News

Cost-effective HIV treatment for developing countries

Researchers have hailed as a major advance the discovery that just two doses of an antiretroviral drug, nevirapene, can sharply cut the risk of passing HIV from mother to child for as little as US$ 4. But some scientists have questioned a controversial suggestion by the authors of the joint Uganda–United States study, whose results were released in mid-July, that all pregnant women in high-prevalence areas could be treated with the drug, regardless of whether they know their HIV status.

In most low-income countries, between 25% and 35% of babies born to HIV-positive women become infected, according to the Joint United Nations Programme on HIV/AIDS (UNAIDS). The programme estimates that as many as 1800 babies become infected every day, 95% of them in Africa. About two-thirds are infected during late pregnancy and birth, and the remainder through breastfeeding. In the industrialized countries, women who have treatment with antiretroviral drugs during pregnancy, and who avoid breastfeeding, can reduce the risk of infecting their babies to 5% or lower. But in poorer settings, such treatment — which costs up to US$ 1000 — is rarely available or practicable.

Three years ago, researchers in Thailand found that a less expensive course of zidovudine (AZT) administered during the last month of pregnancy and the first week of the infant's life could cut the risk of mother-to-child transmission by 50%, raising hopes that more babies worldwide might be spared infection. Then, earlier this year, a multicentre trial in several African countries, coordinated by UNAIDS and known as PETRA, showed that an even shorter course of AZT plus another drug, lamivudine (3TC), could cut the risk by about a third, even when women breastfed.[a] But even this approach relies on beginning treatment in the last week of pregnancy, whereas many women in African countries may not attend a clinic until they are in labour.

Now researchers at Mulago Hospital, Kampala, and colleagues in the USA led by a team at Johns Hopkins University, Baltimore, have tested a simpler regime. They assigned women at random to one of two groups. The first received a single dose of nevirapene in labour and their infants received another dose within three days of birth. The second group received a series of doses of AZT during labour and their babies received regular twice-daily doses for a week after birth. In the nevirapene group, 13.1% of babies were infected by 16 weeks of age, compared with 25% in the AZT group. Nevirapene therefore cut the transmission rate by 47% compared with the short course of AZT.[b] The costs of the drug are estimated to be just US$ 4. "The implications of this study for developing countries, where 95% of the AIDS epidemic is occurring, are profound," said Dr Brooks Jackson, lead investigator at Johns Hopkins, when the results were announced by the US National Institute of Allergy and Infectious Disease, which funded the trial.

The researchers immediately suggested that in areas where HIV infection rates are high, all women might be given the treatment in labour, regardless of whether they know their HIV status or not. UNAIDS estimates that as many as nine out of every 10 infected women in sub-Saharan Africa may be unaware that they are infected. However, the idea of mass-treatment worries some researchers. "For a start, even at US$ 4, it is going to be too costly," says Marie-Louise Newell, an epidemiologist and coordinator of a major European study of mother-to-child HIV transmission at the Institute of Child Health, University College London Medical School. "But also, this approach does not inform a woman about her HIV infection, and so reduces her ability to cope with her own life or to reduce the risk of transmission to others." Others agree that the best principle remains to offer women voluntary testing and counselling, and treatment if they are found to be positive. The priority remains to prevent young adults from becoming infected in the first place.

Meanwhile, the risk to infants of infection through breast milk remains. The coordinators of the Uganda–United States trial plan further research to discover whether continued weekly doses of nevirapene over the first few months of the infant's life can protect against infection via this route. ■

End of the line for tuberculosis "therapy"

Years after the first claims for its usefulness were made, an experimental immunotherapy for tuberculosis has been shown to have no effect, quashing any hopes that it would help to reduce the burden of the world's biggest single microbial killer.

In earlier, widely publicized studies, researchers had claimed that vaccination with *Mycobacterium vaccae*, a bacterium related to *M. tuberculosis*, boosted tuberculosis patients' immune responses and hastened their recovery. But the first randomized controlled trial of the therapy, in Durban, South Africa, has found that patients given *M. vaccae* alongside their standard short-course drug treatment fared no better or worse than those given drug treatment and a placebo.

More than 370 people in Durban with newly diagnosed pulmonary tuberculosis were allocated at random to receive either standard drugs and a placebo injection or standard drugs and an *M. vaccae* injection on the eighth day of therapy. After eight weeks, 65 patients in the placebo group had a negative sputum culture, compared with 70 in the *M. vaccae* group. There was no difference in the time taken to achieve the first negative sputum culture between the groups. The Durban Immunotherapy Trial Group reported the results this summer.[c] "Frankly, there is no evidence of its utility," Paul Fine, a member of the group at the London School of Hygiene and Tropical Medicine, told the *Bulletin*. Results of a larger trial involving some 1200 patients are due to be reported at two tuberculosis conferences in mid-September.

[a] Shorter short-course treatment protects some infants from HIV. *Bulletin of the World Health Organization*, 1999, **77** (4): 362 (http://www.who.int/bulletin/news/vol.77no.4/short-coursehiv.htm).

[b] National Institute of Allergy and Infectious Diseases, Department of Health and Human Services, press release 14 July 1999 (http://www.niaid.nih.gov/cgi-shl/simple/release.cfm).

[c] **Durban Immunotherapy Trial Group**. Immunotherapy with *Mycobacterium vaccae* in patients with newly diagnosed pulmonary tuberculosis: a randomised controlled trial. *The Lancet*, 1999, **354**: 116–119.

Lee Reichman of New Jersey Medical School in Newark[d] says that the earlier claims for *M. vaccae* may have been based on poorly designed trials. He calls for more urgent efforts to improve prevention and treatment of tuberculosis. ■

EMBO raises objection to E-biomed plans

The European Molecular Biology Organization (EMBO) says it will not be involved in any efforts to set up an electronic depository for non-peer-reviewed biomedical research. The announcement, in a statement posted on EMBO's website,[e] came in response to proposals for the electronic publication of all biomedical research, being developed by the National Institutes of Health (NIH).[f, g] EMBO, with headquarters in Heidelberg, Germany, supports the principle of a single electronic website where all life-sciences data are readily searchable and says that the question of its existence has long been "when, rather than whether". But the organization's executive director, Frank Gannon, says that a depository for material without peer review, which forms a key part of the NIH's proposal, could "severely undermine biomolecular research", and should therefore be monitored. EMBO has proposed that, alongside the two categories proposed by the NIH — that is, fully refereed and non-refereed material — a third should be set up with a panel of assessors to check that researchers' science is sound, without all the further requirements of traditional peer review. ■

Vitamin A supplements and malaria symptoms

Simple supplements of vitamin A may reduce the severity of malaria symptoms, according to a study of children in Papua New Guinea. If this finding is confirmed, researchers believe it could herald an "effective and low-cost strategy" to reduce the grip of the disease on endemic areas.

Vitamin A is vital for the normal function of the immune system. However, many children in malaria-endemic areas do not obtain sufficient amounts of this micronutrient from their diet, so that their immune systems are compromised. Earlier research has shown that vitamin A supplementation, which is very cheap, can reduce the morbidity of some other infectious diseases. So researchers in Papua New Guinea and the USA decided to find out whether malaria symptoms, measured by the number of febrile episodes, could also be cut with this approach. In a randomized controlled trial they found that children given regular high-dose vitamin A supplements for just over one year suffered 30% fewer febrile episodes than children who received placebo.[h] Children who received the supplements also had lower densities of the *Plasmodium falciparum* parasite. ■

[d] **Reichman LB**. Whither *Mycobacterium vaccae*? *The Lancet*, 1999, **354**: 90.

[e] http://www.embo.org/EI_Pub.html

[f] http://www.who.int/bulletin/news/vol.77no.7/ebiomed.htm

[g] The *Bulletin* notes that the E-biomed proposal is undergoing rapid changes, including a possible change of name to E-biosci. These modifications may address the objections raised by EMBO and other interested parties.

[h] **Shankar AH et al.** Effect of vitamin A supplementation on morbidity due to *Plasmodium falciparum* in young children in Papua New Guinea: a randomised trial. *The Lancet*, 1999, **354**: 203–209.