

Mucosal immune system of genital tract with

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Are there differences between female and male genital tract regarding humoral responses?

Jiri Mestecky: In general, both female and male genital tracts differ in several significant aspects from other mucosal tissues. Specifically, a considerable proportion of antibodies found in genital tract secretions are derived from the circulation, which is not the case, for example, in the intestinal tract secretions, which are overwhelmingly produced locally by resident plasma cells in the gut and then selectively transported into the external secretions. This fact has many important implications for the efficacy of various routes of immunization. Specifically, we know that systemic immunization, which induces good antibodies in the circulation, does not significantly influence the level of specific antibodies in the intestinal tract, saliva, tears, and other secretions. This obviously is not the case for the genital tract where systemic immunization may result in the appearance of specific antibodies in secretions of the genital tract from the circulation.

In addition to differences between the genital and intestinal mucosal immune system, one also has to consider a marked difference between males and females. Due to the very pronounced hormonal regulation and the existence of the menstrual cycle, the levels of antibodies in female genital tract secretions are highly variable and depend to a great extent on the stage of the menstrual cycle. Furthermore, most of the antibodies of both local and circulatory origin gain their way into the vagina through the uterus. Consequently, hysterectomized females have ~95% decrease in the total level of immunoglobulins in genital tract secretions. Information concerning the local origin of antibodies in the male genital tract secretions (ejaculate and pre-ejaculate) is not quite clear: the role of the epididymis, prostate, and glands of Littre distributed in the male urethra have all been considered, but we do not know the importance of these individual tissues and their contribution to the total pool of antibodies in male genital tract secretions.

Which factors play a role in the mucosal immune system of the genital tract?

Jiri Mestecky: In addition to the profound hormonal influences in the female genital tract as to the level of antibodies, the genital tract differs from other mucosal tissues by the lack of organized lympho-epithelial structures, which are important in the induction of local as well as disseminated immune responses. In comparison to the intestines where such lympho-epithelial structures, called Pey-

er's patches, exist in abundance, both male and female genital tracts lack analogous structures. Consequently, the local application of antigens in the female genital tract, or immune responses to microorganisms present in the female genital tract, or infections of both male and female genital tracts (e.g., gonococcus, *Chlamydia trachomatis*, and other potential agents) induces rather limited

and, at best, localized immune responses without any significant systemic involvement or involvement of other mucosal tissues. For example, the ingestion of certain microbial antigens results in the induction of antibodies not only in the intestinal tract, but also in tears, saliva, and milk of immunized individuals due to the dissemination of specific antibody-form-

ing cells from the inductive sites to the effector sites, such as intestinal mucosa, and salivary, lacrimal and mammary glands. This does not appear to be the case in the genital tract. Local immunization with a number of different antigens resulted in the induction of very low titres of locally produced antibodies without concomitant antibodies in other external secretions.

How can your findings be considered for the development of new immunization strategies against sexually transmitted infections?

Jiri Mestecky: It is obvious that immunization strategies for the induction of protective humoral responses against sexually transmitted diseases in the male and female genital tracts will have to be different than for other mucosal infections, for example, intestinal or respiratory tracts. It is very likely that the systemic immunization followed by local

immunization may represent the best potential means of inducing such desired responses.

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