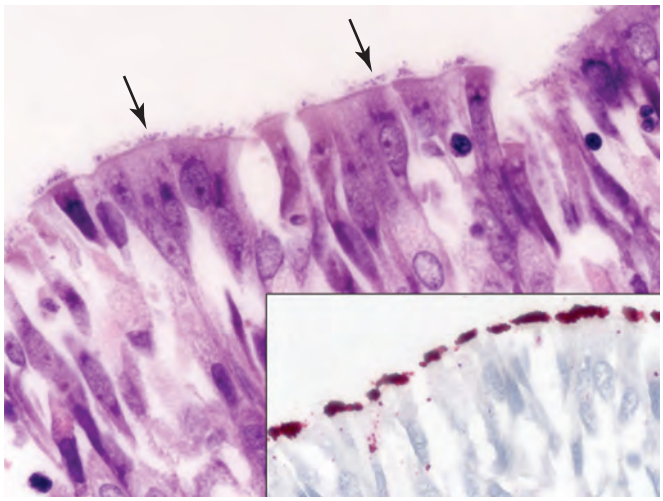

Figure 8-22 Whooping cough showing a haze of bacilli *(arrows)* entangled with the cilia of bronchial epithelial cells. The inset highlights the haze of bacilli by immunohistochemistry using a monoclonal antibody reactive to the lipooligosaccharide A of *Bordetella pertussis*. (Images courtesy Dr. Christopher Paddock of the Centers for Disease Control, Atlanta, Ga.)

toxin is a typical A-B toxin that is composed of five subunits. The A unit, like cholera toxin, ADP-ribosylates and inactivates guanine nucleotide-binding proteins, so these G proteins can no longer transduce signals. The B component contains four subunits that bind to extracellular molecules and allow the A subunit to enter cells. The B subunit can also bind to cell surface molecules such as TLR-4 and through these it can initiate signaling events in cells. Collectively, pertussis toxin subunits impair host defenses by inhibiting neutrophils and macrophages and paralyzing cilia, among other effects.

B. pertussis also produces a toxic adenylate cyclase that enters host cells and converts ATP to cAMP. The rise in cAMP inhibits phagocytosis and the oxidative burst in neutrophils, and can cause apoptosis of macrophages. In addition, pertussis toxin inhibits neutrophil recruitment into the airways and has inhibitory effects on macrophages; the mechanisms underlying these effects are not understood.

MORPHOLOGY

Bordetella bacteria cause a laryngotracheobronchitis that in severe cases features bronchial mucosal erosion, hyperemia, and copious mucopurulent exudate (Fig. 8-22). Unless superinfected, the lung alveoli remain open and intact. In parallel with a striking peripheral lymphocytosis (up to 90%), there is hypercellularity and enlargement of the mucosal lymph follicles and peribronchial lymph nodes.

Pseudomonas *Infection*

***Pseudomonas aeruginosa* is an opportunistic aerobic gram-negative bacillus that is a frequent, deadly pathogen of people with cystic fibrosis, severe burns, or neutropenia.** Many people with cystic fibrosis die of pulmonary failure secondary to chronic infection with *P. aeruginosa*. *P. aeruginosa* can be very resistant to antibiotics, making these infections difficult to treat. It often infects extensive skin burns, which can lead to sepsis. *P. aeruginosa* is a common cause of hospital-acquired infections; it has been cultured from washbasins, respirator tubing, nursery cribs, and even antiseptic-containing bottles. It also causes corneal keratitis in wearers of contact lenses, endocarditis and osteomyelitis in intravenous drug abusers, external otitis (swimmer's ear) in healthy individuals, and severe external otitis in people with diabetes.

Pathogenesis. *P. aeruginosa* produces several toxins that contribute to local tissue damage. The organism secretes an A-B exotoxin called *exotoxin* A that, like diphtheria toxin, inhibits protein synthesis by ADP-ribosylating the ribosomal protein EF-2, leading to the death of host cells. *P. aeruginosa* also secretes damaging enzymes that destroy extracellular matrix (elastase), kill leukocytes (leukocidin), and destroy cell membranes (hemolysins). In the lungs of people with cystic fibrosis, *P. aeruginosa* secretes a mucoid exopolysaccharide called *alginate*, which forms a biofilm that protects bacteria from antibodies, complement, phagocytes, and antibiotics. The organism rapidly develops antibiotic resistance through other mechanisms as well, making treatment difficult.

MORPHOLOGY

Pseudomonas causes a **necrotizing pneumonia** that is distributed through the terminal airways in a fleur-de-lis pattern, with striking pale necrotic centers and red, hemorrhagic peripheral areas. On microscopic examination, masses of organisms are seen that tend to be most concentrated in the walls of blood vessels, where host cells undergo coagulative necrosis (Fig. 8-23). This picture of gram-negative **bacterial vasculitis** accompanied by thrombosis and hemorrhage, although not pathognomonic, is highly suggestive of *P. aeruginosa* infection.

Bronchial obstruction caused by mucus plugging and subsequent *P. aeruginosa* infection are frequent complications of cystic fibrosis. Despite antibiotic treatment and the host immune response, chronic *P. aeruginosa* infection may result in bronchiectasis and pulmonary fibrosis (Chapter 15).

In skin burns, *P. aeruginosa* proliferates widely, penetrating deeply into the veins and spreading hematogenously.

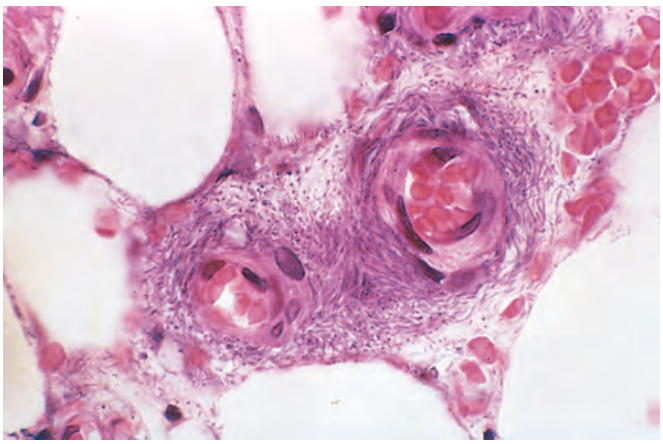

Figure 8-23 *Pseudomonas* vasculitis in which masses of organisms form a perivascular blue haze.