Microbicides Make a Comeback

February 13, 2009 By David Evans

HIV microbicides—which incorporate HIV transmission-blocking molecules into gels and creams for the vagina and rectum—got a boost of confidence after two presentations Monday, February 9, at the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal. An analysis of one study showed first signs of efficacy in humans, and another showed that a gel could completely block viral infection in monkeys.

The HIV prevention field has had a very sad couple of years. Several promising microbicide candidates have completely bombed in large human studies, just as one of the largest vaccine trials to date found that the test might have actually increased the candidates' chances of acquiring HIV. The two presentations on Monday at CROI came as welcome news.

The first presentation involved a gel formulation of the antiretroviral (ARV) drugs tenofovir (found in Viread, Truvada and Atripla) and emtricitabine (found in Emtriva, Truvada and Atripla). Charles Dobard, PhD, from the Centers for Disease Control and Prevention (CDC) in Atlanta reported on a study conducted in monkeys known as pigtail macaques. Dobard and his team first applied no gel, a gel without any drug in it, a gel with just tenofovir or a gel with both tenofovir and emtricitabine into the female monkeys' vaginas. They then applied a hybrid virus—a combination of simian immunodeficiency virus (SIV) and HIV called SHIV—into the monkeys' vaginas 30 minutes later. They did this twice a week a total of 20 times, or until the monkeys became infected with SHIV.

Of the 11 monkeys who either received no gel or the gel without active drugs, 10 of them became infected with SHIV. Infection occurred, on average, after four applications of virus. Of the 12 monkeys who received either of the two gels with active drug, none became infected with SHIV.

Dobard explained that most of the active drug remained in the vaginal tissue and did not make its way into the bloodstream, thus potentially reducing the chance that a person using a tenofovir or tenofovir plus emtricitabine gel who became infected with HIV might develop resistance to these drugs—both of which are widely used to treat HIV.

Another promising study was presented by Salim Abdool Karim, PhD, from the Centre for the AIDS Programme of Research in South Africa in Congella. Karim and his colleagues enrolled 3,099 HIV-negative women into a trial comparing a microbicide called BufferGel with a microbicide called Pro 2000/5, a placebo gel or no gel at all. All the women, who resided in Malawi, South Africa, Zambia, Zimbabwe and the United States, received extensive HIV risk reduction counseling and condoms.

The highest rate of infection occurred in the women who used BufferGel. This rate was nearly equivalent to the rate in women who used either a placebo gel or no gel. However, the rate in women who received the Pro 2000/5 gel was roughly 30 percent lower. While this did not reach

statistical significance, meaning that the result was small enough to have occurred by chance, it is the first time thus far that an HIV microbicide study has shown even a hint of efficacy.

Karim explained that when he and his colleagues conducted a subanalysis of the infection rate in women who reported a high degree of Pro 2000/5 gel use and a low use of condoms, the reduction in HIV rate was nearly 78 percent.

Further studies of both tenofovir gel and Pro 2000/5 in humans are ongoing.
