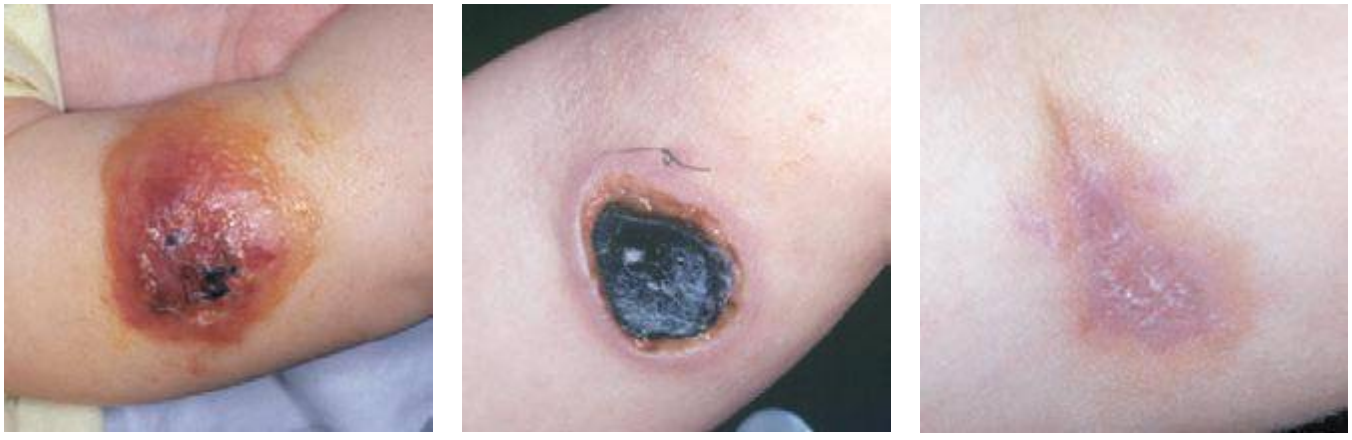

A B C

FIGURE 261e-2 Clinical manifestations of a pediatric case of cutaneous anthrax associated with the bioterrorism attack of 2001. The lesion progresses from vesicular on day 5 (***A***) to necrotic with the classic black eschar on day 12 (***B***) to a healed scar 2 months later (***C***). *(Photographs provided by Dr. Mary Wu Chang. Part A reproduced with permission from KJ Roche et al: N Engl J Med 345:1611, 2001 and Parts B and C reproduced with permission from A Freedman et al: JAMA 287:869, 2002.)*

form most likely to be responsible for death in the setting of a bioterrorist attack. It occurs following the inhalation of spores that become deposited in the alveolar spaces. These spores are phagocytized by macrophages and transported to the mediastinal and peribronchial lymph nodes where they germinate, leading to active bacterial growth and elaboration of the bacterial products edema toxin and lethal toxin. Subsequent hematogenous spread of bacteria is accompanied by cardiovascular collapse and death. The earliest symptoms are typically a viral-like prodrome with fever, malaise, and abdominal and/or chest symptoms that progress over the course of a few days to a moribund state. Characteristic findings on chest x-ray include mediastinal widening and pleural effusions (Fig. 261e-3). Although initially thought to be 100% fatal, the experiences at Sverdlovsk in 1979 and in the United States in 2001 (see below) indicate that with prompt initiation of antibiotic therapy, survival is possible. The characteristics of the 11 cases of inhalational anthrax diagnosed in the United States in 2001 following exposure to contaminated letters postmarked September 18 or October 9, 2001, followed the classic pattern established for this illness, with patients presenting with a rapidly progressive course characterized by fever, fatigue or malaise, nausea or vomiting, cough, and shortness of breath. At presentation, the total white blood cell counts were ~10,000 cells/μL; transaminases tended to be elevated, and all 11 had abnormal findings on chest x-ray and computed tomography (CT). Radiologic findings included infiltrates, mediastinal widening, and hemorrhagic pleural effusions. For cases in which the dates of exposure were known, symptoms appeared within 4–6 days. Death occurred within 7 days of diagnosis in the five fatal cases (overall mortality rate 55%). Rapid diagnosis and prompt initiation of antibiotic therapy were key to survival.

TREATMENT ANTHRAX

Anthrax can be successfully treated if the disease is promptly recognized and appropriate therapy with antibiotics and antitoxin is initiated early. Although penicillin, ciprofloxacin, and doxycycline are the currently licensed antibiotics for this indication, clindamycin and rifampin also have in vitro activity against the organism and have been used as part of treatment regimens. Until sensitivity results are known, suspected cases are best managed with a combination of broadly active agents (Table 261e-3). The *B. anthracis* toxins lethal factor and edema factor share a component known as protective antigen. Raxibacumab, a monoclonal antibody directed toward protective antigen, was licensed in 2012 under the animal rule (see below) for treatment of adult and pediatric patients with inhalational anthrax in combination with appropriate antibacterial drugs. Patients with inhalational anthrax are not contagious and do not require special isolation procedures.

Vaccination and Prevention The first successful vaccine for anthrax was developed for animals by Louis Pasteur in 1881. At present, the single vaccine licensed for human use is a product produced from the cell-free culture supernatant of an attenuated, nonencapsulated strain of *B. anthracis* (Stern strain), referred to as *anthrax vaccine adsorbed* (AVA). Clinical trials for safety in humans and efficacy in animals are currently under way to evaluate the role of recombinant protective antigen as an alternative to AVA. In a postexposure setting in nonhuman primates, a 2-week course of AVA plus ciprofloxacin was found to be superior to ciprofloxacin alone in preventing the development of clinical disease and death. Although the current recommendation for postexposure prophylaxis is 60 days of antibiotics, it would seem prudent to include immunization with anthrax vaccine if available. Given the potential for *B. anthracis* to be engineered to express penicillin resistance, the empirical regimen of choice in this setting is either ciprofloxacin or doxycycline. In settings where these approaches are not available or appropriate, one can administer the antitoxin monoclonal antibody raxibacumab.

PLAGUE

See also Chap. 196.

***Yersinia pestis* as a Bioweapon** Although it lacks the environmental stability of anthrax, the highly contagious nature and high mortality rate of plague make it a close to ideal agent of bioterrorism, particularly if delivered in a weaponized form. Occupying a unique place in history, plague has been alleged to have been used as a biologic weapon for centuries. The catapulting of plague-infected corpses into besieged fortresses is a practice that was first noted in 1346 during the assault of the Crimean city of Kaffa by the Mongolian Tartars. Although unlikely to have resulted in disease transmission, some believe that this event may have played a role in the start of the Black Death pandemic of the fourteenth and fifteenth centuries in Europe. Given that plague was already moving across Asia toward Europe at this time, it is unclear whether such an allegation is accurate. During WWII, the infamous Unit 731 of the Japanese army was reported to have repeatedly dropped plague-infested fleas over parts of China, including Manchuria. These drops were associated with subsequent outbreaks of plague in the targeted areas. Following WWII, the United States and the Soviet Union conducted programs of research on how to create aerosolized *Y. pestis* that could be used as a bioweapon to cause primary pneumonic plague. As mentioned above, plague was thought to be an excellent bioweapon due to the fact that in addition to causing infection in those inhaling the aerosol, significant numbers of secondary cases of primary pneumonic plague would also likely occur due to the contagious nature of the disease and person-to-person transmission via respiratory aerosol. Secondary reports of research conducted during that time suggest that organisms remain viable for up to 1 h and can be dispersed for