Neuro-Sciences

M. Leprae, Clostridium tetani and C. botulinum

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MYCOBACTERIUM LEPRAE

- *Mycobacterium leprae,* the cause of leprosy, is an acid-fast bacillus that has not been grown in artificial medium or tissue culture beyond, possibly, a few generations.
- However, it can be grown in the footpads of normal mice, in thymectomized irradiated mice, and in the armadillo, which may also be infected naturally.
- Its growth in animals is very slow, with an estimated doubling time of 12 to 14 days.

LEPROSY

- Leprosy is a chronic granulomatous disease of the peripheral nerves and superficial tissues, particularly the nasal mucosa.
- Disease ranges from slowly resolving anesthetic skin lesions to the disfiguring facial lesions responsible for the social stigma and ostracism of the individuals with leprosy (lepers).

Important✅

EPIDEMIOLOGY

- The exact mode of transmission is unknown but appears to be by generation of small droplets from the nasal secretions from cases of lepromatous leprosy. Traumatic inoculation through minor skin lesions or tattoos is also possible.
- The incubation period is generally 2 to 7 years but sometimes up to four decades.
- The infectivity of *M.* leprae is low. Most new cases have had prolonged close contact with an infected individual. Biting insects may also be involved.

PATHOGENESIS

- *M. leprae* is an obligate intracellular parasite that must multiply in host cells to persist. In humans the preferred cells are macrophages and Schwann cells.

IMMUNITY

- Immunity to *M. leprae* is CMI mediated. The range of disease correlates with DTH responsiveness to lepromin, a skin test antigen derived from leprous tissue similar to tuberculin.

CMI : cell-mediated immunity
DTH : Delayed-type hypersensitivity

MANIFESTATIONS

- Two major forms of the disease are recognized, tuberculoid and lepromatous. However, intermediate forms occur, and the first form may merge into the second.
- Tuberculoid Leprosy
- Tuberculoid leprosy involves the development of macules or large, flattened plaques on the face, trunk, and limbs, with raised, erythematous edges and dry, pale, hairless centers. When the bacterium has invaded peripheral nerves, the lesions are anesthetic.

Important for clinical

Not for the exam

- Lepromatous Leprosy
- In lepromatous multibacillary leprosy, CMI is deficient, and patients are anergic to lepromin.
- Histologically, lesions show dense infiltration with leprosy bacilli, and large numbers may reach the bloodstream. Skin lesions are extensive, symmetric, and diffuse, particularly on the face, with thickening of the looser skin of the lips, forehead, and ears, resulting in the classic leonine appearance. Damage may be severe, with loss of nasal bones and septum, sometimes of digits, and with testicular atrophy in men.

Modified acid-fast stain (Ziehl–Neelsen stain), not exactly as TB stain, the concentration of the acid differ.

DIAGNOSIS

- Laboratory diagnosis of lepromatous leprosy involves preparation of acid-fast stained scrapings of infected tissue, particularly nasal mucosa or ear lobes. Large numbers of acid-fast bacilli are seen.
- Tuberculoid leprosy is diagnosed clinically and by histologic appearance of full-thickness skin biopsies.
- PGL-1–based serologic tests have been evaluated for their usefulness in serodiagnosis.

rifampin : Shorten treatment duration

TREATMENT AND PREVENTION

- Sulfones, such as dapsone, which blocks *para*-aminobenzoic acid metabolism in *M. leprae*. When combined with rifampin, it usually controls or cures tuberculoid leprosy when given for 6 months.
- In lepromatous leprosy and multibacillary intermediate forms of the disease, a third agent (clofazimine) is added to help prevent the selection of resistant mutants, and treatment is continued at least 2 years.
- Prevention requires early diagnosis and treatment of cases in close contacts.

Flaccid or spastic paralysis
- Flaccid paralysis causes your muscles to shrink and become flabby. It results in muscle weakness. (caused by enterovirus)
- Spastic paralysis involves tight and hard & dense muscles. It can cause your muscles to twitch uncontrollably, or spasm.
(People with Tetanus has **spastic paralysis**)

CLOSTRIDIUM TETANI

- *C. tetani* is a slim, Gram-positive rod, which may stain Gram negative in very young or old cultures.
- It forms spores readily in nature and in culture, yielding a typical round terminal spore that gives the organism a drumstick appearance. (Terminal & bulging spores)
- It requires strict anaerobic conditions. Its definite identification depends on demonstrating its neurotoxic exotoxin (tetanospasmin) which blocks the release of inhibitory neurotransmitters used by inhibitory afferent motor neurons generating spasms.
- Formaldehyde treatment removes toxicity but retains antigenicity (Toxoid) and thus stimulates production of antitoxin.

TETANUS

- **Back muscle** spasms often cause arching, called **opisthotonos.**
- lockjaw patient need a tube to eat & drink.
- it may affect respiratory muscles (diaphragm), in this case if we don't use a oxygen tent the patient will die.

- The striking feature of tetanus is severe muscle spasms (or "lockjaw" when the jaw muscles are involved). This occurs despite minimal or no inflammation at the primary site of infection, which may be unnoticed even though the outcome is fatal.
- The disease is caused by in vivo production of a neurotoxin that acts centrally, not locally. Immunization with inactivated toxin, even after stepping on a rusty nail, prevents tetanus.

EPIDEMIOLOGY

- The spores of *C. tetani* exist in many soils, and the organism is sometimes found in the lower intestinal tract of humans and animals.
- The spores are introduced into wounds contaminated with soil or foreign bodies. It occurs in recently delivered infants when the umbilical cord is severed or bandaged in a nonsterile manner.
- Nonsterile techniques can lead to tetanus.

MANIFESTATIONS

- The incubation period of the disease is from 4 days to several weeks, it varies with distance to CNS . The shorter incubation period is usually associated with wounds in areas supplied by the cranial motor nerves. In general, shorter incubation periods are associated with more severe disease.
- The diagnosis is clinical; neither culture nor toxin testing are useful, the masseter muscles are often the first to be affected, resulting in inability to open the mouth properly (trismus) causing lockjaw.

- As other muscles become affected, intermittent spasms can become generalized to include muscles of respiration and swallowing. In extreme cases, massive contractions of the back muscles (opisthotonos) develop.
- Untreated patients with tetanus retain consciousness and are aware of their plight, in which small stimuli can trigger massive contractions. Respiratory failure leads to death.
- Mortality (15 to more than 60%) is highest in neonates and in elderly patients.

TREATMENT

- Specific treatment of tetanus involves neutralization of any unbound toxin with large doses of human tetanus immune globulin (HTIG), which is derived from the blood of volunteers hyperimmunized with toxoid.
- Most important in treatment are nonspecific supportive measures, including maintenance of a quiet dark environment, sedation, and provision of an adequate airway, until axons regenerate.
- Benzodiazepines are also used to indirectly antagonize the effects of the toxin.

PREVENTION

- Routine active immunization with tetanus toxoid, combined with diphtheria toxoid and pertussis vaccine (DPT) for primary immunization in childhood and DT for adults, can completely prevent the disease. Boosters required every 10 years.
- Passive immunization with a prophylactic dose of HTIG is used as soon as possible to unimmunized subjects with tetanus-prone wounds.

autoclave temperature = 121°C & 15 psi of pressure.

CLOSTRIDIUM BOTULINUM

- *C. botulinum* is a large G ram-positive rod.
- Its spores resist boiling for long periods, and moist heat at 121°C is required for certain destruction.
- Germination of spores and growth of *C. botulinum* can occur in a variety of alkaline or neutral foodstuffs when conditions are sufficiently anaerobic.
- It grows under these anaerobic conditions and elaborates a family of neurotoxins of extraordinary toxicity. **Botulinum toxin** is the most potent toxin known in nature.

- The estimated lethal dose for humans of less than 1 μg.
- It acts on the presynaptic membranes at neuromuscular junctions with consequent blockage of synaptic acetylcholine release causes paralysis of the motor system and dysfunction of the autonomic nervous system.
- The toxins (A to G) are heat labile and destroyed rapidly at 100°C but are resistant to the enzymes of the gastrointestinal tract.

BOTULISM

- Botulism begins with cranial nerve palsies and develops into descending symmetrical motor paralysis, which may involve the respiratory muscles.
- No fever or other signs of infection occur.
- The time course depends on the amount of toxin present and whether it was ingested preformed in food or produced endogenously in the intestinal tract or a wound.

EPIDEMIOLOGY

- Spores are widely distributed in soil, pond, and lake sediments.
- If spores contaminate food, they may convert to the vegetative state, multiply, and produce toxin in storage under proper conditions.
- This may occur with no change in food taste, color, or odor.
- The alkaline conditions provided by vegetables, such as green beans, and mushrooms and fish support the growth, and the acidic conditions provided by foods such as canned fruit do not support the growth.

- Botulism most often occurs after ingestion of inadequately heated home-canned foods.
- Botulism often occurs in small family outbreaks in the case of home-prepared foods or less often as isolated cases connected to commercial products (such as inadequately sterilized commercial fish products).
- Infant and wound botulism results when the toxin is produced endogenously, beginning with environmental spores that are either ingested or contaminate wounds.

MANIFESTATIONS

- Food-borne botulism usually starts 12 to 36 hours after ingestion of the toxin.
- The first signs are nausea, dry mouth, and, in some cases, diarrhea.
- Cranial nerve signs, including blurred vision, pupillary dilatation, and nystagmus, occur later. Symmetrical paralysis begins with the ocular, laryngeal, and respiratory muscles and spreads to the trunk and extremities.
- The most serious finding is complete respiratory paralysis. Mortality is 10 to 20%.

Infant Botulism

- A syndrome associated with *C. botulinum* that occurs in infants between the ages of 3 weeks and 8 months is now the most commonly diagnosed form of botulism.
- The organism is apparently introduced on weaning or with dietary supplements, especially honey, and multiplies in the infant's colon, with absorption of small amounts of toxin.
- The infant shows constipation, poor muscle tone, lethargy, and feeding problems and may have paralyses similar to those in adult.

Wound Botulism

- Very rarely, wounds infected with other organisms may allow *C. botulinum* to grow.
- Wound botulism in parenteral users of cocaine and maxillary sinus botulism in intranasal users of cocaine has been reported.
- Disease similar to that from food poisoning may develop, or it may begin with weakness localized to the injured extremity.
- Botulism without an obvious food or wound source is occasionally reported in individuals beyond infancy.

DIAGNOSIS

- The toxin can be demonstrated in blood, intestinal contents, or remaining food, but these tests require inoculation of mice and are performed only in reference laboratories.
- *C. Botulinum* may also be isolated from stool or from foodstuffs suspected of responsibility for botulism.

TREATMENT AND PREVENTION

- Intensive supportive measures, particularly mechanical ventilation, is the single most important determinant of clinical outcome and mortality should be less then 10%.
- The administration of large doses of horse *C. botulinum* antitoxin is thought to be useful in neutralizing free toxin. Frequent hypersensitivity reactions makes it unsuitable for use in infants.
- Antimicrobial agents are given only to patients with wound botulism.

- Adequate pressure cooking or autoclaving in the canning process kills spores, and heating food at 100°C for 10 minutes before eating destroys the toxin.
- Food from damaged cans or those that present evidence of positive inside pressure should not even be tasted because of the extreme toxicity of the *C. botulinum toxin*.