Developing a Microbicide for HIV

Forty million people are now infected with HIV-1, one in every hundred fifty people on planet Earth. Speaking to the Physics and Chemistry Teachers Clubs of New York on 15 September 2006, David Fairhurst called it a pandemic, one which is still growing, with 14,000 new infections daily. Moreover, resource-poor nations are carrying the burden, he said, with women and girls bearing the brunt, a majority of them married and monogamist mothers. This is due to biological, cultural, and social factors, Fairhurst pointed out: male dominance and initiation of sex leave women with no choice to take measures to protect themselves.

It is because of the brunt borne by women that the Bill and Melinda Gates Foundation has committed sizeable funds to preventing the spread of HIV. Fairhurst is a consultant for the International Partnership for Microbicides (IPM), set up by initial funding from the Gates Foundation; it now has additional donors from many countries and organizations. The requirements to stop a pandemic, he said, were prevention -- to all susceptible, treatment -- of those already infected, and support and care -- for those in need. The US has committed funds to prevent the spread of HIV, Fairhurst noted, but strings attached to these funds have caused very little to be taken up in developing countries. Ways to provide prevention include behavior change, condoms, a vaccine, and microbicides. Although the search for a vaccine has nothing to show after 25-30 years of work, frustrated by a variety of factors, microbicides show real promise -- and Fairhurst said that this is why the Gates Foundation has promised continued funding to develop them. Microbicides can be applied either vaginally or rectally and they are expected to prevent HIV-1 from entering or replicating in cells. They can work by different mechanisms of action, such as inactivating gp120, part of the envelope protein complex of HIV-1.

Fairhurst listed three broad categories of microbicidal agents: membrane disruptive agents (which, however, destroy the outer envelope layer and cellular membrane), charge-dependent inhibition of viral attachment (based on the fact that HIV is net negative), and anti-retroviral drugs (which, potentially, could build up resistance). Microbicides can be made in many forms. Fairhurst also listed quite a few categories of delivery systems, which varied according to the frequency of attention required and duration of drug activity. One form is a semi-solid topical delivery system (TDS) based on a gel, which he said could be water-based, oil-based, anhydrous, or silicone fluid-based. Creating a TDS, he said, is a matter of understanding chemistry and the physicochemical interactions of the ingredients. It's a science, not an art, and without a systematic approach there is no guide for changing a formulation to improve it.

A first generation gel was developed in 2004, and it is now in Phase I trials in Rwanda, Tanzania, and Uganda. These trials are complicated by a scarcity of indigenous doctors able torun clinical trials and a shortage of facilities, Fairhurst noted, but Phase III trials are slated for next year, with a product expected on the market in 2010. He is currently working on a second generation drug based on two active ingredients, each providing different mechanisms of action to increase effectiveness.

But even if a product is effective, Fairhurst cautioned, it may be unattractive to women, and husbands may object to its use. Moreover, there is no "one size fits all" -- women in Africa and Asia have different needs and requirements. IPM has initiated market research to try and answer these questions.