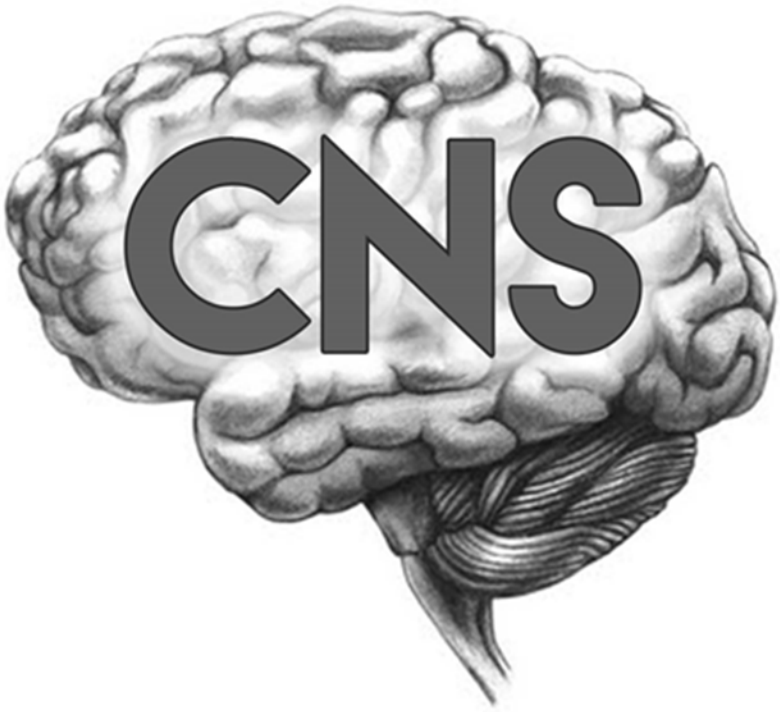

MICROBIOLOGY

○ Sheet ☑ Slide ○ Handout

Number

2

Subject

Doctor

Sameer Naji

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Neuro-Science I

Gp B Streptococci, Listeria, M. Leprae, Clostridium tetani and C. botulinum

Dr. Sameer Naji, MB, BCh, PhD (UK)
Ass. Professor
Dept. of Basic Medical Sciences
Faculty of Medicine
The Hashemite University

Group B Streptococci (Streptococcus agalactiae)

- Group B streptococci (GBS) produce short chains and diplococcal pairs of spherical or ovoid Gram-positive cells. Colonies are larger and β-hemolysis is less distinct than with group A and may even be absent.
- In addition to the Lancefield B antigen, GBS produce polysaccharide capsules of nine antigenic types (Ia, Ib, II through VIII) all of which contain sialic acid in the form of terminal side chain residues.

GROUP B STREPTOCOCCAL DISEASE

- The typical GBS case is a newborn in the first few days of life who is not doing well.
- Fever, lethargy, poor feeding, and respiratory distress are the most common features.
- Localizing findings are usually lacking, and the diagnosis is revealed only by isolation of GBS from blood or cerebrospinal fluid.
- The mortality rate is high even when appropriate antibiotics are used.

EPIDEMIOLOGY

- GBS are the leading cause of sepsis and meningitis in the first few days of life acquired from mother's vaginal flora during pregnancy and delivery (GBS can be found in the vaginal flora of 10 to 30% of women).
- GBS produce disease in approximately 2% of the colonized newborn babies (1.8 cases/ 1000 live births).
- The risk is much higher with prematurity (decrease of infant's innate resistance) or ruptured amniotic membranes.

CLINICAL ASPECTS

- The clinical findings are nonspecific and similar to those found in other serious infections in the neonatal period.
- Respiratory distress, fever, lethargy, irritability, apnea, and hypotension are common. Fever is sometimes absent, and infants may even be hypothermic. Pneumonia is common, and meningitis is present in 5 to 10% of cases.
- Mortality rate approaches 20% even with appropriate and prompt treatment.

- GBS infections in adults are uncommon and fall in two groups:
- Peripartum chorioamnionitis and bacteremia, the mother’s side of the neonatal syndrome.
- Pneumonia and a variety of skin and soft tissue infections similar to those produced by other pyogenic streptococci.
- Maternal and other adult infections can be serious but usually not fatal unless patients are immunocompromised.

DIAGNOSIS

- Culture of blood, cerebrospinal fluid, or other appropriate specimen is the only standard method.

TREATMENT

- Neonatal infections are often initially treated with combinations of penicillin (or ampicillin) and an aminoglycoside as GBS are slightly less susceptible to β-lactams than other streptococci.

PREVENTION

- Current strategies are focused on reducing contact of the infant with the organism.
- In colonized women, attempts to eradicate the carrier state have not been successful, but intrapartum antimicrobial prophylaxis has been shown to be protective and all newborns at risk receive such prophylaxis.
- Third trimester vaginal culture and/or clinical factors determine the risk.
- Prevention by immunization with capsular polysaccharide shows to be feasible.

LISTERIA MONOCYTOGENES

- *Listeria monocytogenes* is a Gram-positive rod with some bacteriologic features that resemble those of both corynebacteria and streptococci. In stained smears of clinical and laboratory material, the organisms resemble diphtheroids.
- *Listeria* are not difficult to grow in culture, producing small, β-hemolytic colonies on blood agar. This species is able to grow slowly in the cold even at temperatures as low as 1°C.

- *Listeria* species are catalase positive, which distinguishes them from streptococci, and produce a characteristic tumbling motility in fluid media at 25°C that distinguishes them from corynebacteria.
- Eleven *L. monocytogenes* serotypes are recognized based on flagellar and somatic surface antigens, but the majority of human cases are limited to only three serotypes (1/2a, 1/2b, 4b).

EPIDEMIOLOGY

- The reservoir is the intestine of animals and humans (colonization varies from 2 to 12%).
- Food-borne transmission is from animal products.
- *L. monocytogenes* grows at refrigerator temperatures, allowing scant numbers to reach an infectious dose during storage.
- It may be transmitted transplacentally to the fetus, and may also be transmitted to newborns in the birth canal in a manner similar to group B streptococci.
- Most cases occur at the extremes of life.

MANIFESTATIONS

- Listeriosis usually does not present clinically until there is disseminated infection.
- In foodborne outbreaks, sometimes GIT manifestations of primary infection such as nausea, abdominal pain, diarrhea, and fever occur. Disseminated infection in adults is usually occult.
- It has a tropism for the CNS causing Meningitis and encephalitis.
- Neonatal and puerperal infections lead to stillbirth and dissemination.

DIAGNOSIS

- Diagnosis of listeriosis is by culture of blood, cerebrospinal fluid (CSF), or focal lesions.
- In meningitis, CSF Gram stains are usually positive. The first indication that *Listeria* is involved is often the discovery that the β – hemolytic colonies subcultured from a blood culture bottle are Gram-positive rods rather than streptococci.

TREATMENT AND PREVENTION

- *L. monocytogenes* is susceptible to penicillin G, ampicillin, and trimethoprim/sulfamethoxazole, all of which have been used effectively. Ampicillin combined with gentamicin is considered the treatment of choice for fulminant cases.
- Intense surveillance to prevent the sale of *Listeria*-contaminated ready-to-eat meat products has led to a marked decrease in the incidence of new infections.
- There is no vaccine.

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).

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.

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.

- 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.

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.

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.

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. 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

- 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.

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.*