News

EU faces world's fastest growing HIV epidemic

Fledgling democracies in Eastern Europe and the former Soviet Union — ten of which are set to join the EU on 1 May — are facing the world's fastest growing HIV epidemic, warned the United Nations Development Programme (UNDP) in a new report released in Moscow on 17 February 2004.

The report was published ahead of a high-level meeting in Dublin on 23 February during which experts on HIV/AIDS warned ministers from 55 countries in Europe and Central Asia that the region's rapidly accelerating HIV/AIDS epidemic could cripple Europe's economic and social development.

According to the report, *Reversing the Epidemic: Facts and Policy Options*, future members of the EU (such as Estonia, Latvia and Lithuania) along with the Russian Federation and Ukraine are facing increasing growth rates of new HIV infections that are amongst the highest in the world. One in every one hundred adults in these three countries is thought to be carrying the virus — a threshold above which efforts to turn back the epidemic have failed in many other countries.

Examining the epidemic in the 28 countries which compose Eastern Europe, the Baltics and the Commonwealth of Independent States, the 117-page study reported that between 1.2 million and 1.8 million people in the region were infected with the virus last year compared with just 30 000 in 1995. However, only 9% of those in need of antriretroviral treatment are currently receiving it.

UN Secretary-General, Kofi Annan, warned of the grave economic impact posed by an epidemic which, in Eastern Europe, sees 80% of new infections occurring among young people.

"No nation can afford to see its future workers and leaders struck down by AIDS before they reach maturity," said Annan in a video message for the Dublin conference entitled, *Breaking the Barriers: Partnership to Fight HIV/AIDS in Europe and Central Asia.*

In a joint statement issued at the conference, UN agencies including WHO, UNAIDS and UNICEF, and the World Bank and the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), called on European Ministers to take decisive action to prevent the further spread of AIDS across Europe and to treat those in need.

"There is no time to waste — European Ministers must urgently scale up and roll out effective HIV prevention and treatment programmes," said Dr Peter Piot, UNAIDS Executive Director. "Given that the EU will form the biggest trading bloc in the world, covering more than 500 million people, it is in the EU's best interest to prevent the AIDS epidemic from crippling Europe's social and economic development."

"Europe cannot divide over the issue of AIDS treatment, and only provide treatment in richer countries," said WHO Director-General, Dr LEE Jong-wook. Treatment should be a right for all, including for sex workers and injecting drug users."

Sex-workers and injecting drug users are some of those at highest risk of contracting HIV. Other high-risk groups include men who have sex with men, and prisoners. Experts report a rise in the use of intravenous drugs, the sharing of dirty needles and unsafe sex since the collapse of communism in 1991. Overcrowded and insanitary prisons

REUTERS/Sergei Karpukhin

A young Russian waves a flag whilst taking part in the "March For Life" in central Moscow, on World AIDS Day, 1 December 2003. One in every one hundred adults in the Russian Federation is thought to be HIV-positive — a threshold above which efforts to turn back the epidemic have failed in many other countries.

are also contributing to the problem. Prison reform and the decriminalization of injection drug use are essential in combating the epidemic, says the UNDP report.

The impact of the epidemic has been compounded by insufficient public awareness, frequent stigmatization and lack of adequate policy instruments to cope with the disease, said UNDP in a statement accompanying the release of the report.

"Members of at-risk groups are often subject to social exclusion, poverty, stigmatization or incarceration factors which actually heighten the spread of the disease," said Kalman Mizsei, Assistant UNDP Administrator and Regional Director for Europe and the Commonwealth of Independent States.

According to WHO, the percentage of people reporting premarital sexual relations more than doubled between 1993 and 1999, from 9% to 22%. Lack of education may be the underlying cause — in Tajikistan for example, only 10% of girls have ever heard of HIV/AIDS.

"Schools are the best defence against HIV infection," said Carol Bellamy, Executive Director of UNICEF. "They offer the best mechanism to deliver HIV prevention information."

A draft declaration adopted at the Dublin conference entitled *Partnership to Fight HIV/AIDS in Europe and Central Asia*, aims to offer 80% of drug users access to treatment and harm reduction services by 2005 and to provide "universal access to HAART [highly active antiretroviral therapy] in Europe and Central Asia by 2010," among other targets.

According to the UNDP report, lessons can be learnt from success stories in countries such as Poland, the Czech Republic and Slovakia which have leveraged progress in building democracies into effective responses to HIV/AIDS.

World Bank figures indicate that funding to tackle the epidemic in the region needs to increase from an estimated US$ 300 million in 2003 to US$ 1.5 billion by 2007.

GFATM, which has approved over US$ 400 million over five years for 22 programmes in 16 countries in Eastern Europe and Central Asia, recently announced the re-launch of its AIDS grant to one of the worst-hit countries — Ukraine. The decision follows the suspension of funding in January 2004 due to the slow pace of the projects which had received GFATM funds and the country's escalating HIV/AIDS crisis. A new fund management structure is now in place to tackle these concerns.

"But money alone is not the issue," warned Shigeo Katsu, World Bank Regional Vice President for Europe and Central Asia. "It is crucial to improve the information base for programs, to support what works against HIV/AIDS, and to break down the policy and social barriers to effective actions across the region." ■

Sarah Jane Marshall, *Bulletin*

MMR controversy raises questions about publication ethics

Ten members of a team of 13 doctors who published a controversial study in the UK-based medical journal, the *Lancet* (1998;351:637), suggesting a possible link between the triple mumps, measles and rubella (MMR) vaccination and autism and bowel disease withdrew this interpretation of their findings last month — an interpretation which triggered a collapse in confidence in the UK's MMR programme and reduced immunization coverage to below WHO recommended levels by 2002.

The move came after it emerged that the study's Senior Author failed to disclose a potential financial conflict of interest either to editors of the *Lancet* or to the paper's co-authors.

"We judge that it should have been so disclosed … we believe that our conflict of interest guidelines at the time should have triggered such a disclosure," said Richard Horton, Editor of the *Lancet*, in a statement issued on 23 February 2004.

The case has since sparked a major debate on the ethics of publishing research findings, in particular on how editors can ensure that all conflicts of interest relating to the authors of research are declared.

Horton said he would not have published the study had he known that its Senior Author, Dr Andrew Wakefield, had a US$ 102 000 contract with the then Legal Aid Board to conduct a separate study involving tests on 10 children in support of claims by their families against vaccine manufacturers. Furthermore, a "significant minority of children" described in the 1998 Lancet paper were also part of the Legal Aid Board-funded project. The Legal Aid Board, replaced by the Legal Services Commission in 1999, is a public body in the UK offering legal services to those who cannot afford the associated fees but are deemed to have a case.

The *Lancet* devoted several pages in the 6 March edition to printing the retraction (*Lancet* 2004;363:750), statements from some of the researchers justifying the ethical conduct of the study as well as a commentary by the editor.

"We wish to make it clear that in this paper no causal link was established between MMR vaccine and autism as the data was insufficient," the 10 researchers wrote. Wakefield and two other co-authors of the study did not join the retraction.

Triple vaccine MMR is used in 94 of WHO's 192 Member States according to 2002 data, including 46 countries in western and eastern Europe, and the former Soviet Union, as well as Indonesia, Malaysia and Australia.

Although WHO and many other public health bodies insisted the MMR vaccine was safe at the time the study was published, the researchers' findings dented public confidence in the UK where many parents stopped having their children vaccinated with MMR and fears around the safety of the vaccine spread to other parts of Europe and the Americas.

In the UK, immunization coverage had dropped to 83% by 2002 — the lowest level since 1989 and well below the 95% WHO recommended level — and in Ireland, similarly low immunization coverage led to a measles outbreak with 234 cases last year.

Last year US health officials expressed fears that measles cases could be imported from the UK and Ireland to parts of North America where immunization was low.

WHO experts do not attribute recent measles outbreaks in the Marshall Islands, Asia and Italy to the MMR scare in the UK.

But while damage, in terms of a reduction in immunization coverage appears to have been limited to the UK, the case underlines the devastating effect the interpretation of research findings can have on public health.

The case has sparked soul searching among the UK's medical bodies, ethics committees and medical publications on how to avoid research misconduct in

future. The UK's General Medical Council is conducting a preliminary investigation into the matter and other reviews of ethics are under way.

During its annual meeting in October last year, The Council on Publication Ethics (COPE), an association of scientific editors, called for the establishment of a National Council for Research Integrity to respond to research misconduct in the UK. Whilst the operational details of the Council remain unclear — for example, whether it should be statutory or voluntary, meeting participants agreed that an independent body was urgently needed and many of them pointed to the conflict of interest generated by institutions having to investigate themselves.

In his commentary, Horton underlined the responsibility of editors in recognizing the implications for public health of publishing research. He said that he and his editorial staff had failed to recognize the potential effect the publication of the 1998 study could have on public health. "These are difficult judgements to make in hindsight. For example our sensitivity to potential conflicts of interest is very much higher today than it was in 1998," he wrote. ■

Fiona Fleck, *Geneva*

Scientific publishers divided over US trade embargo ruling

A fresh interpretation of the rules governing trade between the US and countries such as the Islamic Republic of Iran and Sudan has shocked American publishing houses as well as scientists and editors worldwide.

The ruling, confirmed by the US Department of the Treasury at a meeting attended by representatives from 30 publishers on 9 February 2004, says that it is illegal for scientific journals to continue peer reviewing and editing manuscripts whose authors come from Cuba, the Libyan Arab Jamahiriya, Sudan, the Islamic Republic of Iran, or Iraq — all countries against which the US applies full trade sanctions.

The Association of American Publishers, which represents American publishers and has offices in New York and Washington, says it believes the Office of Foreign Assets Control, which issued the ruling last September, has interpreted the law incorrectly.

The Association of American Publishers is discussing whether to challenge the ruling in the courts. Allan Adler, Vice President for Legal and Government Affairs at the association, said: "If the rulings, and more particularly the regulations, were upheld in a judicial challenge, it would be a significant blow to press freedom in the US."

Arash Etemadi, Managing Editor of the *Iranian Journal of Endocrinology and Metabolism*, said: "This ruling will affect the free exchange of information in the scientific world. The governments of all countries should respect free exchange of scientific information, particularly in the case of medical publications, which deal with the life and well-being of the community."

Etemadi said he knew of colleagues who had held back submitting papers for consideration by American journals because of the ruling.

The ruling has received a divided response from the American scientific publishing community. Some publishers, including the American Association for the Advancement of Science, which publishes the respected journal *Science*, have decided to continue considering manuscripts from the countries concerned regardless. Others, such as the journals of the Institute of Electrical and Electronics Engineers (IEEE), have stopped accepting such papers — a move which has infuriated its members who make up the majority of the 5100 signatures on a petition calling for the organization to "cease discrimination against IEEE members from countries that are embargoed by the US Government." In October 2003, IEEE asked the US Government to grant them a licence authorizing them to edit manuscripts from embargoed countries but it is still waiting for a reply.

"Decisions to edit and publish should not be determined by the policies of governments or other agencies outside the journal itself," said the World Association of Medical Editors, in a policy statement issued on 23 March 2004 (http://www.wame.org/wamestmt.htm#geopolitical). The group, which runs a global email network for its members, reported that many of its member editors were troubled by the ruling.

"Our statement will not be able to change US policy, but we think it is important to have one, to give strength to individual editors who decide to oppose the policy," said Robert Fletcher, Chair of the Association's Editorial Policy Committee. "They will know that a large number of editors around the globe are backing them."

The ban does not apply to the publication of articles, but to the peer review and editing of articles in order to improve them for publication. A spokeswoman for the US Treasury said: "If someone writes a poem in Iran, then that can be reprinted in the US. But where there is substantial editing and collaboration with authors on an article, this is considered to be performing a service — and we cannot perform a service for a fully sanctioned country."

Speaking in early March, she said the US Treasury was reviewing this process, to establish how best to allow the free flow of information, while still maintaining full trade embargoes against the five countries.

The trade embargoes are not new. They are enshrined in the 1988 Omnibus Trade and Competitiveness Act. This exempts information and informational materials from the embargoes, although the exemption has been interpreted in the US as applying only to material that is "fully created" — such as camera-ready copy.

Publishers had apparently not realized that this meant they should not carry out peer review, editing or subediting on manuscripts from affected countries. The issue came to light only last year when IEEE asked the Office of Foreign Assets Control directly for clarification of the ruling, after the Institute's bank had queried a payment to a hotel in Tehran, the Islamic Republic of Iran, where it was co-sponsoring a conference.

The Office of Foreign Assets Control ruled in September 2003 that "the collaboration on and editing of manuscripts submitted by persons in Iran, including activities such as the reordering of paragraphs or sentences, correction of syntax, grammar, and replacement of inappropriate words by US persons, prior to publication, may result in a substantively altered or enhanced product and is therefore prohibited … unless specifically licensed." Selection of reviewers in order to enhance or alter manuscripts was similarly prohibited. ■

Sharon Kingman, *London*

Sexual abuse on the rise in Africa — governments must act

Delegates at the first African Conference on Sexual Health And Rights which took place in Johannesburg 25–29 February 2004, urged governments to prioritize sexual health and recognize it as a fundamental human right amidst reports of the rising incidence of sexual abuse in Africa.

Delegates voiced their support of WHO's Declaration of Sexual Rights and the need for greater openness around sex, traditionally a taboo topic in Africa.

Congress manager Andrew Oberholzer said that delegates committed themselves to advancing sexual health and rights by building on progress made at the International Conference of Population and Development in Cairo in 1994 and achievements such as the African Charter on Human and People's Rights and the Rights of Women in Africa. They also appealed to governments to allocate resources to implement these rights.

"We want to present a united front to lobby at a government level to promote and implement legislation to protect people's sexual rights," said Oberholzer, Managing Director of the Southern African Sexual Health Association, a non-profit organization aimed at improving the sexual well-being of all South Africans. Some 200 delegates attended the conference including health-care practitioners and experts, and activists from sexual and health rights organizations throughout Africa.

Participants heard how the widespread lack of sexual rights on the continent has fuelled the abuse of women and children and the spread of HIV/AIDS. WHO's *World report on violence and health* in 2002 reports widespread sexual violence — from rape and sexual abuse to forced marriage and female genital mutilation.

Curbing the sexual abuse of children was high on the agenda of the three-day congress with reports that offenders were getting younger, abuse was rising and the majority of cases went unreported. Nor is child abuse confined to girls, according to Luke Lamprecht from Johannesburg's Teddy Bear clinic. He reported that the majority of their cases were teenage boys abused by men. During the conference, activists and doctors lobbied for changes in legislation to protect children.

The promotion of women's sexual health rights was also an objective of the conference. "Many women are not economically empowered in Africa and as a result are not sexually empowered," said Oberholzer. This limits their freedom to decide on contraception, including condom use, and consensual sex.

The congress added momentum to a move to bring specialist organizations together under the umbrella of the African Federation for Sexual Health and Rights.

Meanwhile in Amsterdam, 100 experts on reproductive rights met on 9 March for a two-day meeting, organized by the United Nations Population Fund (UNFPA) to review progress on the advancement of sexual and reproductive health and rights since the adoption of the Programme of Action at the International Conference of Population and Development in Cairo in 1994. Participants at last month's meeting, Cairo and Beyond: Reproductive Rights and Culture, identified a need for greater political and financial commitment to reproductive and sexual rights.

"We pledge to break the silence and taboos on culture and religion and their relation to reproductive and sexual health and rights, and establish a permanent dialogue on these vital issues," said Agnes van Ardenne, Netherlands Minister for Development Cooperation, and Thoraya Admed Obaid, UNFPA Executive Director, in a joint statement.

The Dutch government has recently established an online network to discuss issues related to culture and reproductive rights at: www.reproductiverightsandculture.org. ■

Claire Keeton, *Johannesburg*

In brief

Drug-resistant TB spreading in Eastern Europe and Central Asia

Tuberculosis (TB) patients in parts of Eastern Europe and Central Asia are 10 times more likely to have multidrug-resistant TB (MDR-TB) than in the rest of the world, according to a new WHO report.

Anti-Tuberculosis Drug Resistance in the World – Third Global Report named Estonia, Kazahkstan, Latvia, Lithuania, parts of the Russian Federation and Uzbekistan as six global hotspots with drug resistance in new patients as high as 14%.

"TB drug resistance is an urgent public health issue for countries from the former Soviet Union," said Dr Mario Raviglione, Director of WHO's Stop TB Department.

Highest prevalence of MDR-TB coincides with one of the world's fastest growing HIV infection rates in Eastern Europe and Central Asia (see related news story, *EU faces world's fastest growing HIV epidemic*, in this issue of the *Bulletin* (p. 331).

"With people's immune systems compromised, MDR-TB has a perfect opportunity to spread rapidly and kill," said Assistant Director-General of WHO's department of HIV/AIDS, TB and Malaria, Dr Jack Chow.

The report also identified China, Ecuador, Israel and South Africa as key areas of concern.

Nigeria declares polio vaccine safe

Nigerian President, Olusegun Obasanjo, announced in mid-March that independent tests conducted in South Africa, India and Indonesia had confirmed the safety of polio vaccines used in the country during immunization campaigns, following concerns expressed by Muslim leaders over the safety of the vaccine.

Mohammed Maccido, a Muslim leader, appeared with the Nigerian president saying that he accepted the results of the tests. "I hereby urge all our people to bring out all their children to be immunized," he said. The next polio immunization campaign is scheduled for 23–26 May 2004.

However, a spokesman for the northern state of Kano which refused to participate in February's vaccination campaign amid suspicions that the vaccine would spread infertility and HIV, said he remained unconvinced. Kano state Governor, Ibrahim Shekarau, told the BBC that he was withholding a decision on whether to accept the findings until he had seen the report.

The Nigerian boycott has been blamed for the spread of polio to eight African countries where it had previously been eradicated. The country now accounts for nearly half the world's polio cases.

In focus

Clinical trials without ethical review under the spotlight

A recent series of unethical, and in some cases illegal, clinical trials in India is fuelling concern over the incidence of clinical trials conducted without ethical approval in other countries where legislation may be either inadequate or not implemented.

In a series of articles last year, Dr Chandra Gulhati, editor of an independent pharmaceuticals journal, the *Monthly Index of Medical Specialities in India*, shed light on the illegal trials and illegal promotion of the anti-cancer drug, Letrozole, as a fertility drug in India.

More than 400 women, who had been trying in vain to conceive, were enrolled without their knowledge or consent to take part in clinical trials across India to see if the drug induced ovulation.

The drug was a copy of a patented Novartis product, Letrozole by Mumbai-based generics firm, Sun Pharmaceuticals. The women were under the impression they were receiving expensive fertility treatment.

Letrozole has been approved globally for the treatment of breast cancer in postmenopausal women, but it is not approved for any other use in any country, including India.

Since then, India has seen a huge public outcry over the regulatory authorities' failure to crack down on a recent series of illegal and legal, but unethical clinical trials.

A Delhi-based nongovernmental organization is filing a complaint about the Letrozole case to India's Supreme Court and last month, the Indian Government pledged to push through tougher, more effective legislation to tackle the problem this year.

Dr Gulhati contends that although the company and doctors who carried out the tests broke the law no one has been put under criminal investigation by the Indian authorities.

The Letrozole trials are a shocking example of a widespread global phenomenon. A recent survey of more than 200 health researchers concluded that a quarter of clinical trials conducted in developing countries do not undergo ethical review. The survey was commissioned by the former US National Bioethics Advisory Commission and published in February's edition of the *Journal of Medical Ethics* (2004;30:68-72).

John Williams, director of the ethics section of the World Medical Association in Paris, said drug approval agencies in developed countries such as the US Food and Drug Administration and EMEA (European Agency for the Evaluation of Medicinal Products) require ethics committee approval of trials for the sale and distribution of any drug.

"These are strong incentives to seek such approval," Professor Williams said, adding that editors of major journals also require such approval for studies submitted for publication.

"There are efforts under way to strengthen ethical review throughout the world through SIDCER and its regional committees," Professor Williams said, referring to the Strategic Initiative for Developing Capacity in Ethical Review, an international project to develop the ethical review of biomedical research globally.

WHO has been involved in this project and in October 2002 opened its own ethics unit, whose goals include harmonizing ethical review standards for clinical trials and ensuring such studies are effectively regulated in WHO's 192 Member States.

"This is a problem for many countries, not only developing countries," said Dr Marie-Charlotte Bouësseau from WHO's department of Ethics, Trade, Human Rights and Health Law.

Most, but not all developing countries have ethical review committees in the form of research institutes or other scientific panels. "WHO has already been working with many countries in Latin America and Asia to make their ethical review committees work more effectively and recently started working with several African countries too," said Bouësseau.

"We need to provide training to ensure that these panels are independent and able to review clinical trials without prejudice," she said.

The Letrozole case illustrates this problem well. Dr Gulhati said pharmaceuticals in India often have a "cosy relationship" with regulators and bribe researchers, hired to conduct purportedly independent clinical trials, with expensive gifts like cars, paid speaking engagements, over-paid consultancy work and free overseas holidays. He said there was no independent safety monitoring of clinical trials and that participants sometimes do not even know they are participating in tests.

"Neither the regulatory authorities nor the Ethics Committees seek conflict of interest information from investigators," Dr Gulhati said, adding: "Most of the clinical trials here are conducted without any arrangement for compensation in case of study-related injury, disability or even death."

These initiatives come at a time when pharmaceuticals and biotechnology companies try to save time and money by conducting clinical trials in developing countries, where there are plenty of willing subjects and often more relaxed regulatory regimes.

Dr Eugene Braunwald of Harvard Medical School, who is chairman of a clinical trials group of doctors, told the *New York Times* recently that half as many US patients are enrolling in clinical trials compared to five years ago.

The trend of outsourcing clinical trials to developing countries has sparked concerns about unscrupulous biotech and drugs firms exploiting the healthy, in the hope of earning some cash, and the sick, who hope to get free treatment.

A key question for regulators is whether US drug manufacturers should apply FDA standards when they conduct trials abroad. This will be less of an issue once developing countries tighten laws and make their ethical review panels truly independent. ■

Fiona Fleck, *Geneva*

Contributions are welcome for the Letters section, in response to articles that have appeared in the *Bulletin* or on matters of major public health importance. Letters are usually between 400 and 850 words, with a maximum of six references; they will be edited and may be shortened.

Manuscripts should be submitted to the *Bulletin* via our submissions web site accessed at http://submit.bwho.org or via a link from www.who.int/bulletin where there are "Help" and "FAQ" (frequently asked questions) buttons to assist authors.