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Microbicides strike an upbeat note

The Microbicides 2004 conference (London, UK; March 28–31) ended in upbeat mood with the prospect of three or four phase III clinical trials starting this year. Two of these recently began, and a large-scale trial of two microbicide gels—dextrin sulphate (EmmelleR) and Pro-2000/5—will begin later this year in several African countries including South Africa, Tanzania, and Zambia.

The trial, organised jointly by the UK Medical Research Council (MRC) and Imperial College London, through the government-funded Microbicides Development Programme, will recruit about 12 000 women and is expected to last 3 years. Both trial drugs are polyanions, which are thought to inhibit HIV infectivity by interacting with surface glycoproteins.

Microbicides, first developed nearly 20 years ago, fell into disrepute when a vaginal gel containing nonoxynol-9, already registered as a spermicide, was found to enhance, not inhibit, viral transmission. But interest in micro-

bicides has resurfaced as prospects for a vaccine against HIV recede. Around 60 candidate vaginal microbicides are in development, and they work in various



Soweto women can benefit from microbicides

ways. Some prevent the virus from attaching to and infecting human cells, some inhibit viral replication, some (non-specific surface-acting agents) directly inactivate the virus, and others boost the natural vaginal defences.

Whatever the mode of action, vaginal microbicides—formulated as gels, creams, films, or suppositories—will give women a better chance of protecting themselves if their partners

will not use condoms. “Even if a microbicide were found to be only 35% effective in reducing HIV infection rates, this would be a considerable incentive to develop more effective products and would provide a means of potentially protecting hundreds of thousands, if not millions, of women”, says Andrew Nunn, of the MRC.

UK scientists at King’s College London are also leading the European Microbicides Project (EMPRO), which will develop new microbicides with €11.7 million (US\$14 million) funding from the European Commission. EMPRO’s objectives include microbicide discovery, large-scale production at reasonable cost, and carrying out phase-I trials. Meanwhile, the USA-based International Partnership for Microbicides has taken over the development of another microbicide, TMC 120, from the Belgian pharmaceutical company Tibotec, with a royalty-free licence and company funding through phase-II trials.

Dorothy Bonn

New human coronavirus isolated

Researchers have isolated a new human coronavirus from a 7-month-old Dutch child with bronchiolitis and conjunctivitis (*Nature Medicine*, published online March 21; doi:10.1038.nm1024).

“We identified a new virus called human coronavirus NL63 (HCoV-NL63), which was found in 7% of such patients in our centre in January 2003”, Lia van der Hoek and Ben Berkhout (Academic Medical Centre, Amsterdam) explained.

Because the virus grows easily in the laboratory, Hoek and Berkhout believe HCoV-NL63 may also be an attractive model system for testing antiviral drugs. HCoV-NL63 is not as pathogenic as the coronavirus that caused severe acute respiratory syndrome (SARS), but is associated with non-fatal upper and lower-respiratory-tract infection in young children and immunocompromised adults. Like three other known human coronaviruses, its incidence peaks in

winter. The team now plans to look at its prevalence in the general population, its association with the common cold in healthy adults, and its replication cycle, which includes identification of the receptor that determines its host cell tropism.

According to Peter Rottier (Utrecht University, Netherlands) detection of the new virus will also help to reduce the unnecessary use of antibiotics. “If SARS does not return in its serious form, this new virus might well become the most significant human coronavirus”, he said.

Luis Enjuanes, of Campus Universidad Autonoma, Madrid, Spain, believes that the newly discovered coronavirus probably will not have a very high impact in terms of human disease. “We already know of two other human coronaviruses that infect human beings on a regular basis without important consequences under normal conditions”, he pointed out.

Christian Drosten (Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany) calls the discovery “doubtlessly remarkable”. However, he added that clarification of the involvement of the virus in other diseases—eg diarrhoea—will also be very important. “Antiviral agents can be sought only now that the virus is known. Promising candidates are beginning to be found for other coronaviruses. These may cross-react with the new one (especially protease inhibitors)”, he commented.

The immune response to the virus also needs to be clarified. “In case the virus is highly prevalent, causes more severe disease, and is efficiently eliminated by the immune system, it may be worthwhile to develop a vaccine. But vaccination for other coronaviruses has proven difficult in animals”, Drosten concluded.

Khabir Ahmad