social engagedness. "If factors like diet are found to influence the disease," says Unverzagt, "the public health implications could be tremendous. If modifying such factors could delay the onset of Alzheimer by 5 to 10 years, you could really forestall some of the looming public health problems posed by the disease."

The study is believed to be the first cross-cultural study of dementia to use the same methodology and the same group of researchers at different sites. Previous studies have compared rates from different countries, but drawing conclusions from such comparisons is often difficult because of methodological differences.

"Such cross-cultural studies are extremely difficult to do," Dr Denis Evans, director of the Rush Institute for Healthy Aging, in Chicago, commented to the *Bulletin*. "They've done a magnificent job with that. They carried out the same procedures 4000 miles apart. This is very encouraging for people who have thought about doing this sort of work."

In an accompanying editorial, Dr Lindsay Farrer of the Boston University School of Medicine, Massachusetts, says "preliminary evidence suggests that a high-fat diet may increase the risk of developing" Alzheimer disease and "studies have revealed that [Alzheimer] cases are less active physically than controls in early life." Currently, though, most experts say that the only established risk factors are genetics and increasing age. ■

Catherine Dold, *Boulder, Colorado, USA*

US health care takes a battering

The United States' health care system fails to deliver consistent, high-quality health care to its citizens, and without a major overhaul the problem will continue, according to a new report from the Institute of Medicine (IOM) of the US National Academies. The report outlines the problems hobbling the country's health care system and describes changes necessary to fix it.

"The American health care system offers the sophistication of a space station delivered with the efficiency of a third-world post office," says Dr Lucian L. Leape, a physician at the Harvard School of Public Health and a member of the IOM committee that drafted the report. The report blames "a highly fragmented delivery system that largely lacks even rudimentary clinical information capabilities" for the gap between the calibre of care possible and the quality typically delivered. The committee also criticizes a health care system that "frequently falls short in its ability to translate knowledge into practice and to apply new technology safely and appropriately."

The shortcomings the committee found aren't unique to the US. Dr Tessa Tan-Torres Edejer, with WHO's Global Programme on Evidence for Health Policy, says: "The few data that we have suggest that the same problems exist in just about every country, with some countries relatively worse, and some better off. Invariably, the countries that look for problems, find them." Australia and Mexico are two countries she recalls that conducted recent studies revealing malfunctioning areas of their health care delivery systems. "There are probably many others but these are not reported in the scientific press because they are meant for internal use."

The problems of the US health care system can't be resolved without a complete overhaul of the current system, the IOM committee argues. "The current care system cannot do the job. Trying harder will not work. Changing systems of care will." To this end, the committee established a list of guidelines for improving health care in the US. These include a shift toward patient-focused care. "Right now the system is designed around what doctors can deliver, rather than on the care that patients need," says Leape. The report says patients must be given greater control over their care, and greater access to current health information.

The report also calls for better communication between health care practitioners. "The big secret about the American health care system is that no-one is in charge," Leape told the *Bulletin*. He says the current system consists of separate care