10. **Gupta R,** Warren T, Wald A. Genital herpes. *Lancet* 2007;**370**:2127—37.
11. **Maguire RA,** Bergman N, Phillips DM. Comparison of microbicides for efficacy in protecting mice against vaginal challenge with herpes simplex virus type 2, cytotoxicity, antibacterial properties, and sperm immobilization. *Sex Transm Dis* 2001;**28**:259—65.
12. **Mesquita PM,** Wilson SS, Manlow P, *et al*. Candidate microbicide PPCM blocks human immunodeficiency virus type 1 infection in cell and tissue cultures and prevents genital herpes in a murine model. *J Virol* 2008;**82**:6576—84.
13. **Tuyama AC,** Cheshenko N, Carlucci MJ, *et al*. ACIDFORM inactivates herpes simplex virus and prevents genital herpes in a mouse model: optimal candidate for microbicide combinations. *J Infect Dis* 2006;**194**:795—803.
14. **Rosenthal KS,** Killius J, Hodnichak CM, *et al*. Mild acidic pH inhibition of the major pathway of herpes simplex virus entry into HEp-2 cells. *J Gen Virol* 1989;**70**:857—67.
15. **Padian NS,** van der Straten A, Ramjee G, *et al*. Diaphragm and lubricant gel for prevention of HIV acquisition in southern African women: a randomised controlled trial. *Lancet* 2007;**370**:251—61.
16. **Hogrefe W,** Su X, Song J, *et al*. Detection of herpes simplex virus type 2-specific immunoglobulin G antibodies in African sera by using recombinant gG2, Western blotting, and gG2 inhibition. *J Clin Microbiol* 2002;**40**:3635—40.
17. **van der Straten A,** Shiboski S, Montgomery ET, *et al*. Patterns and predictors of adherence to diaphragm use in a phase III trial in sub-Saharan Africa: a trajectory analysis. *J Acquir Immune Defic Syndr* 2009;**50**:419—26.
18. **Rupp R,** Rosenthal SL, Stanberry LR. VivaGel (SPL7013 Gel): a candidate dendrimer—microbicide for the prevention of HIV and HSV infection. *Int J Nanomedicine* 2007;**2**:561—6.
19. **Karim QA,** Karim SS, Frohlich JA, *et al*. Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women. *Science* 2010;**329**:1168—74.

LETTER

Spontaneous remission of sexually transmitted diseases must be considered in randomised controlled trials

Randomised controlled trials that test biomedical interventions to reduce sexually transmitted infections (STIs) have had very mixed results,[1 2] as have behavioural trials.[3 4] It is only in the past 10 years that the field has recognised that chlamydia resolves itself without treatment in 50% of the cases,[4] although the estimates range from 13% to 60%.[5–7] The length of time to clear chlamydia infection varies from 60 days in women to up to 15 months in men.[5] The speed of resolution is also subject to individual-level factors (eg, infection clears sooner in older people), making it difficult to determine sample sizes for randomised controlled trials with STI outcomes.

In a recent five-country trial,[1] the determination of sample size to identify the necessary number of participants to demonstrate a reduction in bacterial STI was based primarily on chlamydia (65.8% of the bacterial infections observed at recruitment; 10.3% prevalence) and trichomoniasis among women (17.2% of infections; 4.89% prevalence). When we examined all the bacterial STIs 1 year later, the rates of chlamydia were more than 60% lower and the rates of trichomoniasis were 40% lower. Potentially, half of the new chlamydia and trichomoniasis infections may have spontaneously resolved, as suggested by the above studies, but the actual incidence rates may have been 25% more than those observed at 12 months (assuming a consistent rate of infection over time).

The emerging data on spontaneous remission rates raises serious questions on how to design effective evaluations to demonstrate reductions in STIs. Randomised controlled trials must be designed to have shorter periods between assessments. It is also likely that there is a variance in the rates of clearance, although it is unclear in what direction and for whom the variations will apply. Thus, the design of future multisite trials must *cautiously* estimate STI infections, given the emerging data on spontaneous remissions or clearing of infections, and consider much shorter follow-up periods, even for long-term longitudinal trials.

Mary Jane Rotheram-Borus,[1] Zunyou Wu,[2] Li Li,[1] Roger Detels,[1] Li-Jung Liang,[1] and the NIMH Collaborative HIV/STD Prevention Trial Group

[1]University of California at Los Angeles, Semel Institute for Neuroscience and Human Behavior, Center for Community Health, Los Angeles, California, USA; [2]National Center for AIDS/STD Control and Prevention, Chinese Centers for Disease Control and Prevention, Beijing, China

Correspondence to Dr Mary Jane Rotheram-Borus, University of California, Semel Institute for Neuroscience and Human Behavior, 10920 Wilshire Boulevard, Suite 350, Los Angeles, CA 90024, USA; cchpublications@mednet.ucla.edu

Funding NIMH provided funding for this multisite study.

Competing interests None.

Patient consent All human subjects signed the informed consent forms that were reviewed and approved by the Institutional Review Boards at UCLA and the China CDC.

Ethics approval UCLA SG-IRB; RTI IRB; Chinese Centers for Disease Control IRB.

Provenance and peer review Not commissioned; internally peer reviewed.

Accepted 16 February 2011
Published Online First 1 April 2011

Sex Transm Infect 2011;**87**:305.
doi:10.1136/sextrans-2011-050009

REFERENCES

1. **NIMH Collaborative HIV/STD Prevention Trial Group**. Results of the NIMH Collaborative HIV/STD prevention trial of a community popular opinion leader intervention. *J Acquir Immune Defic Syndr* 2010;**54**:204—14.
2. **The Explore Study Group.** Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomised controlled study. *Lancet* 2004;**364**:41—50.
3. **Wawer MJ,** Sewankambo NK, Serwadda D, *et al*. Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomized community trial. Rakai Project Study Group. *Lancet* 1999;**353**:525—35.
4. **Gisselquist D,** Potterat JJ. Confound it: latent lessons from the Mwanza trial of STD treatment to reduce HIV transmission. *Int J STD AIDS* 2003;**14**:179—84.
5. **Golden MR,** Schillinger JA, Markowitz L, *et al*. Duration of untreated genital infections with *Chlamydia trachomatis*: a review of the literature. *Sex Transm Dis* 2000;**27**:329—37.
6. **Brunham RC,** Rey-Ladino J. Immunology of chlamydia infection: implication for a *Chlamydia trachomatis* vaccine. *Nat Rev Immunol* 2005;**5**:149—61.
7. **Parks KS,** Dixon PB, Richey CM, *et al*. Spontaneous clearance of *Chlamydia trachomatis* infection in untreated patients. *Sex Transm Dis* 1997;**24**:229—35.