Tetanus

**Background:** Tetanus is an infectious disorder characterized by increased muscle tone and spasms caused by the release of a neurotoxin, tetanospasmin, by *Clostridium tetani* following inoculation into a human host. It occurs in several clinical forms, including generalized, cephalic, localized, and neonatal disease.

- Tetanus results from infection with *C. tetani*, a mobile, spore-forming, anaerobic, gram-positive bacillus.
- This bacillus is found in or on soil, manure, dust, clothing, skin, and 10-25% of human GI tracts.
- The spores need tissue with the proper anaerobic conditions to germinate; the ideal medium is wounds with tissue necrosis.
- The spores may survive for years in some environments and are resistant to disinfectants and to boiling for 20 minutes.
- *C. tetani* only germinate and multiply if there is also low oxygen tension. Tetanus can therefore only develop where there is trauma with devitalised tissue necrosis, or where there are foreign bodies in the wound. Earth or calcium salts in the tissues and contamination with aerobic bacteria such as *Staphylococcus* are contributory factors.
- Only a very small anaerobic area is necessary to produce enough tetanus toxin to be fatal.
- In particular, it is important to note that there are no local complaints related to the site of entry of the infection and toxin, because the wound is often a trivial one. In some cases, no wound or injury can be detected.
- Under anaerobic conditions, the spores of *C. tetani* germinate and produce 2 toxins:
  - tetanolysin (a hemolysin with no recognized pathologic activity)
  - tetanospasmin, which is responsible for the clinical manifestations of the disease.

**Pathogenesis**

- Tetanospasmin is released in the wound and binds to the peripheral motor neuron terminal, enters the axon, and via retrograde intraneuronal transport, or via the blood reaches the nerve cell body in the brainstem and spinal cord.
- The toxin migrates across the synapse to presynaptic terminals where it blocks the release of the inhibitory neurotransmitters glycine and gamma-aminobutyric acid (GABA).
- This diminished inhibition is responsible for the observed muscle rigidity.
- Loss of inhibition may also affect preganglionic sympathetic neurons in the lateral gray matter of the spinal cord and produce sympathetic hyperactivity and high levels of circulating catecholamines.
- The toxin binding may be irreversible; recovery depends on the sprouting of new axonal terminals.

**Mortality/Morbidity:**

The rating scale for the severity and the prognosis of tetanus is described below.

Score 1 point for each of the following:
- Incubation period less than 7 days
- Period of onset less than 48 hours
- Acquired from burns, surgical wounds, compound fractures, or septic abortion
- Narcotic addiction
- Generalized tetanus
- Temperature greater than 104°F (40°C)
- Tachycardia greater than 120 beats per minute (>150 beats per min in neonates)

- Total score indicates the severity and the prognosis as follows:
  - Score of 0-1 indicates mild severity with less than a 10% mortality rate.
  - Score of 2-3 indicates moderate severity with a 10-20% mortality rate.
  - Score of 4 indicates severe tetanus with a 20-40% mortality rate.
  - Score of 5-6 indicates very severe tetanus with greater than a 50% mortality rate.
Generalized tetanus:
- The incubation period is 2-30 days (the average is 6-12 days), largely depending on the distance of the site of injury from the CNS.
  - sustained trismus
  - sore throat with dysphagia (early sign), difficulty swallowing
  - characteristic sardonic smile (risus sardonicus) - altering the expression considerably to produce a sneer when the patient attempts to smile
  - neck stiffness
  - abdominal rigidity
  - back stiffness
  - persistent spasm of the back musculature may cause opisthotonus
  - hydrophobia, drooling, sweating
  - patients often are afebrile
  - irritability; restlessness; diaphoresis;
  - waves of opisthotonus are highly characteristic of the disease. With progression, the extremities become involved in episodes of painful flexion and adduction of the arms, clenched fists, and extension of the legs.
  - Noise or tactile stimuli may precipitate spasms and generalized convulsions.
  - If spasms occur rapidly, the prognosis is worse. Spasms usually occur within 48 hours of the onset of muscle stiffness, and then occur with increasing frequency and without apparent stimulus.
  - Late in the disease, involvement of the autonomic nervous system may result in:
    - severe arrhythmias,
    - oscillation of the blood pressure and of the pulse (hypertension and tachycardia alternating with hypotension and bradycardia)
    - profound diaphoresis,
    - hyperthermia,
    - rhabdomyolysis,
    - laryngeal spasm,
    - urinary retention.
  - In most cases, the patient remains lucid.
  - The condition may progress for 2 weeks despite antitoxin therapy because of the time needed for intra-axonal antitoxin transport.

Localized tetanus:
- Localized tetanus involves the extremity with a contaminated wound and shows considerable variation in severity. This is an unusual form of tetanus.
- In mild cases, patients may have weakness of the involved extremity, presumably due to partial immunity.
- In more severe cases, intense painful spasms occur and usually progress to generalized tetanus.

Cephalic tetanus:
- Cephalic tetanus generally follows head injury or occurs with infection of the middle ear.
- Symptoms consist of isolated or combined dysfunction of the cranial motor nerves (most frequently the seventh cranial nerve).
- It may remain localized or progress to generalized tetanus (rapid progression are typical).
- This is an unusual form of tetanus with an incubation period of 1-2 days.
- The prognosis for survival is usually poor.

Tetanus neonatorum:
- This is generalized tetanus resulting from infection of a neonate.
- The usual cause is the use of contaminated materials to sever or dress the umbilical cord in newborns of unimmunized mothers.
The usual incubation period after birth is 3-10 days (which is why it is sometimes referred to as the disease of the seventh day).

- The newborn usually exhibits irritability, poor feeding, rigidity, facial grimacing, and severe spasms with touch.
- The mortality rate exceeds 70%.

**Complications:**
- Complications include spasm of the vocal cords and/or spasms of the respiratory muscles that cause interference with breathing.
- Other complications include fractures of the spine or long bones, hypertension, abnormal heartbeats, coma, generalized infection, clotting in the blood vessels of the lung, pneumonia, and death.
- Patients experience severe pain during each spasm. During the spasm, the upper airway can be obstructed, or the diaphragm may participate in the general muscular contraction.
- Sympathetic overactivity is the major cause of tetanus-related death in the intensive care unit. Sympathetic hyperactivity usually is treated with labetalol at 0.25-1 mg per minute as needed for blood pressure control or with morphine at 0.5-1 mg/kg per hour by continuous infusion.
- Neonatal tetanus follows infection of the umbilical stump, most commonly resulting from a failed aseptic technique in a mother who is inadequately immunized. The mortality rate of neonatal tetanus exceeds 90%, and developmental delays are common among survivors.

**Prognosis:**
- Current statistics indicate that the mortality rate in mild and moderate tetanus is approximately 6%; for severe tetanus, the mortality rate may be as high as 60%.

**Special Concerns:**
- Strychnine poisoning is the only condition that truly mimics tetanus.

**Lab Studies:**
- The diagnosis of tetanus is based entirely on clinical findings.
- The leukocyte count may be high.
- Serum antitoxin levels of more than or equal to 0.01 are considered protective and make tetanus unlikely, although rarely cases have been reported despite the presence of protective antitoxin levels.
- Serum muscle enzyme levels (eg, creatine kinase, aldolase) may be elevated.

**Medical Care:** The goals of treatment are:
- **Initial supportive therapy:** The patient should be placed in a quiet room in an intensive care unit. If ventilation is compromised, the patient should be sedated, intubated, and provided with a soft nasal feeding tube. A tracheostomy may be needed.
- **Wound debridement and care:** Wounds should be explored, carefully cleansed, and properly debrided.
- **Stopping toxin production:** Antimicrobials are used to decrease the number of vegetative forms (source of toxin) of *C tetani* in the wound.
  - The current antimicrobial drug of choice is **metronidazole** with penicillin as an alternative treatment. Other antimicrobials that have been used are clindamycin, erythromycin, tetracycline, and vancomycin.
- **Neutralizing unbound toxin:** Human tetanus immunoglobulin (TIG) is recommended for treatment.
  - A single total dose of **3000-6000 U** is recommended for children and adults.
  - Available preparations must be administered intramuscularly at the time of diagnosis to prevent further circulating toxin from reaching the CNS.
• In countries in which TIG is not available, equine tetanus antitoxin may be available. Tetanus antitoxin is administered as a single dose of **100,000-150,000 U** after appropriate testing for sensitivity and desensitization, if necessary.

• **Controlling disease manifestations:** A benzodiazepine (midazolam administered intravenously at 5-15 mg/h is suitable) should be used to produce sedation, decrease rigidity, and control spasms. If the spasms are not controlled with benzodiazepines, long-term neuromuscular blockade is required.

• **Managing complications:** Specific therapy for autonomic system complications and control of spasms should be initiated.
  o Sympathetic hyperactivity is treated with combined alpha and beta blockade or morphine.
  o Epidural blockade with local anesthetics may be needed.
  o Hypotension requires fluid replacement and dopamine or norepinephrine administration.
  o Parasympathetic overactivity is rare, but if bradycardia is sustained, a pacemaker may be needed.

• **Clinical tetanus does not induce immunity against future attacks; therefore, all patients should be fully immunized with tetanus toxoid during the convalescent period.**

**Prevention:**

• An effective vaccine termed tetanus toxoid has been available for many years. Administer tetanus toxoid in combination with diphtheria toxoid and pertussis vaccine (DTP) to children at ages 2 months, 4 months, 6 months, 12-15 months, and between 4-6 years. Administer tetanus and diphtheria (TD) toxoid to children aged 7 years or older. Recommend a tetanus booster shot every 10 years.