bacteremia (see below for duration); dosages must be reduced for patients with renal insufficiency. One small nonrandomized study supports a combination of ampicillin and TMP-SMX. Case reports document success with vancomycin, imipenem, meropenem, linezolid, tetracycline, and macrolides, although there are also reports of clinical failure or disease development with some of these agents. Acquired resistance to antimicrobial agents has been sought but not found in large strain collections. Cephalosporins are *not* effective and should not be used. Neonates should receive ampicillin and gentamicin at doses based on weight.

DURATION

The duration of therapy depends on the syndrome: 2 weeks for bacteremia, 3 weeks for meningitis, 6–8 weeks for brain abscess/encephalitis, and 4–6 weeks for endocarditis in both neonates and adults. Early-onset neonatal disease may be more severe and should be treated for >2 weeks.

COMPLICATIONS AND PROGNOSIS

Many individuals who are promptly diagnosed and treated recover fully, but permanent neurologic sequelae are common in patients with brain abscess or rhombencephalitis. Focal infections of visceral organs; the eye; the pleural, peritoneal, and pericardial spaces; the bones; and both native and prosthetic joints have all been reported. Of 100 liveborn, treated neonates in one series, 60% recovered fully, 24% died, and 13% had long-term neurologic or other complications.

PREVENTION

Healthy persons should take standard precautions to prevent foodborne illness: fully cooking meats, washing fresh vegetables, carefully cleaning utensils, and avoiding unpasteurized dairy products. In addition, persons at risk for listeriosis, including pregnant women, should avoid soft cheeses (hard cheeses and yogurt are not problematic) and should avoid or thoroughly reheat ready-to-eat and delicatessen foods.

177 Tetanus

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Tetanus is an acute disease manifested by skeletal muscle spasm and autonomic nervous system disturbance. It is caused by a powerful neurotoxin produced by the bacterium *Clostridium tetani* and is completely preventable by vaccination. *C. tetani* is found throughout the world, and tetanus commonly occurs where the vaccination coverage rate is low. In developed countries, the disease is seen occasionally in individuals who are incompletely vaccinated. In any setting, established tetanus is a severe disease with a high mortality rate.

DEFINITION

Tetanus is diagnosed on clinical grounds (sometimes with supportive laboratory confirmation of the presence of *C. tetani*; see "Diagnosis," below), and case definitions are often used to facilitate clinical and epidemiologic assessments. The Centers for Disease Control and Prevention (CDC) defines tetanus as "the acute onset of hypertonia or … painful muscular contractions (usually of the muscles of the jaw and neck) and generalized muscle spasms without other apparent medical cause." *Neonatal* tetanus is defined by the World Health Organization (WHO) as "an illness occurring in a child who has the normal ability to suck and cry in the first 2 days of life but who loses this ability between days 3 and 28 of life and becomes rigid and has spasms." Given the unique presentation of neonatal tetanus, the history generally permits accurate classification of the illness with a high degree of probability. *Maternal* tetanus is defined by the WHO as tetanus occurring during pregnancy or within 6 weeks after the conclusion of pregnancy (whether with birth, miscarriage, or abortion).

ETIOLOGY

C. tetani is an anaerobic, gram-positive, spore-forming rod whose spores are highly resilient and can survive readily in the environment throughout the world. Spores resist boiling and many disinfectants. In addition, *C. tetani* spores and bacilli survive in the intestinal systems of many animals, and fecal carriage is common. The spores or bacteria enter the body through abrasions, wounds, or (in the case of neonates) the umbilical stump. Once in a suitable anaerobic environment, the organisms grow, multiply, and release tetanus toxin, an exotoxin that enters the nervous system and causes disease. Very low concentrations of this highly potent toxin can result in tetanus (minimum lethal human dose, 2.5 ng/kg).

In 20–30% of cases of tetanus, no puncture entry wound is found. Superficial abrasions to the limbs are the commonest infection sites in adults. Deeper infections (e.g., attributable to open fracture, abortion, or drug injection) are associated with more severe disease and worse outcomes. In neonates, infection of the umbilical stump can result from inadequate umbilical cord care; in some cultures, for example, the cord is cut with grass or animal dung is applied to the stump. Circumcision or ear-piercing also can result in neonatal tetanus.

EPIDEMIOLOGY

Tetanus is a rare disease in the developed world. Two cases of neonatal tetanus have occurred in the United States since 1989. Between 2001 and 2008, a total of 231 cases of tetanus were reported to the U.S. national surveillance system. Most cases occur in incompletely vaccinated or unvaccinated individuals. Vaccination status is known in 50% of cases reported in the United States between 1972 and 2009; among these cases, only 16% of patients had had three or more doses of tetanus toxoid.

Persons >60 years of age are at greater risk of tetanus because antibody levels decrease over time. One-third of recent cases in the United States were in persons >65 years old. Injection drug users—particularly those injecting heroin subcutaneously ("skin-popping")—are increasingly recognized as a high-risk group (15% of all cases in 2001–2008). In 2004, an outbreak of tetanus occurred in the United Kingdom, which had previously reported low rates among drug users. The reasons for this outbreak remain unclear but are thought to involve a combination of heroin contamination, skin-popping, and incomplete vaccination. Since then, only seven sporadic cases have been reported in the United Kingdom.

PATHOGENESIS

Genome sequencing of *C. tetani* has allowed identification of several exotoxins and virulence factors. Only those bacteria producing tetanus toxin (*tetanospasmin*) can cause tetanus. Although closely related to the botulinum toxins in structure and mode of action, tetanus toxin undergoes retrograde transport into the central nervous system and thus produces clinical effects different from those caused by the botulinum toxins, which remain at the neuromuscular junction.

Toxin is transported by intra-axonal transport to motor nuclei of the cranial nerves or ventral horns of the spinal cord. Tetanus toxin is produced as a single 150-kDa protein that is cleaved to produce heavy (100-kDa) and light (50-kDa) chains linked by a disulfide bond and noncovalent forces. The carboxy terminal of the heavy chain binds to specific membrane components in presynaptic α-motor nerve terminals; evidence suggests binding to both polysialogangliosides and membrane proteins. This binding results in toxin internalization and uptake into the nerves. Once inside the neuron, the toxin enters a retrograde transport pathway, whereby it is transported proximally to the motor neuron body in what appears to be a highly specific process. Unlike other components of the endosomal contents, which undergo acidification following internalization, tetanus toxin is transported in a carefully regulated pH-neutral environment that prevents an acid-induced conformational change that would result in light-chain expulsion into the surrounding cytosol.