Gram Negative and Gram Positive Anaerobes

Gram Positive Spore Forming Anaerobic Bacteria (Clostridium Species)

**Clostridium perfringens:**

Structure, Biology, Virulence:
- A) Large Rectangular Gram-positive rods
- B) Multiply very rapidly
- C) Produce many toxins that are directly destructive
  - a. Alpha-lecithinase lysing erythrocytes, platelets and leukocytes
  - b. Beta - necrotizing enteritis (pig-bel)
  - c. Epsilon – vascular permeability of GI wall
  - d. Iota- necrotic activity and vascular permeability

Epidemiology
- A) Soil and water
  - a. Type A-most common cause of infection-soft tissue, food poisoning, septicemia
  - b. Type C- necrotizing enteritis – rare

Clinical Disease
- A) Soft tissue infections following contamination of devitalized tissue-gas gangrene
- B) Food Poisoning-contaminated meat, enterotoxin caused, self limited

Diagnosis
- A) Gram Stain of involved tissue-note, no WBC
- B) Rapid growth in culture

Treatment
- A) Surgical debridement
- B) Penicillin, clindamycin (for toxin)
- C) No treatment for food poisoning

**Clostridium tetani**

Structure, Biology, Virulence
- A) Gram positive, motile, terminal spores, may be confused with gram negative organisms
- B) Tetanospasmin-heat labile, blocks release of neurotransmitters of inhibitory synapses via inactivation of proteins that cause release of glycine and GABA

Epidemiology
- A) Ubiquitous in soil and GI tract
B) At risk population-unvaccinated

Clinical Disease
A) Incubation at site days to weeks without symptoms
B) Axonal transport of toxin with variable manifestations that develops into generalized tetanus preceded most commonly by trismus. Can be confused with non-tetanus paralysis (e.g. stroke)
C) Localized tetanus-wound, cephalic, neonatal

Diagnosis
A) Clinical presentation
B) Culture not useful, rarely recovered, site may not be identified

Treatment
A) Newborns have highest mortality
B) Debridement of wound (if identified), PCN and metronidazole to kill active organisms-will not reverse the manifestations from tetanospasmin
C) Antitoxin at site, systemic (HTIG) to inactivate unbound toxin
D) Symptomatic until synapses functional/newly generated
E) Prophylaxis is most important at time of injury for unvaccinated or vaccinated.

*Clostridium Botulinum*

Structure, Biology, Virulence
A) Large Gram positive rods, sporeforming
B) Seven toxins with four causing human disease (A, B, E, F)
C) Toxin blocks release at cholinergic synapses

Epidemiology
A) Soil worldwide
B) Infant botulism in US most common (but rare)

Clinical Disease
A) Descending paralysis
B) GI then Cranial Nerves, then flaccid paralysis
C) Onset if established in gut flora producing toxin in vivo, respiratory failure
D) Wound botulism-at site of contamination with local toxin production

Diagnosis
A) Clinical presentation
B) Toxin identified in food or stool

Treatment/prevention
A) Supportive measure
B) Elimination from GI tract (infants)-metronidazole
C) Antitoxin to inactivate unbound toxin
D) Prevention- heat potentially contaminated food (60-100C) for 10 min
E) Food preparation (canning) done properly, no honey to infants under 1 yr

**Clostridium difficile**

Structure, biology, Virulence
A) Gram positive spore forming rod. Spores are the major source of spread
B) Two toxins- enterotoxin and cytotoxin

Epidemiology
A) acquired from environment (hospital), exposure to antibiotics allow for selection
B) Recent hyper toxin A producing strain associated with hypervirulence and high mortality and persistence (2003)

Clinical Disease
A) Diarrhea
B) High degree of clinical relapse
C) Increase mortality with hyper toxigenic strain, toxic megacolon, especially in elderly

Diagnosis
A) Clinical suspicion, especially hospitalized patients receiving antibiotics
B) Leukocytosis
C) PCR detection in stool

Treatment
A) Antibiotics- Vancomycin, Metronidazole (less severe), Fidaxomycin
B) Fecal Transplant

Prevention
A) Isolation of patients to prevent spread
B) Terminal cleaning of rooms of infected patients

Other Clostridium species of importance
A) *Clostridium septicum* - Typically associated with bacteremia in high risk patients- leukemia, colon cancer, high degree of mortality
B) *Clostridium sordellii* – Fatal toxic shock syndrome following medical abortions and natural child birth, leukocytosis prominent feature, pathogenesis poorly understood. Also associated with injection drug users, less fatal.

**Other Gram Positive Anaerobic Bacteria-non spore forming**
Actinomyces
A) Gram positive rods
B) Form filamentous hyphae
C) Sulfur granules
D) Slow growing- abscess forming in cervicofacial, thoracic, pelvic, intraabdominal locations
E) Difficult to diagnose, slow growing
F) Treated with penicillin as first line plus drainage when possible

Propionobacterium acnes
A) Skin organism, associated with acne
B) microaerophilic
C) often considered contaminant in blood cultures- but may not be if persistent, associated with prosthetic material (joint or other device/hardware)
D) Penicillin therapy is first line, resistant to metronidazole due to microaerophilic!

Peptostreptococcus
A) Undergone substantial reassignment of genetic classification with new species
B) Inhabitants of mouth and GI tract
C) Often found among mixed infections-brain, intraabdominal, lung
D) Requires debridement and antibiotics (penicillin, metronidazole, carbapenems.

Gram negative anaerobes

Bacteroides fragilis group
Structure, physiology, virulence
A) Prevalent in gut, part of normal flora, Gram negative large rods
B) > 90 species and renamed species of other genera
C) Virulence-outside of GI tract can cause disease, polysaccharide capsule is protective against immune system (prevents phagocytosis)
D) Heat labile toxin- can cause diarrhea in strains that carry toxin, usually associated with animals and poor conditions
E) Hallmark is abscess formation

Clinical Disease
A) Part of normal flora, normal protective, contributes to normal immune development
B) Outside of GI tract- intraabdominal abscess, brain abscess, lung abscess, soft tissue infections, in high risk (diabetes), bacteremia (most often with
intraabdominal infection)-20% mortality.

Diagnosis
A) Clinical suspicion
B) Culture of organism(s), often mixed infections with aerobes

Treatment
A) surgical drainage often required
B) Antibiotics- beta-lactam/beta lactam inhibitors, carbapenems, tigecycline, metronidazole most active

Other Gram Negative Anaerobic Bacteria of importance

Fusobacterium
A) Highly virulent toxin producers (LPS)
B) F necrophorum- Lemierre's syndrome, potent endotoxin, metastatic infection, jugular venous involvement from peritonsilar infection
C) F nucleatum- aspiration associated pneumonia, ear infection, brain abscess, sinusitis, liver abscess.

Prevotella and Porphyromonas Species
A) Formerly classified as Bacteroides
B) Species specific associated infections- pelvic, oral, pleuropulmonary
C) Adhesin, molecules allow for adherence to epithelium, cytokine inducers
D) Abscess formers, often in mixed infections
E) More susceptible to antibiotics than Bacteroides (including clindamycin, moxifloxacin, cefoxitin in addition to those listed for Bacteroides)