bioassay for serum tetanus toxin may be helpful, but a negative result does not exclude the diagnosis. Polymerase chain reaction also has been used for detection of tetanus toxin, but its sensitivity is unknown.

The few conditions that mimic generalized tetanus include strychnine poisoning and dystonic reactions to antidopaminergic drugs. Abdominal muscle rigidity is characteristically continuous in tetanus but is episodic in the latter two conditions. Cephalic tetanus can be confused with other causes of trismus, such as oropharyngeal infection. Hypocalcemia and meningoencephalitis are included in the differential diagnosis of neonatal tetanus.

TREATMENT TETANUS

If possible, the entry wound should be identified, cleaned, and debrided of necrotic material in order to remove anaerobic foci of infection and prevent further toxin production. Metronidazole (400 mg rectally or 500 mg IV every 6 h for 7 days) is the preferred antibiotic. An alternative is penicillin (100,000–200,000 IU/kg per day), although this drug theoretically may exacerbate spasms. Failure to remove pockets of ongoing infection may result in recurrent or prolonged tetanus.

Antitoxin should be given early in an attempt to deactivate any circulating tetanus toxin and prevent its uptake into the nervous system. Two preparations are available: human tetanus immune globulin (TIG) and equine antitoxin. TIG is the preparation of choice, as it is less likely to be associated with anaphylactoid reactions. Recommended therapy is 3000–5000 IU of TIG as a single IM dose, a portion of which should be injected around the wound. Equine-derived antitoxin is available widely and is used in low-income countries at a dosage of 10,000–20,000 U administered IM as a single dose or as divided doses after testing for hypersensitivity. Some evidence indicates that intrathecal administration of TIG inhibits disease progression and leads to a better outcome. The results of relevant studies have been supported by a meta-analysis of trials involving both adults and neonates, with TIG doses of 50–1500 IU administered intrathecally.

Spasms are controlled by heavy sedation with benzodiazepines. Chlorpromazine and phenobarbital are commonly used worldwide, and IV magnesium sulfate has been used as a muscle relaxant. A significant problem with all these treatments is that the doses necessary to control spasms also cause respiratory depression; thus, in resource-limited settings without mechanical ventilators, controlling spasms while maintaining adequate ventilation is problematic, and respiratory failure is a common cause of death. In locations with ventilation equipment, severe spasms are best controlled with a combination of sedatives or magnesium and relatively short-acting, cardiovascularly inert, nondepolarizing neuromuscular blocking agents that allow titration against spasm intensity. Infusions of propofol have also been used successfully to control spasms and provide sedation.

It is important to establish a secure airway early in severe tetanus. Ideally, patients should be nursed in calm, quiet environments because light and noise can trigger spasms. Tracheal secretions are increased in tetanus, and dysphagia due to pharyngeal involvement combined with hyperactivity of laryngeal muscles makes endotracheal intubation difficult. Patients may need ventilator support for several weeks. Thus tracheostomy is the usual method of securing the airway in severe tetanus.

Cardiovascular instability in severe tetanus is notoriously difficult to treat. Rapid fluctuations in blood pressure and heart rate can occur. Cardiovascular stability is improved by increasing sedation with IV magnesium sulfate (plasma concentration, 2–4 mmol/L or titrated against disappearance of the patella reflex), morphine, or other sedatives. In addition, drugs acting specifically on the cardiovascular system (e.g., esmolol, calcium antagonists, and inotropes) may be required. Short-acting drugs that allow rapid titration are preferred; particular care should be taken when longer-acting β antagonists are administered, as their use has been associated with hypotensive cardiac arrest.

Complications arising from treatment are common and include thrombophlebitis associated with diazepam injection, ventilator-associated pneumonia, central-line infections, and septicemia. In some centers, prophylaxis against deep-vein thrombosis and thromboembolism is routine.

Recovery from tetanus may take 4–6 weeks. Patients must be given a full primary course of immunization, as tetanus toxin is poorly immunogenic and the immune response following natural infection is inadequate.

PROGNOSIS

Rapid development of tetanus is associated with more severe disease and poorer outcome; it is important to note time of onset and length of incubation period. More sophisticated modeling has revealed other important predictors of prognosis (Table 177-1). Few studies have formally addressed long-term outcomes of tetanus. However, it is generally accepted that recovery is typically complete unless periods of hypoventilation have been prolonged or other complications have ensued. Studies of children and neonates have suggested a higher incidence of neurologic sequelae. Neonates may be at increased risk of learning disabilities, behavioral problems, cerebral palsy, and deafness.

PREVENTION

Tetanus is prevented by good wound care and immunization (Chap. 148). In neonates, use of safe, clean delivery and cord-care practices as well as maternal vaccination are essential. The WHO guidelines for tetanus vaccination consist of a primary course of three doses in infancy, boosters at 4–7 and 12–15 years of age, and one booster in adulthood. In the United States, the CDC suggests an additional dose at 14–16 months and boosters every 10 years. "Catch-up" schedules recommend a three-dose primary course for unimmunized adolescents followed by two further doses. For persons who have received a complete primary course in childhood but no further boosters, two doses at least 4 weeks apart are recommended.

Standard WHO recommendations for prevention of maternal and neonatal tetanus call for administration of two doses of tetanus toxoid at least 4 weeks apart to previously unimmunized pregnant women. However, in high-risk areas, a more intensive approach has been successful, with all women of childbearing age receiving a primary course along with education on safe delivery and postnatal practices.

Individuals sustaining tetanus-prone wounds should be immunized if their vaccination status is incomplete or unknown or if their last booster was given >10 years earlier. Patients sustaining wounds not classified as clean or minor should also undergo passive immunization with TIG. It is recommended that tetanus toxoid be given in conjunction with diphtheria toxoid in a preparation with or without acellular pertussis: DTaP for children <7 years old, Td for 7- to 9-year olds, and Tdap for children >9 years old and adults.

In the early 1980s, tetanus caused more than 1 million deaths a year, accounting for an estimated 5% of maternal deaths and 14% of all neonatal deaths. In 1989, the World Health

TABLE 177-1 FACTORS ASSOCIATED WITH A POOR PROGNOSIS IN TETANUS

Adult Tetanus	Neonatal Tetanus
Age >70 years	Younger age, premature birth
Incubation period <7 days	Incubation period <6 days
Short time from first symptom to admission	Delay in hospital admission
Puerperal, IV, postsurgery, burn entry site	Grass used to cut cord
Period of onset[a] <48 h	Low birth weight
Heart rate >140 beats/min[b]	Fever on admission
Systolic blood pressure >140 mmHg[b]	
Severe disease or spasms[b]	
Temperature >38.5°C[b]	

[a]Time from first symptom to first generalized spasm. [b]At hospital admission.