Anaerobes

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Definitions

- **Anaerobes**: Bacteria that require anaerobic conditions to initiate and sustain growth
- **Strict (obligate) anaerobe**: Unable to grow if > than 0.5% oxygen
- **Moderate anaerobes**: Capable of growing between 2-8% oxygen
- **Microaerophilic bacteria**: Grows poorly in air, but better in anaerobic conditions
- **Facultative bacteria (facultative anaerobes)**: Grows both in presence and absence of air

Classification of Medically Important Anaerobes

- **Gram positive cocci**: Peptostreptococcus
- **Gram negative cocci**: Veillonella
- **Gram positive bacilli**: Clostridium perfringens, tetani, botulinum, difficile
  - Propionibacterium
  - Actinomyces
  - Lactobacillus
  - Mobiluncus
- **Gram negative bacilli**: Bacteroides fragilis, thetaiotaomicron
  - Fusobacterium
  - Prevotella
  - Porphyromonas

Epidemiology

- **Endogenous infections**: Indigenous microflora
  - Skin: Propionibacterium, Peptostreptococcus
    - Prevalence in areas exposed to air explained by (1) oxygen consumption by aerobes (2) low oxidation-reduction potential microhabitats
  - Upper respiratory: Propionibacterium
  - Mouth: Fusobacterium, Actinomyces
  - Intestines: Clostridium, Bacteroides, Fusobacterium
  - Vagina: Lactobacillus
- **Profound modification of flora in pathophysiologic states**
- **Antimicrobials and other medications (PPI, antacids)**
- **Surgery (blind loops)**
- **Cancers**

Role of Anaerobes

- **Role in normal host physiology**
  - Prevent colonization & infection by pathogens
    - Bacterial interference through elaboration of toxic metabolites, low pH, depletion of nutrients
    - Interference with adhesion
  - Contributes to host physiology
    - *B. fragilis* synthesizes vitamin K and deconjugates bile acids
Sites of anaerobic infections

Virulence factors

- Attachment and adhesion
  - Polysaccharide capsules and pili
- Invasion
  - Alteration in host tissue (trauma, disease)
  - Aerotolerance
- Establishment of infection
  - Polysaccharide capsule (B. fragilis)
  - Spore formation (Clostridium)
  - Maintenance of reduced environment
- Tissue damage
  - Elaboration of toxins

Clinical features of anaerobic infections

- The source of infecting micro-organism is the endogenous flora of host
- Alterations of host’s tissues provide suitable conditions for development of opportunist anaerobic infections
- Anaerobic infections are generally polymicrobial
- Abscess formation
- Exotoxin formation

Anaerobic cocci

- Epidemiology
  - Normal flora of skin, mouth, intestinal and genitourinary tracts
- Pathogenesis
  - Opportunistic pathogens, often involved in polymicrobial infections
  - Virulence factors not as well characterized
  - Brain abscesses, periodontal disease, pneumonias, skin and soft tissue infections, intra-abdominal infections
- Peptostreptococcus
  - P. magnus: chronic bone and joint infections, especially prosthetic joints
  - P. prevotii and P. anaerobius: female genital tract and intra-abdominal infections
- Veillonella
  - Normal oral flora, isolated from infected human bites

Anaerobic gram positive bacilli

- No Spore Formation
  - Propionibacterium
    - P. acnes
  - Actinomyces
    - A. israelii
  - Lactobacillus
  - Mobiluncus

- Spore Formation
  - Clostridium
    - C. perfringens
    - C. difficile
    - C. tetani
    - C. botulinum
Propionobacterium

- Anaerobic or aerotolerant, produces propionic acid as major byproduct of fermentation
- Colonize skin, conjunctiva, external ear, oropharynx, female GU tract
- \( P. \) acnes
  - Acne
    - Resides in sebaceous follicles, releases LMW peptide, stimulates an inflammatory response
  - Opportunistic infections
    - Prosthetic devices (heart valves, CSF shunts)

Actinomyces

- Facultative or strict anaerobes
- Colonize upper respiratory tract, GI, female GU tract
- Low virulence; development of disease when normal mucosal barriers are disrupted
- Diagnosis:
  - Macroscopic colonies of organisms resembling grains of sand (sulfur granules)
  - Culture

Actinomycosis

- Cervicofacial Actinomycosis
  - Poor oral hygiene, oral trauma
  - Slowly evolving, painless process
  - Chronic granulomatous lesions that become suppurative and form sinuses
  - Treatment: surgical debridement and prolonged penicillin

Lactobacillus

- Facultative or strict anaerobes
- Colonize GI and GU tract
  - Produces \( H_2O_2 \) which is bactericidal to \( Gardnerella vaginalis \)
  - Vagina heavily colonized (10^5/ml) by Lactobacillus crispatus & jensonii
- Clinical disease
  - Transient bacteremia from GU source
  - Endocarditis
  - Bacteremia in immunocompromized host

Mobiluncus

- Obligate anaerobes
- Gram negative or gram variable
- Colonize GU tract in low numbers
- Associated with bacterial vaginosis
  - Detected in vagina of 6% of controls
  - As many as 97% of women with bacterial vaginosis

Clostridium

- Epidemiology
  - Ubiquitous,
    - Present in soil, water, sewage
    - Normal flora in GI tracts of animals and humans
- Pathogenesis
  - Spore formation
    - Resistant to heat, dessication, and disinfectants
    - Can survive for years in adverse environment
  - Rapid growth in nutritionally enriched, oxygen deprived environment
  - Toxin elaboration (histolytic toxins, enterotoxins, neurotoxins)
**Clostridium perfringens**

- **Epidemiology**
  - GI tract of humans and animals
  - Type A responsible for most human infections

- **Pathogenesis**
  - α-toxin: lecithinase (phospholipase C) that lyses erythrocytes, platelets and endothelial cells
  - δ-toxin: necrotizing activity
  - θ-toxin: hemolysin
  - Enterotoxin: binds to brush borders and disrupts small intestinal transport

- **Clinical manifestations**
  - Self-limited gastroenteritis
  - Soft tissue infections: cellulitis, fascitis or Myonecrosis (gas gangrene)

**Clostridial soft tissue infections**

- Crepitant cellulitis
- Fascitis
- Myonecrosis

**Myonecrosis**

**Myonecrosis xray**

**Clostridial myonecrosis**

- **Clinical course**
  - <48 hours incubation
  - Local area with marked pain, swelling, serosanguinous discharge, bullae, slight crepitance
  - May be associated with increased CPK

- **Treatment**
  - Surgical debridement
  - Antibiotics
  - Hyperbaric oxygen
**Clostridium difficile**

- **Epidemiology**
  - Colonizes GI tract of 5% healthy individuals
  - Endogenous infection
    - Antibiotic exposure associated with overgrowth of C. difficile
  - Exogenous infection
    - Spores detected in hospital rooms of infected patients
- **Pathogenesis**
  - Enterotoxin (toxin A)
    - Produces chemotaxis, induces cytokine production and hypersecretion of fluid, development of hemorrhagic necrosis
  - Cytotoxin (toxin B)
    - Induces polymerization of actin with loss of cellular cytoskeleton

**C. difficile colitis**

- **Clinical syndromes**
  - Asymptomatic colonization
  - Antibiotic-associated diarrhea
  - Pseudomembranous colitis
- **Diagnosis**
  - Isolation of cytotoxin or enterotoxin
- **Treatment**
  - Discontinue antibiotics
  - Metronidazole or vancomycin
  - Relapse in 20-30% (spores are resistant)

**Clostridium tetani**

- **Epidemiology**
  - Spores found in most soils
  - Disease in un-vaccinated or inadequately immunized
  - Disease does not induce immunity
- **Pathogenesis**
  - Spore inoculated into wound
  - Tetanospasmin
    - Heat-labile neurotoxin
    - Retrograde axonal transport to CNS
    - Blocks release of inhibitory neurotransmitters (GABA) resulting in spastic paralysis
    - Binding is irreversible
  - Tetanolysin
    - Oxygen labile hemolysin, unclear clinical significance

**C. tetani exotoxin**

**Tetanus**

- **Clinical Manifestations**
  - Generalized
    - Involvement of bulbar and paraspinal muscles
    - Trismus, risus sardonicus, opisthotonus
    - Autonomic involvement
    - Sweating, hyperthermia, cardiac arrhythmias, labile BP
  - Cephalic
    - Involvement of cranial nerves only
  - Localized
    - Involvement of muscles in primary area of injury
  - Neonatal
    - Generalized in neonates; infected umbilical stump
Risus sardonicus and Opisthotonos of Tetanus

Tetanus

- Treatment
  - Debridement of wound
  - Metronidazole
  - Tetanus immunoglobulin
  - Vaccination with tetanus toxoid
- Prevention
  - Vaccination with a series of 3 tetanus toxoid
  - Booster dose every 10 years

Clostridium botulinum

- Epidemiology
  - Commonly isolated in soil and water
  - Human disease associated with A, B, E, F
- Pathogenesis
  - Botulinum toxin targets cholinergic nerves
  - Prevents release of acetylcholine
  - Recovery depends upon regeneration of nerve endings

C. Botulinum Exotoxin

Botulism

- Clinical Syndromes
  - Foodborne botulism
    - Mostly associated with home-canned foods and preformed toxin
    - Onset of symptoms 1-2 days: blurred vision, dilated pupils, dry mouth, constipation
    - Bilateral descending weakness of peripheral muscles; death related to respiratory failure
  - Infant botulism
    - Consumption of foods contaminated with botulinum spores
    - Disease associated with neurotoxin produced in vivo
    - Wound botulism

Botulism

- Diagnosis
  - Isolation of organism
    - Culture implicated food and stool of patient
  - Isolation of toxin
    - Mouse bioassay
- Treatment
  - Supportive care
    - Elimination of organism from GI tract
    - Gastric lavage
    - Metronidazole or penicillin
  - Trivalent botulinum toxin (A, B, E) to bind circulating botulinum toxin
- Prevention
  - Prevention of spore germination (Acid PH, storage <4°C)
  - Destruction of preformed toxin (20 min at 80°C)
Anaerobic gram negative bacilli

- **Bacteroides**
  - *B. fragilis*
  - *B. thetaiotaomicron*
- Fusobacterium
- Prevotella
- Porphyromonas

Anaerobic gram negative bacilli

- Epidemiology
  - Colonize human body in great numbers
  - Stabilize resident bacterial flora
  - Prevent colonization by pathogens
  - Anaerobes are predominant bacteria in upper respiratory tract, GI and GU tract
  - Outnumber aerobic bacteria by 10-100 fold
  - Many species, but few pathogens

Anaerobic gram negative bacilli

- Clinical Diseases
  - Chronic sinus infections
  - Periodontal infections
  - Brain abscess
  - Intra-abdominal infection
  - Gynecological infection
  - Skin and soft tissue

Bacteroides

- Epidemiology
  - *B. fragilis* associated with 80% of intra-abd infx
- Pathogenesis
  - Polysaccharide capsule
    - Increases adhesion to peritoneal surfaces (along with fimbriae)
    - Protection against phagocytosis
  - Differs from LPS of aerobic GNR
    - Less fatty acids linked to Lipid A component
    - Less pyrogenic activity
  - Superoxide dismutase and catalase
  - Elaborate a variety of enzymes

Bacteroides

- Infections
  - Intra-abdominal infections (peritonitis, abscess); bacteremias; decubitus and diabetic ulcers
- Treatment
  - Drainage of abscess and debridement of necrotic tissue
  - Antibiotics