Tetanus

Maria Banica & Sophie Nam

BISC 209

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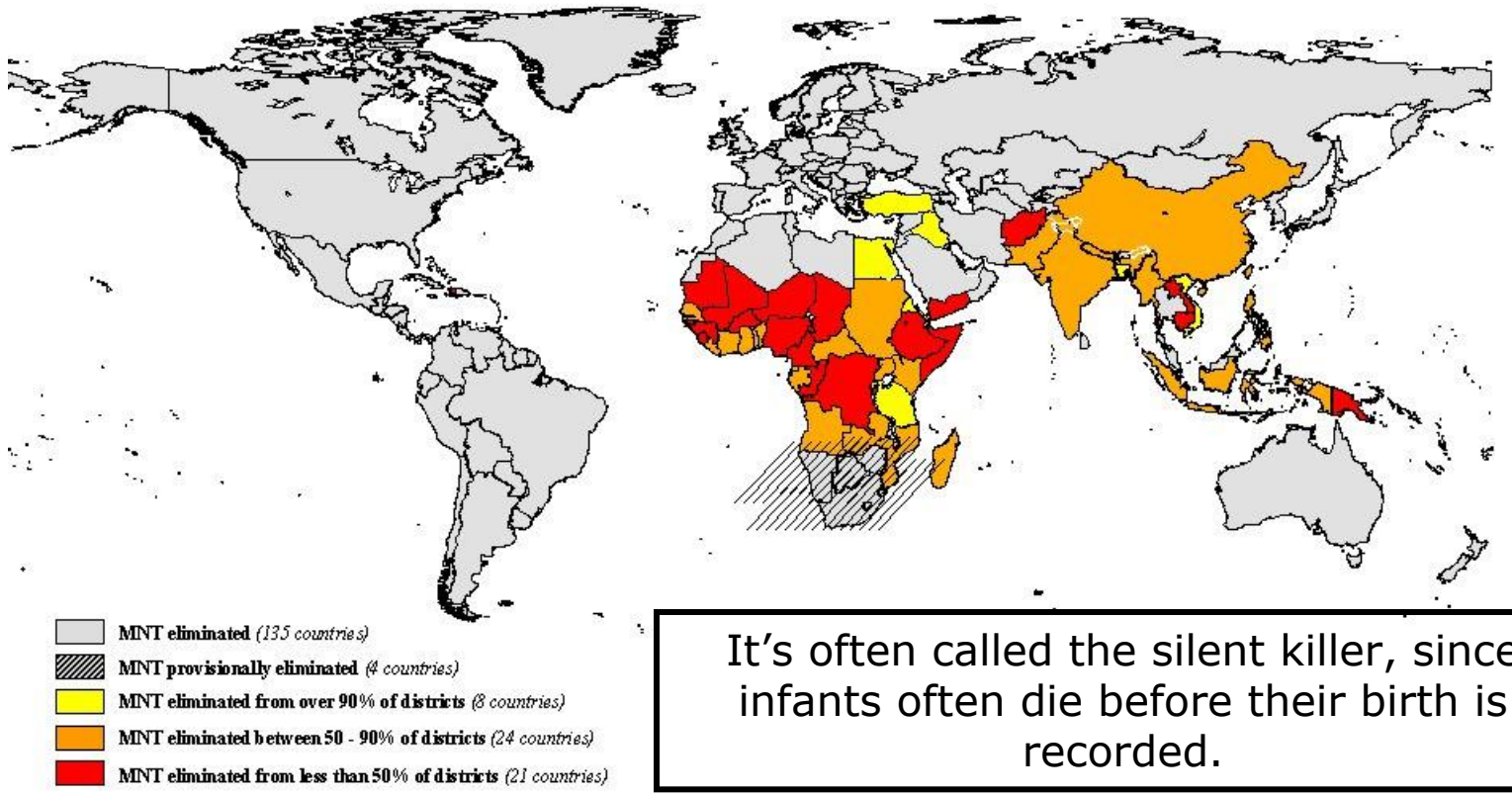
Brief history of disease

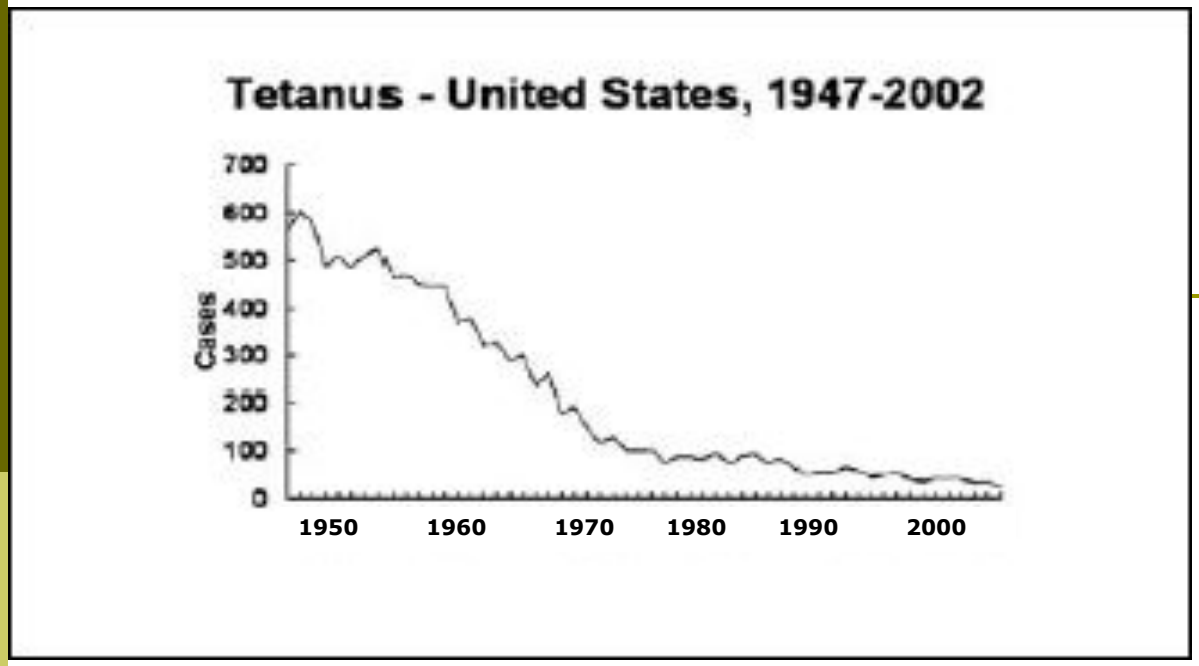
- 5th century BC: Hippocrates first **described** the disease
- 1884: Carle and Rattone discovered the **etiology** *(cause/origin of disease)*
  - Produced tetanus by injecting pus from a fatal human case
  - Nicolaier was able to do the same by injecting soil samples into animals
- 1889: Kitasato **isolated** the organism from human victim, showed that it could produce disease when injected into animals. Reported that **toxin** could be **neutralized** by specific antibodies.
- 1897: Nocard demonstrated the protective effect of **passively transferred antitoxin** ☐ used in WWI
- 1924: Descombey developed tetanus toxoid for **active immunization** ☐ used in WWII

Distribution

In developing countries, neonatal tetanus is a leading cause of neonatal mortality, accounting for over 250,000 deaths annually.



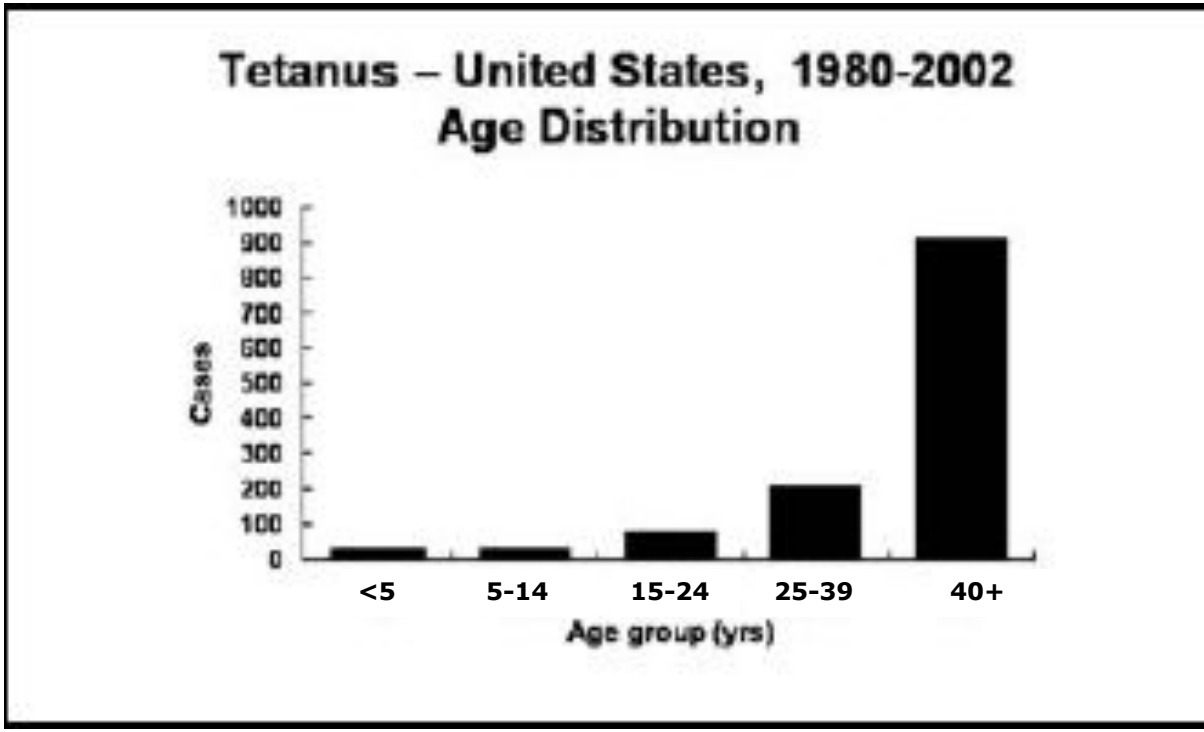
It's often called the silent killer, since infants often die before their birth is recorded.



A sharp decrease after tetanus toxoid was introduced into routine childhood immunization in the late 1940s.

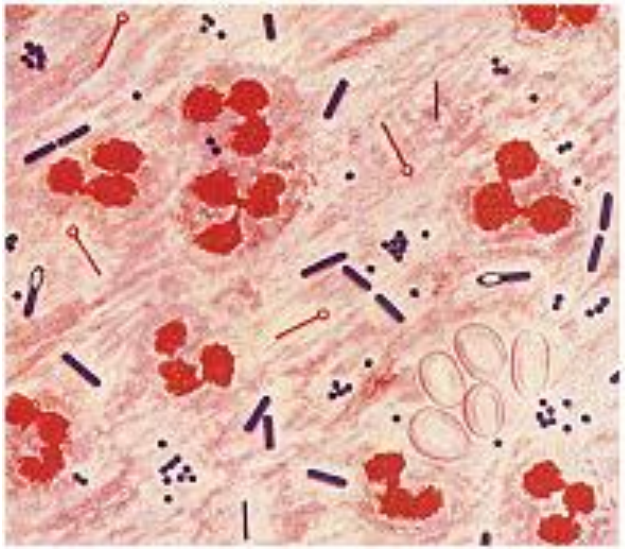
All time low in 2002 – 25 cases (0.4 cases in 100,000 population)

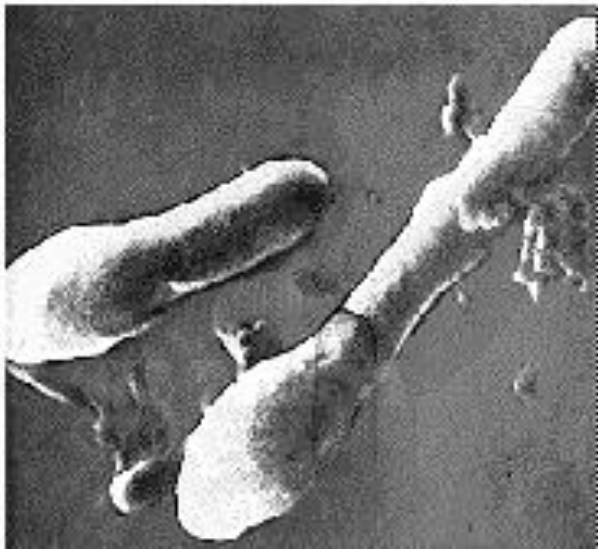
* Affects those over the age of 40 the most ☐ is taken to mean that waning immunity is a significant risk factor.



Causative agent

- *Clostridium tetani*





Left. Stained pus from a mixed anaerobic infection. At least three different clostridia are apparent.

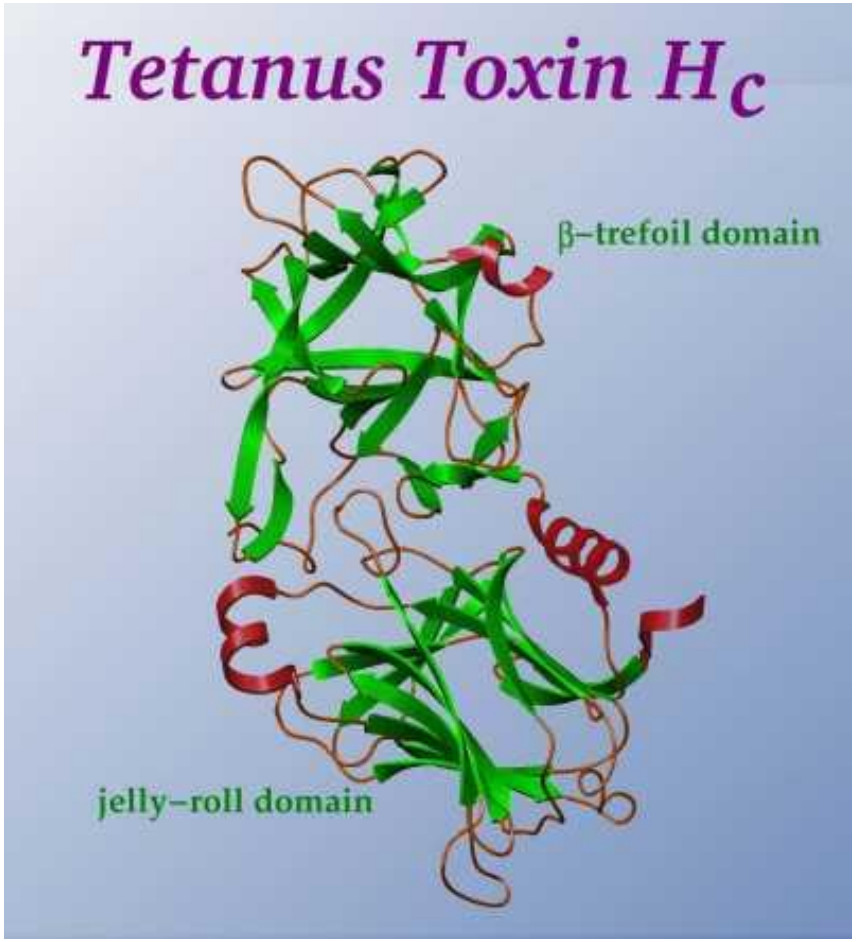
Right. Electron micrograph of vegetative *Clostridium tetani* cells.

Morphology & Physiology

- Relatively large, Gram-positive, rod-shaped bacteria
- Spore-forming, anaerobic.
- Found in soil, especially heavily-manured soils, and in the intestinal tracts and feces of various animals.
- Strictly fermentative mode of metabolism.

Virulence & Pathogenicity

- Not pathogenic to humans and animals by invasive infection but by the production of a potent protein toxin
  - **tetanus toxin** or **tetanospasmin**
  - The second exotoxin produced is tetanolysin—function not known.

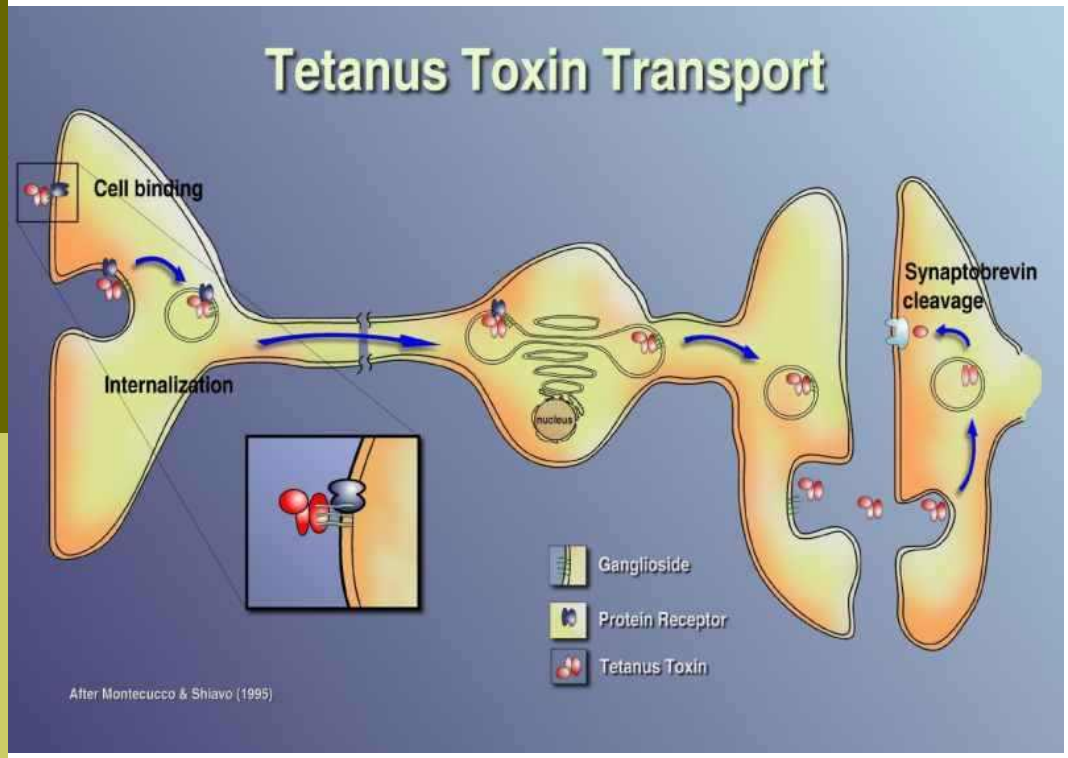


Tetanus toxin

- Produced when spores germinate and vegetative cells grow after gaining access to wounds. The organism multiplies locally and symptoms appear remote from the infection site.

- One of the three most poisonous substances known on a weight basis, the other two being the toxins of botulism and diphtheria.
  - Tetanus toxin is produced in vitro in amounts up to 5 to 10% of the bacterial weight.
  - Estimated lethal human dose of Tetanospamin = 2.5 nanograms/kg body

- Because the toxin has a specific affinity for nervous tissue, it is referred to as a **neurotoxin**. The toxin has no known useful function to *C. tetani*.



- Initially binds to peripheral nerve terminals
- Transported within the axon and across synaptic junctions until it reaches the central nervous system.
- Becomes rapidly fixed to gangliosides at the presynaptic inhibitory motor nerve endings, then taken up into the axon by endocytosis.

- Blocks the release of inhibitory neurotransmitters (glycine and gamma-amino butyric acid) across the synaptic cleft, which is required to check the nervous impulse.
  - If nervous impulses cannot be checked by normal inhibitory mechanisms, it leads to unopposed muscular contraction and spasms that are characteristic of tetanus.

Methods of transmission

- *C. tetani* can live for years as spores in animal feces and soil. As soon as it enters the human body through a major or minor wound and the conditions are anaerobic, the spores germinate and release the toxins.
- Tetanus may follow burns, deep puncture wounds, ear or dental infections, animal bites, abortion.
- Only the growing bacteria can produce the toxin.
- It is the only vaccine-preventable disease that is *infectious but not contagious* from person to person.

Symptoms

- Tetanic seizures (painful, powerful bursts of muscle contraction)
- if the muscle spasms affect the larynx or chest wall, they may cause asphyxiation
- stiffness of jaw (also called lockjaw)
- stiffness of abdominal and back muscles
- contraction of facial muscles
- fast pulse
- fever
- sweating

The back muscles are more powerful, thus creating the arc backward

"Oposthotonus" by Sir Charles Bell, 1809.

Baby has neonatal tetanus with complete rigidity

Types of tetanus: local, cephalic, generalized, neonatal

- *Incubation period: 3-21 days, average 8 days.*

Uncommon types:

- **Local tetanus:** persistent muscle contractions in the same anatomic area as the injury, which will however subside after many weeks; very rarely fatal; milder than generalized tetanus, although it could precede it.

- **Cephalic tetanus:** occurs with ear infections or following injuries of the head; facial muscles contractions.

Most common types:

Generalized tetanus

- descending pattern: lockjaw ☐ stiffness of neck ☐ difficulty swallowing ☐ rigidity of abdominal and back muscles.
- Spasms continue for 3-4 weeks, and recovery can last for months
- Death occurs when spasms interfere with respiration.

Neonatal tetanus:

- Form of generalized tetanus that occurs in newborn infants born without protective passive immunity because the mother is not immune.
- Usually occurs through infection of the unhealed umbilical stump, particularly when the stump is cut with an unsterile instrument.

Methods of diagnosis

- Based on the patient's account and physical findings that are characteristic of the disease.
- Diagnostic studies generally are of little value, as cultures of the wound site are negative for *C. tetani* two-thirds of the time.
  - When the culture is positive, it confirms the diagnosis of tetanus
- Tests that may be performed include the following:
  - Culture of the wound site (may be negative even if tetanus is present)
  - Tetanus antibody test
  - Other tests may be used to rule out meningitisOther tests may be used to rule out meningitis, rabies, strychnine poisoning, or other diseases with similar symptoms.

Clinical treatment

- If treatment is not sought early, the disease is often fatal.
- The **bacteria** are killed with antibiotics, such as penicillin or tetracycline; further toxin production is thus prevented.
- The **toxin** is neutralized with shots of tetanus immune globulin, TIG.
- Other drugs may be given to provide sedation, relax the muscles and relieve pain.
- Due to the extreme potency of the toxin, immunity does not result after the disease.

Method of prevention - immunization

- A person recovering from tetanus should begin active immunization with tetanus toxoid (Td) during convalescence.
- The tetanus toxoid is a formalin-inactivated toxin, with an efficiency of approx. 100%.
- The DTaP vaccine includes tetanus, diphteria and pertussis toxoids; it is routinely given in the US during childhood. After 7 years of age, only Td needs to be administered.
- Because the antitoxin levels decrease over time, booster immunization shots are needed every 10 years.

What else can be done?

- Remove and destroy the source of the toxin through surgical exploration and cleaning of the wound (debridement).
- Bedrest with a nonstimulating environment (dim light, reduced noise, and stable temperature) may be recommended.
- Sedation may be necessary to keep the affected person calm.
- Respiratory support with oxygen, endotracheal tube, and mechanical ventilation may be necessary.

RESOURCES

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