/COMMENTARY

Taking Aim at Sexually Transmitted Diseases

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Immunization has obliterated smallpox, set measles and polio melitis on the road to extinction, and curbed our fear of many other maladies. Yet not a single vaccine is commercially available to combat any one of the wide range of dangerous bacteria and viruses that can infect the human reproductive system. These include *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, *Treponema pallidum*, herpes simplex virus II, human papilloma virus, and human immunodeficiency virus.

Given this disparity, it could plausibly be argued that sexually transmitted diseases have been unjustly neglected targets for research. Women—in particular—seem to have been discriminated against (just as they have been, according to recent evidence, with respect to coronary care). More generally and historically—from syphilis to AIDS—science may have paid insufficient attention to conditions that might be seen as the "wages of sin."

In reality, technical obstacles are more likely than sociopolitical prejudice to be responsible for apparent inaction toward the conquest of particular diseases. The central difficulty in dealing with infections of the female reproductive tract, for example, has been that of securing an effective antibody response in the superficial layers of the vaginal and cervical epithelium, the sites attacked by the various pathogens. Many different teams have attempted to take on the problem, usually basing their strategy on the fact that antigenic stimulation at one mucosal site can lead, through the migration of activated lymphocytes, to an immune response in mucosal cells elsewhere in the body.

Over the past decade, several groups have found that antigens taken orally can provoke lymphoid tissue in the gut to produce corresponding immunoglobulin A antibodies in the reproductive tract. However, even the strongest immune responses in tissue, such as the Peyer's patches in the small intestine, tend to be accompanied by relatively weak responses in the genital tract.

Very recent studies have begun to indicate that the only hope of eliciting truly effective antibody titers will be through local administration of the antigen. And while dose is important, repeated or continuous exposure to the antigen seems to be particularly significant in determining the level of mucosal immunity. One way of achieving such a sustained antigenic stimulus, over many days or indeed much longer periods of time, would be to use a living virus or bacterium as a vehicle for the immunizing antigen.

Collaborative research between Queensland University of Technology (Brisbane, Australia) and the University of Siena (Italy) now indicates that this approach might win a breakthrough in the battle against *C. trachomatis* and the rest. They decided to evaluate, as putative vaccines, members of the genus *Lactobacillus*. These are the dominant commensal bacteria in the human vagina, with no pathogenic potential whatever. In the last few years, moreover, following the first transformation of *L. casei* by electroporation in 1988, the genetic manipulation of lactobacilli has become a practical proposition. The expression of foreign antigens in such strains is now on the agenda.

The Brisbane and Siena researchers have used the guinea pig as an animal model to assess the possibility of exploiting lactobacilli as human vaccines. They first studied the animal's vaginal flora and selected a common member of that flora, *L. feriantum*, as their candidate for genetic modification. Then they developed an improved electroporation technique to transform one strain of the organism with the broad host range plasmid pNZ17. Preliminary results (reported by C.M. Rush et al. in *J. Med. Microbiol.* **41**:272) show that the recombinant strain had excellent segregational stability in the absence of antibiotic selection. It also persisted, though only for five days, when administered to the vaginal tract of guinea pigs.

Clearly, there is still a long way to go. The researchers believe their approach has great potential in the development of vaccines against pathogens of the female reproductive tract. One of their immediate aims is to encourage effcient colonization by the recombinant organism, by studying the many factors that could have contributed to its relatively short persistence in these early experiments. The main significance of the work so far is in demonstrating that naturally occurring vaginal lactobacilli can be genetically manipulated, in addition to the dairy and culture collection strains that have been modified hitherto. ///