TABLE 261e-3 CLINICAL SYNDROMES, PREVENTION, AND TREATMENT STRATEGIES FOR DISEASES CAUSED BY CATEGORY A AGENTS

Agent	Clinical Syndrome	Incubation Period	Diagnosis	Treatment	Prophylaxis
Bacillus anthracis (anthrax)	Cutaneous lesion: Papule to eschar Inhalational disease: Fever, malaise, chest and abdominal discomfort Pleural effusion, widened mediastinum on chest x-ray	1–12 days 1–60 days	Culture, Gram stain, PCR, Wright stain of peripheral smear	Postexposure: Ciprofloxacin, 500 mg, PO bid × 60 d *or* Doxycycline, 100 mg PO bid × 60 d *or* Amoxicillin, 500 mg PO q8h × 60 d, likely to be effective if strain is penicillin sensitive *Active disease:* Ciprofloxacin, 400 mg IV q12h *or* doxycycline, 100 mg IV q12h *plus* Clindamycin, 900 mg IV q8h and/or rifampin, 300 mg IV q12h; switch to PO when stable × 60 d total *plus* *Antitoxin* Raxibacumab, 40 mg/kg IV over 2.25 h; diphenhydramine to reduce reaction	Anthrax vaccine adsorbed Recombinant protective antigen vaccines are under study Raxibacumab when alternative therapies are not available or appropriate
Yersinia pestis (pneumonic plague)	Fever, cough, dyspnea, hemoptysis Infiltrates and consolidation on chest x-ray	1–6 days	Culture, Gram stain, direct fluorescent antibody, PCR	Gentamicin, 2.0 mg/kg IV loading then 1.7 mg/kg q8h IV *or* Streptomycin, 1.0 g q12h IM or IV Alternatives include doxycycline, 100 mg bid PO or IV; chloramphenicol, 500 mg qid PO or IV	Doxycycline, 100 mg PO bid *or* Levofloxacin, 500 mg PO daily Formalin-fixed vaccine (FDA licensed; not available)
Variola major (smallpox)	Fever, malaise, headache, backache, emesis Maculopapular to vesicular to pustular skin lesions	7–17 days	Culture, PCR, electron microscopy	Supportive measures; consideration for cidofovir, tecovirimat, antivaccinia immunoglobulin	Vaccinia immunization
Francisella tularensis (tularemia)	Fever, chills, malaise, myalgia, chest discomfort, dyspnea, headache, skin rash, pharyngitis, conjunctivitis Hilar adenopathy on chest x-ray	1–14 days	Gram stain, culture, immunohistochemistry, PCR	Streptomycin, 1 g IM bid *or* Gentamicin, 5 mg/kg per day div q8h IV for 14 days *or* Doxycycline, 100 mg IV bid *or* Chloramphenicol, 15 mg/kg up to 1 g IV qid *or* Ciprofloxacin, 400 mg IV bid	Doxycycline, 100 mg PO bid × 14 days *or* Ciprofloxacin, 500 mg PO bid × 14 days
Viral hemorrhagic fevers	Fever, myalgia, rash, encephalitis, prostration	2–21 days	RT-PCR, serologic testing for antigen or antibody Viral isolation by CDC or U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID)	Supportive measures Ribavirin 30 mg/kg up to 2 g × 1, followed by 16 mg/kg IV up to 1 g q6h for 4 days, followed by 8 mg/kg IV up to 0.5 g q8h × 6 days	No known chemoprophylaxis Consideration for ribavirin or monoclonal antibodies in high-risk situations
Botulinum toxin (*Clostridium botulinum*)	Dry mouth, blurred vision, ptosis, weakness, dysarthria, dysphagia, dizziness, respiratory failure, progressive paralysis, dilated pupils	12–72 h	Mouse bioassay, toxin immunoassay	Supportive measures including ventilation, HBAT equine antitoxin from the CDC Emergency Operations Center, 770-488-7100	Administration of antitoxin

Abbreviations: CDC, U.S. Centers for Disease Control and Prevention; FDA, U.S. Food and Drug Administration; HBAT, heptavalent botulinum antitoxin; PCR, polymerase chain reaction; RT-PCR, reverse transcriptase polymerase chain reaction.

to disseminated intravascular coagulation, and gangrene of the digits and/or nose may develop in patients with advanced septicemic plague. It is thought that this appearance of some patients gave rise to the term *Black Death* in reference to the plague epidemic of the fourteenth and fifteenth centuries. Some patients may develop pneumonia (secondary pneumonic plague) as a complication of bubonic or septicemic plague. These patients may then transmit the agent to others via the respiratory route, causing cases of primary pneumonic plague. Primary pneumonic plague is the manifestation most likely to occur as the result of a bioterrorist attack, with an aerosol of bacteria spread over a wide area or a particular environment that is densely populated. In this setting, patients would be expected to develop fever, cough with hemoptysis, dyspnea, and gastrointestinal symptoms 1–6 days following exposure. Clinical features of pneumonia would be accompanied by pulmonary infiltrates and consolidation on chest x-ray. In the absence of antibiotics, the mortality rate of this form of plague is on the order of 85%, and death usually occurs within 2–6 days.

TREATMENT PLAGUE

Streptomycin, tetracycline, doxycycline, and levofloxacin are licensed by the U.S. Food and Drug Administration (FDA) for the treatment of plague. Levofloxacin was approved for this indication in 2012 via the animal rule (see below). Multiple additional antibiotics licensed for other infections are commonly used and are likely effective. Among these are aminoglycosides such as gentamicin, cephalosporins, trimethoprim/sulfamethoxazole, chloramphenicol, and ciprofloxacin (Table 261e-3). A multidrug-resistant strain of