News

Viral load best predictor of HIV transmission

The higher the concentration of human immunodeficiency virus type 1 (HIV-1) in the bloodstream, the greater the risk of transmitting the virus to a partner during heterosexual intercourse, a large study conducted in sub-Saharan Africa has found. The number of copies of HIV-1 ribonucleic acid (RNA) in the blood, an indicator of viral load, was a better predictor of whether transmission would occur than many other factors, such as the presence of other sexually transmitted diseases (*New England Journal of Medicine*, 2000, **342**: 921–929).

Thomas C. Quinn, Professor of Medicine at Johns Hopkins University in Baltimore, MD, said the study found a clear dose–response relationship between viral load and transmission. "For every 10-fold rise in the concentration of HIV in the bloodstream, transmission more than doubled," he said.

Conducted in the Rakai district of Uganda by researchers from the United States and Uganda, the project involved following 415 couples where only one partner was HIV-positive. All participants received free condoms, voluntary confidential HIV testing and counselling, as well as health education directed at preventing HIV transmission. Researchers visited the couples at 10-month intervals for up to 30 months. At each visit, the participants gave blood samples and these were later tested to determine HIV viral load. Over the period of the study, 90 (22%) of the previously uninfected partners became HIV-positive. Analysis of the blood tests showed that in nearly 80% of these cases, the viral load of the infected partner was above 10 000 copies of HIV-1 RNA/ml of blood. No one who had fewer than 1500 copies of HIV-1 RNA/ml of blood transmitted the virus to his or her partner.

Quinn added that the findings were "strikingly consistent" with studies of viral load in cases of mother-to-child HIV infection. He said: "Theoretically, just as drugs have helped reduce perinatal transmission, antiretroviral regimens that dampen HIV viral load should also be effective against heterosexual transmission of HIV. But we need more studies to confirm this".

Nelson Sewankambo, Dean of Medicine at Makerere University in Uganda and the principal investigator in Uganda for the study, said its findings demonstrated the need to develop "low-cost and feasible methods of reducing viral load for use in resource-poor settings". The study also showed that male circumcision may also play a part in controlling the spread of HIV. Among the 187 seronegative men who had HIV-positive partners, none of the 50 who were circumcised became infected, compared to 40 of the 137 who were not circumcised.

Commenting on the paper in an accompanying editorial (*New England Journal of Medicine*, 2000, **342**: 970–972), Myron S. Cohen of the University of North Carolina at Chapel Hill, NC, said this finding might lead countries where HIV-1 is endemic or epidemic to consider promoting circumcision for its public health benefits. But he added: "However, the promotion or institution of a procedure that has profound cultural implications, risks of complications and benefits that are realized only decades later represents a formidable public health and political challenge". ■

Sharon Kingman, *London*

Japan launches nursing insurance scheme for the elderly

Japan took a major step towards caring for the world's fastest ageing population in April with the introduction of an ambitious new nursing insurance scheme. Modelled on a similar set-up in Germany, the Nursing Care Insurance System makes elderly people more responsible for the costs of their care and encourages the private sector to enter the nursing market. The scheme is designed to lower the government's medical bill, which is rising at the rate of 1 trillion yen (US$ 9.5 billion) per annum, and to make up for a shortage of care-providers.

Each year, 100 000 people are forced to give up their jobs to nurse elderly family members and with the population set to start shrinking within the next five years, the ratio of workers to retirees is expected to fall to 2:1 by 2025, from the current ratio of 4:1. Under the scheme, people over the age of 64 will have to pay 10% of their nursing costs as well as a monthly premium of about US$ 29. In return, they will be entitled to care worth up to US$ 4000 per month depending on circumstances. Limited cover will be available to those aged between 40 to 64.

The complex scheme has got off to a bumpy start. A month before it was to begin, municipal officials faced a backlog of about 700 000 applications. According to a poll by the *Asahi* newspaper, 84% of respondents were unaware of the cover provided. Worried by the political implications, the government has delayed collection of the premiums that are supposed to fund the scheme until after the next election, which must be held by October.

It is not just developed nations that have an interest in the outcome of the scheme, which should reduce the burden on Japan's near bankrupt medical insurance system by US$ 22 billion a year. In China, the proportion of the population aged over 64 has grown from 7% to 14% in just 27 years. The same increase took France more than 115 years.

Nursing insurance is also only part of the solution. In April, the Japanese government cut pensions by 5% and enacted a law to raise the retirement age from 60 to 65 by 2025. The ruling Liberal Democratic Party has initiated moves to allow more foreign nurses to immigrate to Japan. However, political considerations have forced the government to postpone reform of the entire medical insurance system which is widely considered to be the most important change of all. ■

Jonathan Watts, *Tokyo*

New guidelines for treatment of latent tuberculosis infection

New guidelines on the testing and treatment of persons with latent tuberculosis infection have been issued by the American Thoracic Society (ATS) and the Centers for Disease Control and Prevention (CDC). Prepared by a panel of 47 scientists, the document suggests several important changes from previous guidelines and practices (*American Journal of Respiratory and Critical Care Medicine*, 2000, **161**: 221–247).

After further analysis of earlier clinical trials, the new guidelines recommend nine months of daily treatment with isoniazid for adults with latent tuberculosis infection regardless of whether the patient is infected with human immunodeficiency virus (HIV). The document also strongly discourages widespread tuberculin screening or testing of persons at low risk of tuberculosis. Instead, targeted tuberculin testing is recommended for latent tuberculosis infection to identify individuals at high risk of tuberculosis who, if found to be infected, would benefit from the recommended treatment. Persons at highest risk include those with recent tuberculosis infection and those with clinical conditions that are associated with an increased risk for progression to active tuberculosis.

The guidelines include several criteria for different risk groups that define a positive tuberculin test. Children should be screened, if possible by use of a questionnaire, for risk factors for tuberculosis infection. Those at risk are candidates for tuberculin skin tests, which should be interpreted according to the criteria for adults with the exception that a reaction of greater than or equal to 10 mm of induration should be considered as a positive test in children of less than four years of age. The only recommended regimen for treatment for tuberculosis infection in infants, children and adolescents is nine months of isoniazid taken daily (self-supervision) or twice weekly (directly observed therapy).

According to the guidelines, no available data exist to support the use of the other adult regimens in children. Although isoniazid has been the mainstay of treatment for latent tuberculosis infection for more than 30 years, its application has been limited because of poor adherence and because of concerns about toxicity. Recent clinical trials in HIV-infected persons have evaluated shorter, rifampicin-based regimens for latent tuberculosis treatment. Based on these studies, the guidelines recommend a possible two-month regimen of rifampicin and pyrazinamide for use in both HIV-positive and HIV-negative adults.

Dr Cohn emphasized "more data will be needed to determine the acceptability of this regimen in HIV-negative patients". Dr O'Brien stressed that more work would be needed to determine if these guidelines work in practice and if they apply to developing countries. The ATS/CDC statement can be found on the Internet at http://www.thoracic.org/statementframe.html ■

Tudor Toma, *New York*

Guidelines on health databases must consider developing countries

Developing countries must be given special consideration when drawing up guidelines on centralized health databases, warned delegates of the World Health Organization and the World Medical Association at a joint seminar on the ethical implications and optimal design of centralized health databases. The seminar was held in May at the headquarters of WHO, in Geneva.

"WHO has a special responsibility for developing countries, where regulatory frameworks and technical expertise may be scarce, and the level of public awareness, education, and sophistication may be low," explained Dr Daniel Wikler, senior ethicist at WHO. "Developing countries must receive particular attention because current initiatives in wealthy countries might serve as precedents for similar undertakings in developing countries. The interests of developing countries need special attention also because firms and agencies now gaining experience in developed countries may turn to populations in poorer countries in the course of research initiatives".

Representatives from both organizations debated whether producing international ethical guidelines on the use of health databases would be a valuable next step in protecting the public and allowing scientific research to continue. Health databases have been an indispensable resource for researchers over many years, but recent progress in genetics has sparked public fears that the information on these databases could be abused.

Only last year, the government of Iceland awarded a private company, deCODE genetics, an exclusive licence to establish a database of genetic and genealogical data for the whole population. Because of its unique history — mostly of isolation — Iceland is of particular interest to researchers. The ethics of awarding the licence to a private company have been questioned, however.

"Centralized health databases can make a tremendous contribution to the improvement of health through a better scientific understanding of the causes of disease and illness," said Dr Anders Milton, chairman of the World Medical Association. "But the public's right to privacy and consent are essential to the trust and integrity of the patient/physician relationship. Guidelines must address the issues of informed consent, privacy, confidentiality, individual access, and accountability on the part of the owner of the database".

A working group from the World Medical Association will present draft guidelines to the World Medical Association's annual general meeting at Edinburgh in October 2000. ■

Kamran Abbasi, *Bulletin*

EU adopts legislation to promote drug development for rare diseases

The European Union (EU) Executive Commission adopted legislation to stimulate the development of drugs for rare diseases on 27 April 2000. Pharmaceutical companies may now apply to the European Agency for the Evaluation of Medicinal Products (EMEA) to designate pharmaceuticals as "orphan medicinal products". Under the new legislation, companies will be able to request reductions in the fees for market authorizations and for changes requested after registration has been granted. Companies whose products are granted orphan drug status will be entitled to a 10-year period of market exclusivity.

Fernand Sauer, Executive Director of the EMEA, comments: "The prospect of obtaining a 10-year period of market exclusivity for orphan medicinal products in the European Union will provide a strong incentive for sponsors to develop and market orphan medicinal products". He added: "Pharmaceuticals intended to treat diseases which may have high prevalence in some developing countries, but which are classified as rare in the European Union, such as malaria, may also be designated as orphan medicinal products".

Similar legislation was adopted in the United States in 1983, where the inclusion of tax incentives for companies proved to be effective. However, such incentives are not possible in the EU due to the absence of a centralized system of taxation. The Committee for Orphan Medicinal Products, which was established in 1999 and which is the first institutional committee of the EU to include representatives of patient organizations as full members, has been instrumental in introducing the new legislation. Sauer notes: "To date, the EMEA has received seven applications for orphan medicinal product designation. A further 35 sponsors have indicated their intention to submit applications". ■

Barry Whyte, *Bulletin*