Pyogenic Microorganisms
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Contents

• Pyogenic Infections
  – Virulence Factors
  – Pathogenesis
• Immuno-resistance
Serious Pyogenic Infections

- **Bacteremia** – The presence of bacteria in blood
- **Septicemia** – a bacteremic condition that leads to Sepsis
- **Pyemia** – a Septicemic condition that leads to widespread abscesses of metastatic nature
S. Aureus Virulence Factors

- Enzymes: Coagulase, Hyaluronidase, and DNAse
- Protein A: binds to Fc-IgG to inhibit complement fixation and phagocytosis
- Toxins:
  1. Superantigens: TSST-1 that produce toxic shock syndrome, enterotoxins that cause gastroenteritis
  2. Exfoliative toxins: protease activity causes peeling of skin in staphylococcal scalded-skin syndrome
  3. Other toxins: alpha, beta, and delta toxins act on cell membranes, and Panton-Valentine leukocidin (PVL) is associated with severe necrotizing pneumonia in children
S. Aureus Pathogenesis

- Combined effect of extracellular factors and toxins together with invasive properties of the strain
- More dangerous strains of S. Aureus causes focal abscess that can spread via lymphatics or blood.
- Can result in meningitis, endocarditis, and sepsis
- Can also causes disease through toxins: SSSS and TSS
S. Pyogenes Virulence Factors

1. Structural Components
   - carbohydrate-based bacterial capsule composed of hyaluronic acid
   - M protein inhibit opsonization
   - lipoteichoic acid and protein F (Sfbl) allow attachment to various host cells

2. Toxins and Superantigens
   - Streptolysin O is a exotoxin of beta hemolytic Group property
   - Streptolysin S is a cardiotoxic exotoxin that is another beta-hemolytic component
   - Exotoxin A, B, and C are superantigens cause STSS and scarlet fever

3. Enzymes
S. Pyogenes Virulence Factors

- Streptokinase digest fibrin and other proteins
- Hyaluronidase breaks down hyaluronic acid in connective tissue allowing spread
- Streptodornase are DNAses
- C5a Peptidase are used to minimize influx of neutrophils early in infection
• Serious infection of Beta-hemolytic group A S.pyogenes can result in bacteremia with sepsis, which is rapidly fatal
• Usually involve rapidly spreading infection along lymphatics with little focal suppuration.
• From lymphatics infection can spread via blood stream.
S. Agalactiae

- Virulence factor
  - Capsule
  - β-hemolysin

- GBS: The CAMP test is an important test for identification. It is characterized by the presence of group B Lancefield antigen and by its ability to hydrolyze sodium hippurate.
- It is also sensitive to bile, and will lyse in its presence.
- Causes Septicemia in newborns
Streptococcus Agalactiae Pathogenesis

- Normal flora in GI tract, also can spread to the secondary site such as vagina in 10-30% women and large intestine
- Transferred to a neonate passing through the birth canal and can cause serious group B streptococcal infection
- S. Group B infection during the first month of life may present as fulminant sepsis, meningitis, or respiratory distress syndrome.
- Neonatal pneumonia: S. agalactiae invades via alveolar and pulmonary epithelial cells; newborns are especially susceptible to infection because they lack alveolar macrophages to prevent invasion
S. Pneumoniae Virulence Factors

- **Polysaccharide Capsule** that prevents phagocytosis by the host's immune cells
- **surface proteins** that prevent the activation of complement-mediated opsonization.
- **pili** that enable S. pneumoniae to attach to epithelial cells in the upper respiratory tract
Streptococcus Pneumoniae Pathogenesis

- Causes 60-70% of all bacterial pneumonia
- Pneumococci produce their disease through their ability to multiply in tissues.
- From the respiratory tract the infection can reach other sites such as sinuses and middle ear. Infections sometimes can spread from the mastoid to the meningitis, and sometimes bacteria enter blood stream, resulting bacteremia.
- Severe complications include meningitis, endocarditis, and septic arthritis.
S. Epidermis Virulence Factors

- No specific virulence factors

- Ability to form biofilms, which make it harder to treat since the cells inside the biofilm are guarded from antibiotics and the immune system
Staphylococcus Epidermis Pathogenesis

- Normal flora of skin, respiratory tract and GI tract
- Rarely produce suppuration
- causes biofilms to grow on plastic devices placed within the body. This occurs most commonly on intravenous catheters and on medical prostheses.
- Infection can also occur in dialysis patients or anyone with an implanted plastic device that may have been contaminated. Also causes endocarditis, often in patients with defective heart valves.
- In some other cases, sepsis can occur in hospital patients.
N. Gonorrhoeae Virulence Factors

- Type IV pili
- Outer membrane protein
- Por
- Rmp (Protein III)
- Lipooligosaccharide (LOS)
- IgA1 protease
N. Gonorrhoeae Pathogenesis

1. acquired by **sexual contact**; affect the mucous membranes of the **urethra** in males and **endocervix** and **urethra** in females.

2. **Males:** urethritis, with **yellow, creamy pus** and painful urination. **Females:** mucopurulent discharge.

3. It attacks **mucous membranes** of **genitourinary tract, eye, rectum,** and **throat,** producing **acute suppuration**; followed by **chronic inflammation** and **fibrosis**.

4. **bacteremia** leads to skin lesions

5. **Gonococcal ophthalmia neonatorum.** The initial **conjunctivitis** rapidly progresses and if untreated, results in blindness. **Eye inflammation**

6. **urethritis, cervicitis, salpingitis, pelvic inflammatory disease, proctitis, conjunctivitis** and **pharyngitis**.
N. Meningitidis Virulence Factors

- Capsule
- Fimbriae
- Type IV pili and outer membrane
- IgA protease
- Lipooligosaccharide (LOS)
N. Meningitidis Pathogenesis

1. septicemia and meningitis.
2. Fulminant meningococcemia is more severe, with high fever and hemorrhagic rash; there may be DIC and circulatory collapse.
3. begins suddenly with intense headache, vomiting and stiff neck and progresses to coma within a few hours.
4. thrombosis of small blood vessels with perivascular infiltration and petechial hemorrhages. There may be interstitial myocarditis, arthritis and skin lesions.
5. Meningitis with the surface of the brain is covered with a thick purulent exudate.
H. Influenza Virulence Factors

- PRP capsule (most important)
  Lipooligosaccharide
- IgA protease
- Fimbrial adhesin
- HMW1 and HMW2
- Hap Adhesin
- Hia and Hsf Adhesins - facilitate the adherence of the microorganism to host cell.
- OapA Haemocin - Outer membrane proteins Protein D
1. Type B H. influenza is the most virulent, which causes bacteremia, meningitis, pneumonia, empyema, epiglottis, osteomyelitis, cellulitis, joint infections, ear infections, infective and septic arthritis.

2. It is an important cause of meningitis in children, and may cause respiratory tract infections in children and adult.
Some microbes can evade the damage or killing from the host immune system by several ways.

**IMMUNE EVASION BY MICROBES**
Innate immunity

- Evade phagocytosis
- Interfere with the complement system
## Evade phagocytosis

<table>
<thead>
<tr>
<th>Defense</th>
<th>Microbial strategy</th>
<th>Mechanism</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wash-out</td>
<td>Bind to cell</td>
<td>Adhesins</td>
<td>Neisseria</td>
</tr>
<tr>
<td>Inhibit ciliary activity</td>
<td></td>
<td>Ciliotoxic/ Ciliostatic molecule</td>
<td>Bordetella Streptococcus</td>
</tr>
<tr>
<td>Ingestion and killing by phagocyte</td>
<td>Disrupt Chemotaxis cytotoxic</td>
<td>Leucocidins</td>
<td>Staphylococcus</td>
</tr>
<tr>
<td>Inhibit phagocytosis</td>
<td></td>
<td>Capsule</td>
<td>Streptococcus</td>
</tr>
<tr>
<td>Inhibit lysosomal fusion</td>
<td></td>
<td>Inhibitory molecule</td>
<td>Mycobacterium</td>
</tr>
<tr>
<td>Multiply</td>
<td></td>
<td>Unknown</td>
<td>Listeria</td>
</tr>
</tbody>
</table>
Interfere with the complement system

- Herpesviridae and Coronaviridae interfere with the classical complement activation pathway by avoiding complement binding to antibody–antigen complexes, either by removing (shedding or internalization) these antibody–antigen complexes from the cell surface of the infected cell or by the expression of Fc receptors.
- Poxviruses and herpesviruses encode and express proteins with functional similarities to RCA proteins and other complement regulators and can thereby protect their lipid envelopes and the membranes of the cells.
- Poxviridae, Herpesviridae, Retroviridae and Togaviridae can incorporate host complement control proteins in their viral envelope and/or upregulate expression of these proteins in infected cells.
Virus interference with the complement cascade. Viral proteins that interfere with the complement cascade or promote the activity of physiological complement regulators are indicated in red. Physiological complement regulation is shown in blue.
Evasion of Adaptive immunity

• Bacterial Evasion of Humoral immunity
• Bacterial Evasion of Cellular immunity
• Viral Immune Evasion
Bacterial Evasion of Humoral immunity

- Immunoglobulin-evading
- Evasion of Ab responses
- Evasion of complement system
Immunoglobulin-evading

- Bacteria such as Haemophilus influenzae, *Streptococcus pneumoniae*, Helicobacter pylori, Shigella flexneri, Neisseria meningitidis, Neisseria gonorrhoeae and enteropathogenic E. coli
- Produce *immunoglobulin proteases*, which can *degrade antibodies* (immunoglobulins)
Evasion of Ab responses

• Salmonella species can undergo **phase variation of their capsular (K) and flagellar (H) antigens**, that is, they can change the molecular shape of their capsular and flagellar antigens so that antibodies made against the previous form no longer fit the new form.
### Table 4.4. Bacterial strategies to evade the complement system

<table>
<thead>
<tr>
<th>Evasion strategy</th>
<th>Bacterium</th>
<th>Molecules involved</th>
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</thead>
<tbody>
<tr>
<td><strong>Bacterial capsule</strong></td>
<td>GAS</td>
<td>hyaluronic acid-containing capsule</td>
</tr>
<tr>
<td></td>
<td>Group B streptococci</td>
<td>type III capsular polysaccharide and sialic acid</td>
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<tr>
<td></td>
<td><em>Neisseria</em> spp</td>
<td>capsule and capsule containing sialic acid/LPS</td>
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<td></td>
<td><em>Staph. aureus</em></td>
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<td></td>
<td><em>Haemophilus</em> spp</td>
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<td></td>
<td><em>E. coli</em></td>
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<tr>
<td></td>
<td><em>Salmonella</em> spp</td>
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<td></td>
<td>Meningococci</td>
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<tr>
<td><strong>Proteinases</strong></td>
<td><em>P. gingivalis</em></td>
<td>gingipain</td>
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<tr>
<td></td>
<td>GAS</td>
<td>C5a peptidase</td>
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<td></td>
<td><em>Ps. aeruginosa</em></td>
<td>elastase</td>
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<td><strong>Chemical inactivation</strong></td>
<td><em>H. pylori</em></td>
<td>Urea/ammonia</td>
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<tr>
<td></td>
<td><em>Ps. aeruginosa</em></td>
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<tr>
<td><strong>Binding to RCA proteins</strong></td>
<td>GAS</td>
<td>M protein family</td>
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<td></td>
<td><em>Strep. pneumoniae</em></td>
<td>Protein H</td>
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<td></td>
<td><em>Bord. pertussis</em></td>
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<td></td>
<td><em>N. gonorrhoeae</em></td>
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<td></td>
<td><em>B. Burgdorferi</em></td>
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<td></td>
<td><em>Y. enterococci</em></td>
<td></td>
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<tr>
<td><strong>Inhibition of lytic pathway</strong></td>
<td>GAS</td>
<td>Streptococcal inhibitor of complement (SIC)</td>
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<tr>
<td></td>
<td><em>Y. enterococci</em></td>
<td>Ail</td>
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<td></td>
<td><em>S. typhimurium</em></td>
<td>Rck and Trat</td>
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<td></td>
<td><em>E. coli</em></td>
<td>Trat and binding protectin</td>
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<tr>
<td></td>
<td><em>H. pylori</em></td>
<td>binding protectin</td>
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<td></td>
<td><em>Moraxella</em> <em>catarrhalis</em></td>
<td>?</td>
</tr>
</tbody>
</table>
Bacterial Evasion of Cellular immunity

- Inhibit cytokines/interferon/chemokines
- Block antigen presentation
- Secreted modulators or toxins
- Modulators on the pathogen surface
- Antigenic hypervariability
- Subvert or kill immune cells/phagocytes
- ......
Immune evasion by viruses

- **Antigenic variation**
  - Influenza, HIV, rhinovirus

- **Inhibition of the class I MHC antigen processing pathway**
  - Different viruses use different mechanisms
  - NK cells are the host adaptation for killing class I MHC-negative infected cells

- **Production of immune modulators**
  - Soluble cytokine receptors may act as “decoys” and block actions of cytokines (poxviruses)
  - Immunosuppressive cytokines, e.g. IL-10 (EBV)

- **Engagement of inhibitory pathways**
  - LCMV (mice), HIV (humans): PD-1

- **Infection of immune cells**
  - HIV
Viruses inhibit the class I MHC pathway of antigen processing

- Inhibition of proteasomal activity: EBV, human CMV
- Block in MHC synthesis and/or ER retention: adenovirus, human CMV
- Block in TAP transport: HSV
- Removal of class I from ER: CMV
- Interference with CTL recognition by "decoy" viral class I-like molecules: murine CMV
THE END!!! THANKS!! (^O^)/