

## EDITORIALS

### Barriers and boundaries

Control of human immunodeficiency virus (HIV) infection is a prominent item on the agenda of the Sixth International Conference on AIDS in San Francisco, which finishes this Sunday, June 24. Many control programmes rely heavily on the use of condoms as the best method available, other than chastity, to reduce the risk of transmitting or acquiring sexually transmitted diseases (STDs) including AIDS.<sup>1</sup> Condoms are reasonably effective contraceptives but they are not universally acceptable, and correct and consistent use is seldom achieved. There is a great need to widen the choice of methods that can act both as contraceptives and as prophylactics against STDs. Menstruation and menopause provide a respite from the fear of unwanted pregnancy, but women can contract STDs at any time of the menstrual or life cycle. New contraceptive methods that enable women to play a greater part in protecting their own health are urgently required.<sup>2</sup>

Many women, in both developing and developed countries, are exposed to the heterosexual transmission of diseases but are unable to compel their partners to use a condom. At one extreme, a prostitute may fear losing her client if she insists on condom use; at the other, a woman in love with an HIV-positive man may feel that her own safety is less important than the risk of appearing to reject her partner if she insists that he use a sheath. A female method would also help protect men against some of their own risk taking—in a study from Africa of men who acquired an STD from a group of prostitutes, 43% of those who were uncircumcised and had a genital ulcer became HIV positive.<sup>3</sup>

The existing choices for women are severely limited—a handful of spermicidal formulations based on a single class of detergents, mainly nonoxynol-9 (N-9); the reusable diaphragm or cervical cap applied with a spermicide; and the N-9-loaded disposable

'Today' sponge. New methods undergoing laboratory or clinical evaluation include the female condom ('Femshield'), 'Lea's Kap', and new chemical entities that could be used as spermicides. Femshield, invented in Denmark, consists of a heat-sealed polyurethane bag that is held in place by a soft ring outside the introitus and a firmer, loose ring that is used to insert the device in the posterior fornix, in much the same way as a woman inserts a diaphragm.<sup>4</sup> Lea's Kap is a bowl-shaped device made of silicone which fits over the cervix; it has a soft valve to discharge cervical secretions and a removal loop, which also prevents intravaginal rotation of the device. Potential new spermicides, that would also be bactericidal/virucidal, include chlorhexidine, benzalkonium chloride, povidone iodine,<sup>5</sup> and sodium oxychlorosene.<sup>6</sup> Chlorhexidine is an especially interesting candidate as a spermicidal, bactericidal, and virucidal agent because it binds directly to the cervical mucus and attains spermicidal concentrations in the cervical canal. Why is so little effort being made to test these agents?

At a research level, we need to know more about the route taken by HIV when infecting women—does the virus ascend the cervix (possibly even carried by sperm), cross an eroded cervical epithelium, or traverse the vaginal wall after disease or microtrauma? If, for example, HIV ascends through the cervix then a diaphragm or Lea's Kap should give considerable protection, but if the virus crosses the vaginal wall these devices will have less prophylactic value. Laboratory testing of new chemical agents is reasonably straightforward.<sup>7</sup> N-9 retards vaginal transmission of the simian immunodeficiency virus in rhesus monkeys and the feline immunodeficiency virus in cats but, while more work needs to be done with laboratory animals, human trials are also needed and they inevitably present formidable logistic and ethical difficulties.

The random allotment of a placebo to people at risk of a lethal infection is clearly unacceptable. Thus, the

randomised design previously used in volunteers to show that the Today sponge reduces the risk of gonorrhoea and chlamydia<sup>8</sup> needs to be modified for HIV. However, the random allotment of a female method and a placebo, if a condom is used in addition, should be acceptable. Such a protocol would require large numbers of volunteers because, despite the rapid spread of HIV, there are only a few groups (mostly commercial sex workers in Africa) in whom the disease is sufficiently frequent to make such a clinical trial feasible. A small study of the Today sponge among commercial sex workers in Nairobi not only showed no protective action against HIV infection<sup>9</sup> but also raised the question of whether frequent use (as by prostitutes) might not increase the risk of ulceration and thus also HIV acquisition.

The administrative and organisational barriers to development of new female prophylactic methods need the most urgent attention. In Britain, it is expected that Femshield, after passing quality assurance tests, will be marketed later this year. In the USA, the Food and Drug Administration (FDA) has insisted on clinical trials of contraceptive safety and efficacy before marketing and such trials are now underway. Whilst the US Government, through the Agency for International Development (USAID), deserves credit for sponsoring the necessary studies, the FDA requirements themselves merely delay the distribution of a potentially useful method by which a woman can protect herself without adding any information about the value of the device in slowing HIV and STD transmission. A WHO expert meeting on the need for new female prophylactics devised complex and lengthy study protocols and then side-stepped the issue of who might pay for such studies. In the pharmaceutical industry fears of litigation make the manufacturers as afraid of new prophylactic methods as of new contraceptives,<sup>10</sup> and several interesting chemical entities lie unexploited on the laboratory shelves. Fortunately, in-vivo and in-vitro research is being undertaken on chlorhexidine at Manchester University.

Even if the carefully conducted clinical trials now underway rank various methods for their theoretical prophylactic effectiveness, the results may still prove a poor indication of usefulness in the real world. A highly acceptable method that is only partly effective might well have a more powerful public health impact than a highly effective but poorly accepted method.<sup>11</sup> Since HIV prevalence can double every year in groups at high risk of acquiring HIV infection, a moderately effective method available now might well save more lives than an excellent method in five years time. A wide choice of methods also tends to encourage community inventiveness. Femshield, for example, is visible to the man when in use, and in an acceptability trial in Thailand some sex workers essentially told their clients "You use a condom or I use Femshield"—but there was no third choice.

Worldwide there are very few efforts to study the

impact of existing spermicides on HIV acquisition and transmission; one such study is being conducted by Family Health International (a USA research group) in West Africa. An intelligently managed programme with a strict development schedule, perhaps funded by one or more of the European medical research councils, the US National Institutes of Health, or USAID is urgently needed. Responsible short cuts could be taken—eg, the acceptability of new spermicide formulations could be tested while in-vitro studies and phase I clinical trials are being conducted. Boundary disputes between agencies and between those who control resources related to family planning and AIDS prevention must stop. Research in pregnancy prevention and in STD control are complementary. We know that fertility regulation improved immeasurably as women gained access to oral contraceptives and other female methods. HIV control might well take a similar leap forward with the development of female prophylactics.

1. Feldblum PJ, Fortney JA. Condoms, spermicides and the transmission of human immunodeficiency virus: a review of the literature. *Am J Publ Health* 1988; 78: 52-54.
2. Stein ZA. HIV prevention: the need for methods women can use. *Am J Publ Health* 1990; 80: 460-62.
3. Cameron DW, Simonsen NJ, D'Costa LJ, et al. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. *Lancet* 1989; ii: 403-07.
4. Sonnet C, Hart GJ, Bounds W, Williams P, Guillebaud J, Adler MW. Sexual behaviour and attitudes to barrier contraception among family planning clinic attenders. *Br J Fam Plann* 1989; 15: 71-75.
5. Chantler EN. New and existing spermicides with virucidal properties. In: Alexander NJ, Gabelnick HL, Spieler JM, eds. *Heterosexual transmission of AIDS*. New York: Wiley-Liss, 1990: 303-10.
6. Klein RJ, Buimovic-Klein E, Ong KR, Czelusniak SM, Lange M, Friedman-Kien A. Inactivation of human immunodeficiency, herpes simplex, and vaccinia viruses by sodium oxychlorosene. *Lancet* 1987; i: 281-82.
7. Hicks DR, Voeller B, Resnick L, et al. Chemical inactivation of HIV-1 (HTLV-III and HB2) by contraceptives/spermicidal agents. Fourth International Conference on AIDS, Stockholm, Sweden, June 13-16, 1988. Book 2: 278 (abstr 6528).
8. Rosenberg MJ, Rojanapithayakorn W, Feldblum PJ, Higgins JE. Effect of the contraceptive sponge on chlamydial infection, gonorrhoea and candidiasis. *JAMA* 1987; 257: 2308-12.
9. Kreiss J, Ruminjo I, Ngugi E, Roberts P, Ndinya-Achola J, Plummer F. Efficiency of nonoxynol-9 in preventing HIV transmission. Fifth International Conference on AIDS, Montreal, Canada, June 4-9, 1989: 51 (abstr MA036).
10. Mastroianni L, Donaldson PJ, Kane TT. Development of contraceptives—obstacles and opportunities. *N Engl J Med* 1990; 322: 482-84.
11. Witkowski KM. Preventing the heterosexual spread of AIDS: what is the best advice if compliance is taken into account? *AIDS* 1989; 3: 143-45.