Pathogenesis of genital tract disease due to Chlamydia trachomatis.

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Although the pathologic consequences of C. trachomatis genital infection are well-established, the mechanism(s) that result in chlamydia-induced tissue damage are not fully understood. We reviewed in vitro, animal, and human data related to the pathogenesis of chlamydial disease to better understand how reproductive sequelae result from C. trachomatis infection. Abundant in vitro data suggest that the inflammatory response to chlamydiae is initiated and sustained by actively infected nonimmune host epithelial cells. The mouse model indicates a critical role for chlamydia activation of the innate immune receptor, Toll-like receptor 2, and subsequent inflammatory cell influx and activation, which contributes to the development of chronic genital tract tissue damage. Data from recent vaccine studies in the murine model and from human immunoepidemiologic studies support a role for chlamydia-specific CD4 Th1-interferon-g-producing cells in protection from infection and disease. However, limited evidence obtained using animal models of repeated infection indicates that, although the adaptive T cell response is a key mechanism involved in controlling or eliminating infection, it may have a double-edged nature and contribute to tissue damage. Important immunologic questions include whether anamnestic CD4 T cell responses drive disease rather than protect against disease and the role of specific immune cells and inflammatory mediators in the induction of tissue damage with primary and repeated infections.

Continued study of the complex molecular and cellular interactions between chlamydiae and their host and large-scale prospective immunoepidemiologic and immunopathologic studies are needed to address gaps in our understanding of pathogenesis that thwart development of optimally effective control programs, including vaccine development.

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