cells. Chlamydiae are nonmotile, gram-negative, obligate intracellular bacteria that replicate within the cytoplasm of host cells, forming the characteristic membrane-bound inclusions that are the basis for some diagnostic tests. Originally considered to be large viruses, chlamydiae differ from viruses in possessing RNA and DNA as well as a cell wall that is quite similar in structure to the cell wall of typical gram-negative bacteria. However, chlamydiae lack peptidoglycan; their structural integrity depends on disulfide binding of outer-membrane proteins.

GROWTH CYCLE

Among the defining characteristics of chlamydiae is a unique growth cycle that involves alternation between two highly specialized morphologic forms (Figs. 213-1 and 213-2): the elementary body (EB), which is the infectious form and is specifically adapted for extracellular survival, and the metabolically active and replicating reticulate body (RB), which is not infectious, is adapted for an intracellular environment, and does not survive well outside the host cell. The biphasic growth cycle begins with attachment of the EB (diameter, 0.25–0.35 μm) at specific sites on the surface of the host cell. The EB enters the cell through a process similar to receptor-mediated endocytosis and resides in an inclusion, where the entire growth cycle is completed. The chlamydiae prevent phagosome-lysosome fusion. The inclusion membrane is modified by insertion of chlamydial antigens. Once the EB has entered the cell, it reorganizes into an RB, which is larger (0.5–1 μm) and contains more RNA. After ~8 h, the RB starts to divide by binary fission. The intracytoplasmic, membrane-bound inclusion body containing the RBs increases in size as the RBs multiply. Approximately 18–24 h after infection of the cell, these RBs begin to become EBs by a reorganization or condensation process that is poorly understood. After rupture of the inclusion body, the EBs are released to initiate another cycle of infection.

Chlamydiae are susceptible to many broad-spectrum antibiotics and possess a number of enzymes, but they have a very restricted metabolic capacity. None of these metabolic reactions results in the production of energy. Chlamydiae have thus been considered to be energy parasites that use the ATP produced by the host cell for their own metabolic functions. Many aspects of chlamydial molecular biology are not well understood, but the sequencing of several chlamydial genomes and new proteomics research have provided researchers with many relevant tools for elucidating the biology of the life cycle.

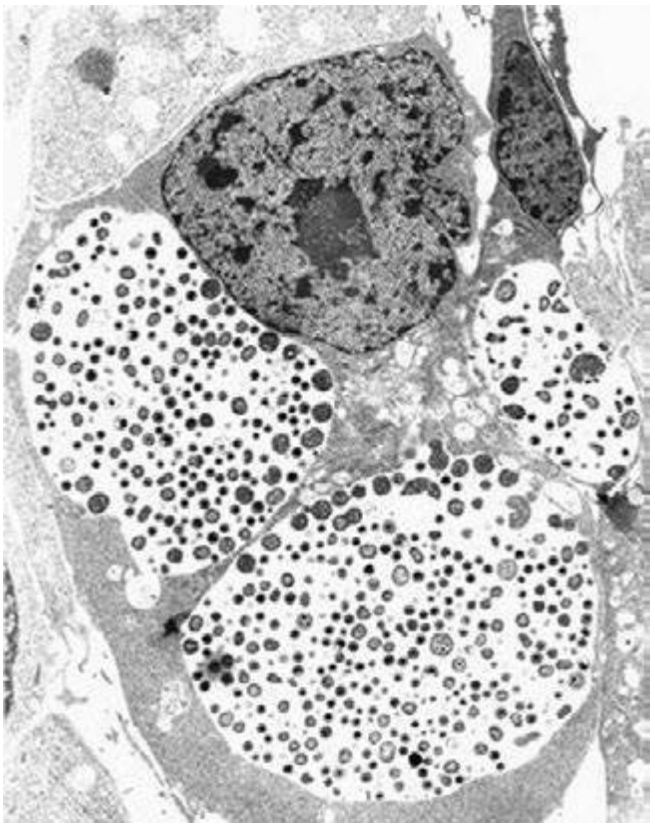

FIGURE 213-1 Chlamydial intracellular inclusions filled with smaller dense elementary bodies and larger reticulate bodies. *(Reprinted with permission from WE Stamm: Chlamydial infections, in Harrison's Principles of Internal Medicine, 17th ed, AS Fauci et al [eds]. New York, McGraw-Hill, 2008, p 1070.)*

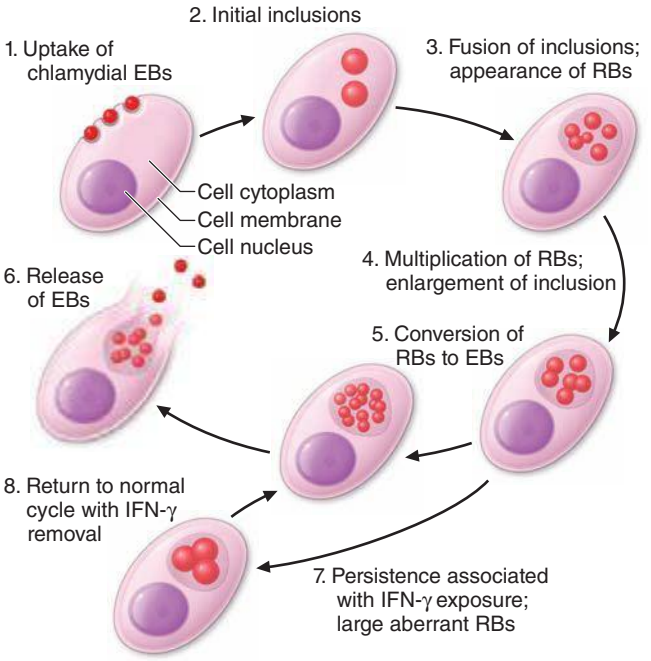

FIGURE 213-2 Chlamydial life cycle. EBs, elementary bodies; RBs, reticulate bodies; IFN-γ, interferon γ. *(Reprinted with permission from WE Stamm: Chlamydial infections, in Harrison's Principles of Internal Medicine, 17th ed, AS Fauci et al [eds]. New York, McGraw-Hill, 2008, p 1071.)*

PATHOGENESIS

Genital infections are mostly caused by *C. trachomatis* serovars D–K, with serovars D, E, and F involved most often. Molecular typing of the major outer-membrane protein gene (*omp1*) from which serovar differences arise has been used to demonstrate that polymorphisms can occur in isolates from patients who are exposed frequently to multiple infections, while less variation is observed in isolates from less sexually active populations. Polymorphisms in the major outer-membrane protein may provide antigenic variation, and the different forms allow persistence in the community because immunity to one is not protective against the others.

The trachoma biovar is essentially a parasite of squamocolumnar epithelial cells; the LGV biovar is more invasive and involves lymphoid cells. As is typical of chlamydiae, *C. trachomatis* strains are capable of causing chronic, clinically inapparent, asymptomatic infections. Because the duration of the chlamydial growth cycle is ~48–72 h, the incubation period of sexually transmitted chlamydial infections is relatively long—generally 1–3 weeks. *C. trachomatis* causes cell death as a result of its replicative cycle and can induce cell damage whenever it persists. However, few toxic effects are demonstrated, and cell death because of chlamydial replication is not sufficient to account for disease manifestations, the majority of which are due to immunopathologic mechanisms or nonspecific host responses to the organism or its byproducts.

In recent years, the entire genomes of various chlamydial species have been sequenced, the field of proteomics has become established, host innate immunity has been more precisely delineated, and innovative host cell–chlamydial interaction studies have been conducted. As a result, many insights have been gained into how chlamydiae adapt and replicate in their intracellular environment and produce disease. These insights into pathogenesis include information