

Predicting the unpredictable real-world impact of ARV-based microbicides

A number of findings in the article by Wilson *et al.* (1), which uses a mathematical model to examine the public health impact of widespread introduction of antiretroviral (ARV)-based microbicides, have been labeled “surprising.”

For example, Wilson *et al.* (1) highlight the “paradox” of a vaginal microbicide potentially benefiting more men than women. Although the goal of microbicide development is to fill a global gap in HIV prevention by providing women with a method that they control, that men might benefit is neither surprising nor unwelcome. For men to benefit, however, certain conditions must exist. First, the product must provide bidirectional protection. Second, drug-resistant HIV must be difficult to transmit. At present, we do not know whether either of these conditions is met, and we will not know until trials are undertaken involving serodiscordant couples.

The Wilson model (1) also suggests that use of an ARV-based microbicide by HIV-positive women could result in widespread drug resistance if the product is readily absorbed into the bloodstream. We cannot discount that ARV-based vaginal microbicides may be absorbed, but pharmacokinetic

studies of current topically applied products suggest that this is not likely to be the case (2–4). Once an ARV-based product is shown to work, however, it will be important to evaluate the impact of its use by HIV-positive women before making it widely available.

The concerns raised in the article highlight the need to continue developing non-ARV-based or combination products, developing drugs specifically for prevention, and enrolling HIV-positive women in safety and bridging studies.

Lori Heise and Sean Philpott¹

Global Campaign for Microbicides, PATH, 1800 K Street NW, Suite 800, Washington, DC 20006

1. Wilson DP, Coplan PM, Wainberg MA, Blower SM (2008) The paradoxical effects of using antiretroviral-based microbicides to control HIV epidemics. *Proc Natl Acad Sci USA* 105:9835–9840.
2. Patton DL, *et al.* (2007) Preclinical safety assessments of UC781 anti-human immunodeficiency virus topical microbicide formulations. *Antimicrob Agents Chemother* 51:1608–1615.
3. Jespers VA, Van Roey JM, Beets GI, Buvé AM (2007) Dose-ranging phase 1 study of TMC120, a promising vaginal microbicide, in HIV-negative and HIV-positive female volunteers. *J Acquir Immune Defic Syndr* 44:154–158.
4. Mayer KH, *et al.* (2006) Safety and tolerability of tenofovir vaginal gel in abstinent and sexually active HIV-infected and uninfected women. *AIDS* 20:543–551.

Author contributions: L.H. and S.P. wrote the paper.

The authors declare no conflict of interest.

¹To whom correspondence should be addressed. E-mail: sphilpott@path.org.

© 2008 by The National Academy of Sciences of the USA