Staph and Strep most common pathogens
obligate anaerobes important also

Staph and Strep
  Cellulitis
  Necrotizing fasciitis
  Toxic shock syndrome
    Wound and tampon associated disease
    Fever, shock, organ failure
    Superantigen toxin
      Activates massive numbers of T cells – cytokine storm

Tetanus – *Clostridium tetani*
  Gram positive, spore forming anaerobic bacillus
  Infection of wounds by spores
  Spastic paralysis, respiratory failure
  Neonatal disease

  Tetanus toxin
    Protease prevents neurotransmitter release by cleaving proteins in neuron
    necessary for neurotransmitter vesicle fusion to membrane
    Toxin acts in central nervous system to prevent release of inhibitory
    neurotransmitters resulting in uncontrolled muscle contraction

  Therapy involves antitoxin antibodies to block unbound toxin, benzodiazepines to
  stimulate inhibitory neurotransmitter receptors

  Prevention
    cleaning of wounds, administration of antitoxin, toxoid vaccine

  Epidemiology
    Most common in developing world, neonatal disease important in developing world
Wound Infections

- **Staphylococcus aureus** and **Streptococcus pyogenes** are the most important pathogens associated with wound infections
  - Cellulitis – infection and inflammation of subcutaneous tissue
  - Wound infections frequently involve obligate anaerobic bacteria
  - Traumatic tissue damage frequently involves areas of tissue necrosis (cell death) and associated absence of oxygen

Complications of S. aureus and S. pyogenes wound infections

- Necrotizing fasciitis
  - Rapidly spreading cellulitis of deeper subcutaneous tissue, may involve muscle damage and necrosis, associated with significant mortality
  - Toxic shock syndrome
  - Toxin-mediated rapidly-progressing febrile illness associated with shock, organ failure, and significant mortality

Toxic Shock Syndrome

- Complications of skin and wound infections (Staph and Strep)
- Use of highly adsorbent tampons during menstruation (Staph only)
- Complication of influenza-associated S. aureus pneumonia
- Severe form of scarlet fever (Strep)

Symptoms

- Rapid onset and progression of fever, shock (low blood pressure)
- Sunburn-like rash, ultimately desquamates (peels)
- May progress to organ failure (kidney, liver, gastrointestinal, CNS)

Pathogenesis

- Production of superantigen toxins
  - Toxins mediate the activation of a large percentage of T lymphocytes
  - Bind to T cell receptors in an antigen-nonspecific manner
  - Proliferation and production of cytokines
  - Systemic activation of macrophages which produce cytokines
  - Cytokine storm

Therapy of toxic shock syndrome

- Antibiotics
- Fluid support for shock

Epidemiology of toxic shock syndrome

- Non menstrual staphylococcal TSS most common form (~1/100,000)
- Menstrual TSS (~0.1 – 1/100,000)
- Streptococcal TSS (~0.1/100,000)

Tetanus

- **Clostridium tetani**
  - Gram-positive, anaerobic spore-forming bacillus
  - Found in soil and in low numbers in intestinal flora of mammals

- The disease: tetanus
  - Acquired by infection of wound by spores, may be minor, highly variable incubation period
  - Spastic paralysis – contraction of opposing muscle pairs
  - Symptoms begin with facial muscles (lockjaw) and descend over period of days
  - Most deaths occur in first week of disease from respiratory failure
  - Mortality ~50% in untreated disease, <20% with therapy
  - Adult survivors show complete recovery

- Neonatal tetanus
  - Infection of umbilical stump
  - Progression more rapid
  - Survivors may have permanent neurological and cognitive impairment
Pathogenesis of tetanus

- Spores introduced by trauma, germinate in necrotic tissue
- Tetanus toxin produced, transmitted to CNS via motor neuron
  - AB toxin –
    - B subunit binds to neuron surface and determines neuron trafficking
    - A subunit is a protease specific for protein required for fusion of synaptic vesicle with cytoplasmic membrane of neuron.
- Tetanus toxin inhibits release of inhibitory neurotransmitter from interneuron

Diagnosis of tetanus

- Clinical observation
- Electromyographic studies

Therapy

- Antitoxin: human tetanus immune globulin
- Supportive: maintenance of airway, sedation with benzodiazepines (like valium) - stimulate inhibitory neurotransmitter receptors
- Antibiotic therapy not proven to be effective

Prevention of tetanus

- Thorough debridement of wound and administration of antitoxin (or vaccine booster if immune status known) at time of injury
- Vaccine – tetanus toxoid
- Immunization: primary in infancy (DPT), booster every ten years (Tetanus toxoid) for life

Epidemiology of tetanus

- Spores widely present in environment
- Disease occurs in unimmunized populations.
  - Common in developing world
    - ~150,000 deaths per year worldwide (not including neonatal deaths)
  - Important agent of neonatal infection in developing world
    - ~100,000 neonatal deaths per year

Maternal and Neonatal Tetanus (MNT)

20 Countries eliminated MNT (2000 – August 2011)
leaving 38 countries yet to eliminate MNT

*Plus 16/33 States in India & 18/34 Provinces in Indonesia