Microm 301 Skin Infections
Nov. 19, 2012

Acne vulgaris

*Propionibacterium acnes*
Inflammation of pilosebaceous gland blocked by keratin
Topical and oral antibiotics, retinoids

*Staphylococcus aureus*
Folliculitis, furuncle, carbuncle
Impetigo
Scalded skin syndrome
Culture necessary to identify and treat MRSA with appropriate antibiotics
Pathogenesis
Coagulase, membrane damaging toxins, protein A, exfoliative toxin

*Streptococcus pyogenes*
Impetigo (with *S. aureus*)
Erysipelas
Diagnosis requires culture to rule out MRSA
Treat with antibiotics, resistance not a serious problem unlike Staph

Lyme Disease – *Borrelia burgdorferi*
tick bite, rash, systemic disease, arthritis
Pathogenesis involves low-level stimulation of cytokine production, antigenic variation
Diagnosis involves clinical observation, complicated serology
Antibiotic therapy
Small rodents are natural reservoir, concentration of disease in northeastern U.S.

Measles
Enveloped non-segmented neg stranded ssRNA
Acquired via inhalation of respiratory droplets
Infection of immune cells, epithelial cells
Rash and immunosuppression, secondary bacterial pneumonia
Diagnosis clinical and serology
No specific antiviral therapy
Eliminated from US by vaccination but imported cases and small outbreaks among non-immunized individuals
Infections of the Skin

• Bacterial infections
  • Acne vulgaris – *Propionibacterium acnes*
  • *Staphylococcus aureus* and *Streptococcus pyogenes*
  • Lyme Disease – *Borrelia burgdorferi*

• Viral infections with prominent skin manifestations (rashes)
  • Measles – rubeola virus
• Acne vulgaris
  • Inflammation of pilosebaceous glands
• Pathogenesis – not well understood
  • Induction of fatty acid secretion at puberty by androgen hormones
  • Colonization of gland by Propionibacterium acnes
    • Commensal Gram-positive anaerobic bacillus
    • Uses fatty acids as nutrients, produces acids from fermentation
  • Abnormal deposition of keratin produces obstruction
  • Continued secretion of sebum and bacterial growth induces inflammatory response
• Therapy
  • Topical benzoyl peroxide (antibacterial effect)
  • Topical or oral antibiotics - increasing resistance is a problem
  • Retinoids (for severe disease) – suppresses sebum secretion, production of keratin
• **Staphylococcus aureus**
  • Gram-positive cocci in clusters
  • Normal flora of anterior nares (inner surfaces of nostrils) and skin
  • Divide rapidly, resistant to drying

• Diseases
  • **Folliculitis** – infection and inflammation of hair follicle
    • may follow minor irritation of the follicle
    • furuncle – boil: spreading of inflammation to neighboring dermal tissue
    • carbuncle: infection and inflammation spreads to large area
      • Diabetes patients at risk
  • **Impetigo**
    • Inflammation of epidermis
    • Common in children
    • Caused by *S. aureus* and *Streptococcus pyogenes*
  • **Scalded skin syndrome**
    • Blistering of skin and separation and sloughing of superficial epidermis
    • Neonates and children <5 years
• Diagnosis of *Staphylococcus aureus* and *Streptococcus pyogenes* skin infections
  • Culture and antimicrobial sensitivity testing for MRSA

• Therapy
  • Antibiotics, complicated in MRSA infections
  • Topical antibiotics for mild folliculitis, impetigo
  • Parenteral antibiotics for more serious infections
• Other disease caused by S. aureus

• Wound infections
  • Toxic shock syndrome
• Osteomyelitis – bone infection
• Endocarditis – heart valve infection
• Pneumonia
• Sepsis – bloodstream infection
• Food poisoning
• Pathogenesis of *S. aureus*

• **Coagulase**, clumping factor
  • Binding of bacteria to fibrinogen, *conversion of fibrinogen to fibrin*
    • binding to connective tissue, shielding from phagocytes

• **Membrane damaging toxins**
  • inhibits phagocytic cell functions

• **Polysaccharide capsule**
  • inhibits complement binding

• **Protein A**
  • binds Fc (wrong end!) portion of antibody, inhibits interaction with phagocytic cell
• Pathogenesis of S. aureus (cont.)
  • **Exfoliative toxin**
    • Mediates scalded skin syndrome
    • NOT produced by most strains
    • Protease specific for protein that connects cells in epidermis
  • Superantigen toxin (more on this later)
  • Enterotoxin
Streptococcus pyogenes skin infections

- **Impetigo** – superficial infection of epidermis, inflammation produces pus
  - Infections frequently start out as streptococcal infections, then superinfected by S. aureus

- **Erysipelas** – diffuse infection of dermis, can spread in lymphatic circulation
  - Acquired after minor skin trauma
  - Fever, swelling of skin
  - Lymphedema associated with cancer treatment is a significant risk factor

Complications of streptococcal skin infections

- Acute glomerulonephritis
- (acute rheumatic fever NOT a complication of skin infections, only streptococcal pharyngitis)
• Diagnosis of streptococcal skin infections
  • *Culture and antibiotic sensitivity necessary for impetigo to confirm or rule out MRSA*
  • Erysipelas can be treated empirically, culture necessary if infection does not resolve
• Lyme Disease

• *Borrelia burgdorferi*
  • Spirochaete
    • Cannot be reliably visualized in tissue
    • Very slow growing in artificial media

• Lyme disease
  • Acquired from tick bite
  • Disease occurs in stages, not all patients experience all stages
    • 1. Expanding ring-like rash at site of bite (*erythema migrans*)
    • 2. After resolution of initial lesion, *similar lesions appear at other body sites with fever, headache, aches and pains*. Resolves after weeks.
    • 3. Recurring *arthritis* (joint inflammation) months after initial infection.
      • Small percentage of patients will develop chronic arthritis
• Pathogenesis of Lyme Disease poorly understood
  • Adherence to extracellular matrix
  • Persistence in tissue, dissemination
    • Organism binds activators of plasmin (enzyme which dissolves fibrin)
  • Limited induction of cytokines
    • No lipid A
    • Bacterial lipoproteins stimulate cytokine induction through TLR2
  • Slow development of antibody response
    • Antigenic variation of major surface lipoprotein
• Diagnosis of Lyme Disease
  • Clinical: observation of ECM with potential tick exposure in endemic area
  • Serology: complicated two stage test involving EIA and immunoblot assay

• Therapy for Lyme Disease
  • Antibiotics
    • In a small percentage of patients, chronic arthritis and neurological symptoms are not cured, and continued antibiotic therapy is ineffective
• Pathogenesis of Lyme Disease
  • Poorly understood
    • Adherence to extracellular matrix components
    • Induction of cytokines
    • Antigenic variation of major surface protein impedes effective antibody response

*B. burgdorferi* chromosome

Silent loci – not expressed

Expression locus

variable region
• Epidemiology of Lyme Disease
  • Most common arthropod-borne infection in U.S.
  • Small rodents are most important animal reservoir
  • Transmitted to humans by *Ixodes scapularis* (black legged tick, deer tick)
Tick life cycle and Lyme Disease Transmission

Spring

Female adult lays eggs

Summer

Larva hatch, feed on small rodents, become infected.

Autumn

Larva develop into nymphs.

Winter

Nymphs feed on small rodents or humans, transmit pathogen.

Spring

Nymphs develop into adults, feed on deer, occasionally humans, transmit the pathogen (but deer NOT a reservoir for human disease).
Reported Cases of Lyme Disease—United States, 2011

One dot is placed randomly within the county of residence for each confirmed case. Though Lyme disease cases have been reported in nearly every state, cases are reported based on the county of residence, not necessarily the county of infection.

24,000 cases
Measles

- Measles virus
  - Enveloped, non-segmented negative sense ssRNA virus (paramyxovirus family)

- Measles
  - Acquired via inhalation of respiratory droplet from infected person
  - Begins with fever, cough, conjunctivitis 1 week after infection
  - Oral lesions (Koplik spots) and rash occur a few days later.
  - Symptoms resolve after ~10 days
  - Complications – mortality highest in infants and very young children
    - Secondary bacterial pneumonia – very common and major cause of mortality
    - Measles virus pneumonia in persons with impaired cellular immunity
    - Encephalomyelitis (brain and spinal cord inflammation) ~0.1%
    - SSPE – progressive neurodegenerative disease years later <0.01%
• **Diagnosis of measles**
  • Clinical – in areas where measles is endemic
    • Koplik spots and non-vesicular rash pathognomonic (near-certain diagnostic sign)
  • **Serology**

• **Therapy for measles**
  • No specific antiviral therapy
  • Antibiotics for secondary bacterial pneumonia
• Pathogenesis of measles
  • Initial replication in respiratory macrophages, dendritic cells and lymphocytes
    • Measles virus proteins block RLR-mediated detection of viral RNA
    • Induction of interferon synthesis inhibited by blocking signalling pathway
    • Transcriptional response to interferon inhibited
  • Viremia involves replication in T and B cells and dissemination to many cell types
  • Rash produced by cell mediated immune reaction against infected skin endothelial and epithelial cells
  • Immunosuppression
    • Measles virus infection of activated lymphocytes and antigen-presenting cells inhibits cell mediated AND humoral (antibody mediated) immunity.
    • Immunosuppression can last months after initial disease

• Prevention of measles
  • Attenuated live vaccine
    • Administered to infants in combination with mumps and rubella vaccines
      • NO SCIENTIFIC EVIDENCE THAT THIS VACCINE CAUSES AUTISM
• Epidemiology of measles
  • US
    • Measles no longer endemic in U.S.
    • Most cases imported
    • Outbreaks associated with vaccine refusal continue to occur
  • Global
    • Incidence significantly reduced but measles remains a major cause of infant mortality in the developing world