asymptomatic and so may go untreated. Both *N. gonorrhoeae* and *C. trachomatis* frequently cause asymptomatic infections in women. *C. trachomatis* urethritis can be diagnosed by culture of the bacteria in human cell lines, but amplified nucleic acid tests performed on genital swabs or urine specimens are more sensitive and have supplanted cultures.

Genital infection with the L serotypes of *C. trachomatis* causes *lymphogranuloma venereum*, a chronic, ulcerative disease. Lymphogranuloma venereum is a sporadic disease in the United States and Western Europe, but it is endemic in parts of Asia, Africa, the Caribbean region, and South America. The infection initially manifests as a small, often unnoticed, papule on the genital mucosa or nearby skin. Two to 6 weeks later, growth of the organism and the host response in draining lymph nodes produce swollen, tender lymph nodes, which may coalesce and rupture. If not treated, the infection can subsequently cause fibrosis and strictures in the anogenital tract. Rectal strictures are particularly common in women.

MORPHOLOGY

The features of *C. trachomatis* **urethritis** are virtually identical to those of gonorrhea. The primary infection is characterized by a mucopurulent discharge containing a predominance of neutrophils. Organisms are not visible in Gram-stained smears or sections.

The lesions of **lymphogranuloma venereum** contain a mixed granulomatous and neutrophilic inflammatory response. Variable numbers of chlamydial inclusions are seen in the cytoplasm of epithelial cells or inflammatory cells. Regional lymphadenopathy is common, usually occurring within 30 days of infection. Lymph node involvement is characterized by a granulomatous inflammatory reaction associated with irregularly shaped foci of necrosis containing neutrophils (stellate abscesses). With time, the inflammatory reaction is dominated by nonspecific chronic inflammatory infiltrates and extensive fibrosis. The latter, in turn, may cause local lymphatic obstruction, lymphedema, and strictures. In active lesions, the diagnosis of lymphogranuloma venereum may be made by demonstration of the organism in biopsy sections or smears of exudate. In more chronic cases, the diagnosis rests with the demonstration of antibodies to the appropriate chlamydial serotypes in the patient's serum.

Rickettsial Infections

Members of the *Rickettsiales* are vector-borne obligate intracellular bacteria that cause epidemic and scrub typhus, spotted fevers (*Rickettsia rickettsii* and others), ehrlichiosis, and anaplasmosis. These organisms have the structure of gram-negative, rod-shaped bacteria, although they stain poorly with Gram stain.

- *Epidemic typhus* (caused by *Rickettsia prowazekii*) is transmitted from person to person by body lice. It is associated with wars and poverty, when individuals live in close contact with poor hygiene. Manifestations include a rash that is initially macular, progressing to a petechial, maculopapular rash on the entire body except the face, palms, and soles.

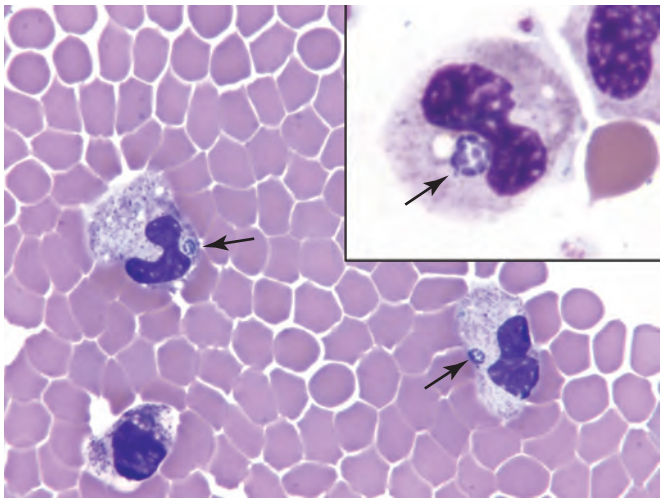

Figure 8-39 Peripheral blood granulocytes (band neutrophils) containing *Anaplasma* inclusions *(arrows)*. (Courtesy Dr. Tad Weiczorek, Faulkner Hospital, Boston, Mass.)

- *Scrub typhus* (caused by *Orienta tsutsugamushi*) is transmitted by chiggers. It is endemic in areas of Asia, Australia, and some islands in the western Pacific and Indian oceans. Fever, headache, myalgia and cough are usual symptoms, sometimes accompanied by a characteristic eschar and associated lymphadenopathy from the chigger bite.
- *Rocky Mountain spotted fever* (caused by *Rickettsia rickettsia*) is transmitted to humans by dog ticks. It is most common in the southeastern and south-central United States. It begins as a nonspecific severe illness with fever, myalgias, and gastrointestinal distress, and progresses to a widespread macular then petechial rash that can involve the palms and soles.
- *Ehrlichiosis* (caused by *Ehrlichia chaffeensis*) and *anaplasmosis* (*Anaplasma phagocytophilum*) are tick-transmitted diseases. The bacteria predominantly infect monocytes (*Ehrlichia chaffeensis*) or neutrophils (*Anaplasma phagocytophilum*). Characteristic cytoplasmic inclusions (morulae), composed of masses of bacteria that occasionally take the shape of a mulberry, are present in leukocytes (Fig. 8-39). Ehrlichiosis and anaplasmosis are characterized by abrupt onset of fever, headache, and malaise, and may progress to respiratory insufficiency, renal failure, and shock. Rash occurs in approximately 40% of people with *E. chaffeensis* infections.

Rickettsial diseases are usually diagnosed clinically and confirmed by serology or immunostaining of the organisms.

Pathogenesis. **The severe manifestations of rickettsial infections are primarily due to infection of endothelial cells and the consequent endothelial dysfunction and injury.** The rickettsiae that cause typhus and spotted fevers predominantly infect vascular endothelial cells, especially those in the lungs and brain. The bacteria enter the endothelial cells by endocytosis, but they escape from the endosome into the cytoplasm. The organisms proliferate in the endothelial cell cytoplasm and then either lyse the cell