

## HIV/AIDS surges in Eastern Europe — Asia-Pacific next?

Twenty years after physicians first spotted the immune deficiency disease that became known as AIDS, the state of the worldwide AIDS epidemic is stirring both dismay and hope, judging from the latest *AIDS Epidemic Update* released on 28 November by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and WHO.

In Eastern Europe and Central Asia, HIV infections are rising faster than anywhere in the world — an estimated one million people were living with HIV/AIDS there in 2001, up from 700 000 the year before — and “a huge epidemic may be imminent” in parts of the former Soviet Union, the UNAIDS/WHO report says. In Asia and the Pacific, low national incidence rates hide “serious” local epidemics that could break into the general population, particularly in China, where as many as one million people may already be infected. In the US, Western Europe, Canada and Australia, complacency is replacing the safer-sex ethic “promoted so successfully for much of the 1980s and 1990s”, posing the threat of resurgent epidemics.

Worldwide, an estimated five million people were newly infected with HIV in 2001 (vs 5.3 million in 2000) and an estimated 40 million people (vs 36.1 million) are believed to be living with the virus — 70% of them in sub-Saharan Africa, the hardest-hit region.

“This is very bad news,” said Dr Gro Harlem Brundtland, Director-General of WHO, in a 29 November statement. “But there is good news, too.” On the upside is evidence that prevention programmes work, that aggressive harm-reduction efforts can restrain HIV/AIDS outbreaks. Thailand’s “well-funded, politically supported and comprehensive prevention programmes” have trimmed new HIV infections from about 140 000 annually a decade ago to about 30 000 annually today. Cambodia’s campaign, too, against high-risk sexual behaviour has reduced HIV prevalence among pregnant women from 3.2% in 1997 to 2.3% in 2000, “suggesting that the country is beginning to bring its epidemic under control”.

Similar harm-reduction programmes have curtailed HIV among intravenous (IV) drug users in Poland and have posted successes even in sub-Saharan Africa. Urban men and women in Zambia report fewer sexual contacts and more condom use. HIV prevalence rates among South African adolescents have dropped slightly since 1998. And in Uganda, “the first African country to have subdued a major HIV/AIDS epidemic”, prevalence rates among pregnant women in urban areas have fallen for the past eight years running, from a peak of 29.5% in 1992 to 11.25% in 2000.

“When there’s the will and commitment from all different sectors — from the political to the religious sectors — it’s possible to reverse the epidemic,” says Dr Jesus Maria Garcia Calleja, a UNAIDS epidemiologist in Geneva, Switzerland. “It’s not a question only of money. It’s a question of the country getting involved in the fight against HIV/AIDS.”

Massive prevention efforts could avert “a much larger and more generalized epidemic” in Eastern Europe and Central Asia, the UNAIDS/WHO report says, because the outbreak there is still at an early stage. Although diagnosed AIDS cases have risen dramatically over the past two years in the Russian Federation, the epidemic is still centred among IV drug users, not just in Russia but also in Ukraine and several Central Asian countries. However, a high proportion of IV drug users are sexually active young men, raising the prospect that HIV infection might explode into the broader population.

What is needed is “a comprehensive response to reduce risky sexual and drug-injecting behaviour among young people, and to tackle the socioeconomic and other factors that promote the spread of the virus,” the report says. It points to signs that governments in the region are planning such an effort.

“The coming year can be the turning point in the fight against this global epidemic,” says WHO’s Brundtland. But she warns that “it will be a long fight.” Dr Peter Piot, UNAIDS executive director, cautions: “It will get worse before it gets better.” ■

Bruce Agnew, *Bethesda, Maryland, USA*

## Haemoglobin variant gives strong protection against malaria



WHO/TDR/Mark Edwards

With a double dose of the haemoglobin C gene, this baby recovering from malaria in a West African hospital might well have escaped the disease.

A genetic variation of haemoglobin, the oxygen-carrying protein found in red blood cells, can almost completely abolish the risk of falciparum malaria, the most lethal form of the disease, according to a study in West Africa reported by African and Italian researchers in the 15 November issue of *Nature*. Having two copies of the gene for the variant, called haemoglobin C, provides “almost complete protection” against the disease, according to malaria researcher and study team leader Dr Mario Coluzzi of the University of Rome La Sapienza.

Moreover, haemoglobin C comes with few unhealthy strings attached. Mild anaemia and, in some adults, gallstones are the only adverse effects. “Compared to all other red blood cell mutations that protect against malaria, haemoglobin C is not associated with serious health problems,” says Dr David Modiano, lead author of the study.

Scientists have known for years that another version of the haemoglobin gene, haemoglobin S, shields against malaria by crippling the red blood cells that malaria parasites need to survive. The abnormal haemoglobin distorts red blood cells into a sickle shape, and these misshapen cells along with any parasites they contain are destroyed by the spleen. But with haemoglobin S, malaria protection comes

at a cost. People with two copies of the haemoglobin S gene often develop potentially lethal sickle-cell anaemia.

Earlier work by other research teams, including an epidemiological study in Mali and laboratory experiments on parasite proliferation, had suggested a link between haemoglobin C and malaria resistance, but the results were inconclusive. The Rome team confirmed the protective effect of haemoglobin C by studying the blood of 4348 children of the Mossi ethnic group in Ouagadougou, Burkina Faso. The majority of the participants were healthy, but 835 of them had malaria caused by the parasite *Plasmodium falciparum*. The scientists determined which forms of the haemoglobin gene each child had inherited.

When the researchers compared the genetic data between the healthy and sick children, they found far fewer haemoglobin C genes among the sick patients. Statistical analysis predicted that 14 of the sick children would have two copies of the haemoglobin C gene if the variant offered no protection against the disease. Instead, only one sick child had a double dose of the gene. Based on their findings, the scientists calculate that having a haemoglobin C gene paired with a normal haemoglobin gene reduces the risk of malaria by 29% compared to having two normal haemoglobin genes. Having two copies of the haemoglobin C gene reduces the risk by a huge 93%. That is slightly more protective than the 73% risk reduction experienced by people having a normal haemoglobin gene paired with a haemoglobin S gene (HbAS genotype), and certainly more protective than the approximately 67% protection afforded by having two copies of the haemoglobin S gene (HbSS), although the lethality of that genotype clearly offsets its protective effect.

Modiano and his colleagues are currently conducting a study of more than 5000 people, children and adults, in Burkina Faso to find out whether haemoglobin C merely keeps the disease in check or if it totally blocks infection. How the haemoglobin could accomplish either task remains a mystery. The abnormal protein might produce slight changes in the way antigens are exposed on the surface of red blood cells, says Modiano. Determining how haemoglobin C fends off malaria might guide the development of vaccines and better

treatments that safely mimic the mechanism of action involved. ■

Charlene Crabb, *Paris, France*

## Anti-inflammatory drugs slash Alzheimer risk

Extended use of nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, may reduce the risk of developing Alzheimer disease by as much as 80%, according to a seven-year prospective study published on 22 November in the *New England Journal of Medicine (NEJM)*. If these results are confirmed in prevention trials, the drugs could have an enormous public health impact, say experts.

“Given the global spread of this disease, with about 11 million sufferers of Alzheimer dementia worldwide,” says WHO mental health expert Dr José Bertolote, “any evidence such as this clearly has the potential to be of public health significance. We have to be hopeful, however, that these early findings will live up to the expectations they raise.”

The new study, conducted by researchers at Erasmus University Medical School in Rotterdam, the Netherlands, followed nearly 7000 people over an average of just under seven years. All subjects were aged 55 or older and free of dementia at the beginning of the study. The researchers evaluated the mental and neurological health of the participants at the beginning, middle and end of the study. Throughout the study, the researchers used computerized pharmacy records to keep track of the subjects’ NSAID use. (NSAIDs were available only by prescription in the Netherlands during most of the study.)

Analysis revealed that study participants who used NSAIDs for two or more years were 80% less likely to develop Alzheimer disease compared to people who didn’t use the drugs. Ibuprofen, naproxen, and diclofenac were the most popular NSAIDs, together accounting for about 83% of the total number of NSAIDs taken by participants in the study.

This isn’t the first study to find a link between NSAIDs and Alzheimer risk. “There have been at least 20 epidemiological studies looking at NSAIDs and Alzheimer disease,” Dr Peter P. Zandi of Johns Hopkins University in

Baltimore, Maryland, USA, told the *Bulletin*. But this latest study is especially strong because it was prospective, involved a large population group, included a long follow-up period, and gathered data from pharmacy records rather than relying on the subjects’ memory of past NSAID use, Zandi and his colleague at Johns Hopkins, Dr John Breitner, wrote in an accompanying editorial in the *NEJM*.

It is unclear how NSAIDs might decrease Alzheimer risk. Inflammation is believed to be involved in Alzheimer. For this reason, “we think that inhibition of inflammation [by these drugs] may play a role”, Dr Bruno Stricker, senior author of the study, told the *Bulletin*. But that is only one hypothesis. A study recently published in the 8 November issue of *Nature* suggested that NSAIDs might lessen Alzheimer risk by reducing brain levels of amyloid- $\beta$ , a protein that accumulates in the brains of people with the disease. The exact mechanism by which these drugs might achieve this result is not entirely clear, but blockage of an enzyme involved in the production of amyloid- $\beta$  is one possibility.

For now, the ability of NSAIDs to prevent Alzheimer disease awaits verification from clinical trials under way. “Widespread use [of NSAIDs for this purpose] should be discouraged until prospective double-blind randomized trials have confirmed this and have assessed the ideal dose and benefit/risk ratio,” Stricker told the *Bulletin*.

But if the benefits of NSAIDs are validated in further trials, the public health gains would be huge. “If a particular drug can be proven to prevent Alzheimer disease, it would have a tremendous public health impact,” Dr Neil Buckholtz, Chief of the Dementias of Aging Branch of the National Institute on Aging in Bethesda, Maryland, USA, told the *Bulletin*. “People have estimated that if you delayed the onset of Alzheimer by five years, you would decrease the number of people with the disease by half and cut the cost too.”

Those numbers could quickly add up. WHO estimates that by the year 2025 more than 22 million people worldwide will have Alzheimer disease. ■

Christie Aschwanden,  
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## WHO attacks tobacco sponsorship of sports



PHOTO DPAC/Oliver Multhaup

Thumbs up for Michael Schumacher (left) and Eddie Irvine for their performance at a recent Grand Prix championship, but thumbs down by WHO for Big Tobacco sponsorship of this and other sports.

In late November, WHO joined forces with the international governing bodies of motor racing, football, and the Olympic Games, as well as with well-known athletes, in a drive to sweep Big Tobacco out of sporting arenas worldwide. The launch of the “Tobacco Free Sports” campaign, as this drive is called, coincided with the gathering in Geneva of government representatives of WHO’s 191 member states for the third round of negotiations on the Framework Convention on Tobacco Control (FCTC), an international treaty that seeks, among other things, strong controls over global advertising and sponsoring activities by the tobacco industry.

“Tobacco is a communicated disease. It is communicated through advertising and sponsorship. The most pernicious and pervasive form of that marketing is found in sports stadiums and arenas worldwide,” said WHO Director-General Dr Gro Harlem Brundtland at the launch.

The main goal of the campaign, Dr Derek Yach, WHO executive director for noncommunicable diseases and mental health, told the *Bulletin*, is “to keep tobacco products out of

sporting events and to encourage more people, especially young ones, to engage in sports. We want to get rid of a bad thing and promote a good one because we see that the two just don’t mix. It’s an unhealthy association.”

Mr Johann Koss, Norwegian four-time Gold Medallist in speedskating and chairman of Olympic Aid, an athlete-led humanitarian nongovernmental organization, couldn’t agree more. “Tobacco and sport do not belong together. As athletes and role models, we will try to eliminate all forms

of tobacco in all levels of sport,” he commented to the *Bulletin*.

What’s more, adds Yach, linking the sport’s excitement to smoking makes sporting events the number one route for tobacco manufacturers to target the world’s youth. Experts estimate that tobacco companies pump at a minimum tens of millions of dollars each year into sponsoring major sports events. In the United States alone, according to the US Federal Trade Commission, the major domestic cigarette companies reported spending more than US\$ 110 million on sporting events in 1999. And their strategy seems to pay off. When British American Tobacco (BAT) took over sponsorship of the India–New Zealand cricket series held in India in 1996, a survey conducted a few months later in the Indian state of Goa (and published in the 17 August 1996 *British Medical Journal*) showed that the likelihood of children experimenting with tobacco almost doubled.

About a year ago, WHO started approaching leading sports organizations to try and hammer out a plan to ban tobacco sponsoring for all major sporting events. For the 22 November launch WHO had teamed up with the CDC, the International Olympic Committee (IOC), the Fédération Internationale de Football Association (FIFA), and the Fédération Internationale de l’Automobile (FIA).

It seems that WHO’s ideas are falling on fertile ground. The FIA plans to introduce a worldwide ban on

### Science historian predicts a billion deaths from tobacco by end of the century

- In a recent study published in the October issue of *Nature Cancer Reviews*, science historian Professor Robert Proctor from the Pennsylvania State University predicts that, if left unchecked, tobacco products will cause up to one billion deaths by the end of the 21st century.
- From historical sources Proctor calculated that there is about one lung cancer death for every three million cigarettes consumed worldwide. In 1990 world consumption already amounted to 6 trillion cigarettes per year. By current global smoking rates and future trends, smoking will have killed about one billion people by 2100, according to Proctor’s calculation.
- Already today, tobacco is responsible for the deaths of more than four million people every year. By 2020, WHO estimates, the toll will be around 8.4 million per year and by 2030, could reach 30 million, mainly because of the increase in smoking in developing countries. By 2020, 70% of smoking-related deaths will occur in developing countries.

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Poster of the international *Tobacco Free Sports* campaign.

tobacco advertising and sponsoring in all FIA-sponsored events from the end of the 2006 season, following a resolution of FIA's World Motor Sport Council from October 2000. This ban includes the FIA's cash cow, Formula One, which enjoys at least US\$ 350 million in tobacco sponsorship, according to an FIA estimate: this is widely believed to be more than is spent on tobacco sponsorship of any other single sport.

The FIFA and the IOC are one step further ahead. Since the late 1980s, the Olympics and the soccer World Cup have been tobacco-free, and the kick-off of the upcoming World Cup in Japan and Korea on 31 May 2002 will coincide with WHO's World No Tobacco Day. A perfect opportunity to spread the message, Yach notes. "The World Cup will be the most watched sporting event ever; it has an enormous power to influence people," he says.

WHO's concerted effort to make sports smoke-free comes on the heels of a similar proposal from tobacco manufacturers themselves. On 10 September, BAT, Philip Morris and Japan Tobacco announced a new code of conduct on international marketing standards to prevent sales activities specifically tailored to appeal to young people. The voluntary measures, due to come into force in early 2003, would eliminate sponsorship of sporting events, advertising on the Internet, TV and radio, and celebrity endorsements.

So why does WHO need its Tobacco Free Sports campaign? "Tobacco

companies can't be trusted," says WHO's Yach. "We urge governments not to accept any self-regulation. They haven't worked in the past and they won't work in the future," he says. For Yach, the announcement of voluntary marketing restrictions is "just another attempt by the industry to persuade governments that there's no need for a strong framework convention".

Currently under negotiation, the framework convention would be the first legally enforceable international treaty on tobacco control attempting to curb deaths from smoking-related illnesses, which, according to WHO estimates, kill about four million people each year [see Box]. With the third round of negotiations completed in late November, Yach is cautiously optimistic: "The basis for a really strong convention is there," he says. Talks will resume next March. Yach thinks that negotiations are "still on target" for the convention to be completed in time for adoption by the World Health Assembly in May 2003. ■

Michael Hagmann, *Zurich, Switzerland*

## WHO head visits DPR Korea

On her first visit to the Democratic People's Republic of Korea in mid-November, WHO Director-General, Dr Gro Harlem Brundtland, found a country struggling with a daunting catalogue of deprivation: "They are poor, they have a big burden of disease,

and children are suffering," she told journalists after her visit.

The main purpose of Brundtland's visit was to open a permanent WHO office in Pyongyang, the capital, where only three other UN organizations have a permanent representative — the World Food Programme, the United Nations Development Programme, and UNICEF. During her visit she met with Mr Kim Yong Nam, President of the Praesidium of the Supreme People's Assembly, Foreign Minister Mr Kim Yong Nam, and Health Minister Dr Kim Su Hak.

Outside of major cities, medical resources, she noted, particularly medicines, are sorely lacking, as are other essentials, such as clean running water and electricity. There is also a lack of reliable information: "We don't have a full picture of everything ... we don't have concrete numbers."

What information there is, however, suggests that some malnutrition persists despite food aid and a better harvest this year. Diseases related to malnutrition are certainly rife, particularly among children. The country is also facing an upsurge of malaria — an estimated 300 000 cases have occurred this year — as well as of tuberculosis, which currently affects about 33 000 people. Overall mortality has also been on the upswing and the current mortality rate is about 30–40% higher than 15 years ago, equivalent to an increase from 1.4 million to 2 million deaths a year in a population of 22 million.

Brundtland said the country "will need to give health a higher priority and channel more of its own resources towards ensuring that basic health services can be provided. But it cannot do so on its own." WHO has appealed to the international community to donate US\$ 8 million to restoring what in the 1960s and 1970s was an extensive, well-functioning health system providing free care to all. ■

John Maurice, *Bulletin*