Gram-positive cocci:
Staphylococcus
Streptococcus

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Staphylococcus

**Virulence factors:**
- Coagulase (CF)
- Glycocalix
- A protein
- Enzymes: hyaluronidase
- Cytolytic exotoxins = hemolysins
- Leukocidin Panton-Valentine
- **Superantigens** (SAgs):
  - exfoliatins
  - enterotoxins
  - toxic shock toxin (TSST-1)
Staphylococcus

**Source of infection** (the origin from which a host acquires the infection):

**Human carriers**

**Transmission:**

- **directly** (contact with carriers or infected individual)
- **indirectly** (contaminated surfaces or medical equipment)

Staphylococci - **resistant to drying** (prolonged survival), disinfectants, antimicrobials
Staphylococcus aureus

- **Skin infections**: localized: superficial or subcutaneous abscesses (furuncles, boils), larger, deeper infections (carbuncles) - can lead to bacteremia

- **Diffuse skin infection** - impetigo (pyoderma)

- **Deep localized infections**: osteomyelitis, arthritis

- **Other infections**: acute endocarditis, septicemia, severe necrotizing pneumonia

- **Toxicoses**: shock syndrome, gastroenteritis, intoxication staphylococcal scaled skin syndrome (marked epithelial desquamation) SSSS
Staphylococcus - types of infections

INFECTION

INVASIVE
- Furuncles
- Carbuncles
- Wound infections
- Postoperative
- Posttraumatic
- Endocarditis (heart surgery)

TOXICOSES
- Food poisoning

MIXED
- Staphylococcal scaled skin syndrome (SSSS)
- TSST-1 shock syndrome
- Bacteremia sepsis
pathogen in situ =
local infections:
furuncles
carbuncles
wound infections
postoperative or
posttraumatic
ostitis/osteomyelitis

What virulence factors are important?
The effects of peptidoglycan fragments and teichoic acids released during GP infections
The effects of peptidoglycan fragments and teichoic acids released during GP infections
diapedesis

lumen of capillary

selectin

endothelial cell

receptor for TNF and interleukin 1 (cytokines)

TNF

II-1
vasodilation

lumen of capillary

leukocytes

endothelial cell

receptor for TNF and interleukin 1 (cytokines)
capillary damage during SIRS
SIRS
Systemic inflammatory response syndrome:
hypotension + hypovolemia + DIC (diffuse intravascular coagulation) + loss of perfusion + ARDS (acute respiratory distress syndrome) = acidosis & decreased cardiac output = irreversible septic shock and MOSF (multiple organ system failure) & death
Superantigens (Type I toxins)

Unusual bacterial toxins that interact with exceedingly large numbers of T4 lymphocytes

This results in the secretion of excessive amounts of cytokine IL-2 and the activation of self-reactive T-lymphocytes
Superantigen

Antigen presenting cell

MHC Class II

T cell receptor

T lymphocyte

Superantigen
superantigen → activation → T-lymphocytes

**circulation**
- fever
- nausea
- vomiting
- diarrhea
- malaise

**IL-2**

**TNFα, IL-1, IL-8, PAF**

endothelial damage
- ARDS
- DIC
- MOSF
- shock

**self-reactive T-lymphocytes**

autoimmune attack

**neutrophils**

proteases
toxic oxygen radicals

**neutrophils**

**ARDS**

**DIC**

**MOSF**

**shock**

**toxic oxygen radicals**

**toxic oxygen radicals**
excessive inflammatory response

- adherence of neutrophils
- IL-8
- damage to capillary walls
  - capillary permeability
  - prolonged vasodilation
  - vascular resistance
  - hypotension
  - hypovolemia
  - blood and plasma leave bloodstream
  - reduced perfusion of blood
  - coagulation pathway
    - DIC
    - reduced perfusion of blood
Superantigens (Type I toxins) - examples

- Toxic shock syndrome toxin-1 (TSST-1) some strains of Staphylococcus
- Staphylococcal enterotoxins (SE)
- Staphylococcal exfoliative toxin
- Pyrogenic exotoxin (Spe) - toxic shock-like syndrome (TSLS) - rare invasive strains and scarlet fever strains of Streptococcus pyogenes (group A)
**Staphylococcus epidermidis**
- Part of normal flora of the skin and anterior nares
- Important cause of infections from prosthetic implants (catheters, heart valves)
- Virulence factors: glycocalyx - biofilm

**Staphylococcus saprophyticus**
- Part of the normal vaginal flora
- A frequent cause of cystitis in women
- Virulence factors: urease, glycocalyx, lipase
<table>
<thead>
<tr>
<th>Species</th>
<th>Hemolysis</th>
<th>Group antigen</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pyogenic, hemolytic streptococci</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em> (A streptococci)</td>
<td>β</td>
<td>A</td>
<td>Frequent pathogen in humans; invasive infections, sequelae</td>
</tr>
<tr>
<td><em>S. agalactiae</em> (B streptococci)</td>
<td>β</td>
<td>B</td>
<td>Meningitis/sepsis in neonates; invasive infections in predisposed persons</td>
</tr>
<tr>
<td>C streptococci</td>
<td>β(α; γ)</td>
<td>C</td>
<td>Rare; purulent infections (similar to <em>S. pyogenes</em> infections)</td>
</tr>
<tr>
<td>G streptococci</td>
<td>β</td>
<td>G</td>
<td>Rare; purulent infections (similar to <em>S. pyogenes</em> infections)</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>α</td>
<td>–</td>
<td>Pneumococci; respiratory tract infections; sepsis; meningitis</td>
</tr>
<tr>
<td><em>S. bovis</em></td>
<td>α; γ</td>
<td>D</td>
<td>Not enterococci, although in group D; rare sepsis pathogen; if isolated from blood work up for pathological colon processes</td>
</tr>
</tbody>
</table>
### Oral streptococci (selection)

<table>
<thead>
<tr>
<th>Species</th>
<th>Antigen(s)</th>
<th>Phenotypes</th>
<th>Clinical Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. salivarius</td>
<td>α; γ</td>
<td>A, C, E, F, G, H, K</td>
<td>Greening (viridans) streptococci; occur in oral cavity; endocarditis; caries (S. mutans, S. sanguis, S. mitis)</td>
</tr>
<tr>
<td>S. sanguis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. mutans</td>
<td></td>
<td>Occasionally detectable</td>
<td>Purulent abscesses</td>
</tr>
<tr>
<td>S. mitis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>S. anginosus</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>S. constellatus</td>
<td></td>
<td>S. milleri group</td>
<td></td>
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<tr>
<td>S. intermedius</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>etc.</td>
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</tbody>
</table>

### Enterococci (Enterococcus)

<table>
<thead>
<tr>
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<th>Antigen(s)</th>
<th>Phenotype</th>
<th>Clinical Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. faecalis</td>
<td>α; γ; β</td>
<td>D</td>
<td>Occur in human and animal intestines; low-level pathogenicity; endocarditis; nosocomial infections. Often component of mixed florae.</td>
</tr>
<tr>
<td>E. faecium</td>
<td>α</td>
<td>D</td>
<td></td>
</tr>
</tbody>
</table>
Streptococcus

**Virulence factors:**
- Hyaluronic acid capsule
- M protein
- Streptolysin O
- Pyrogenic streptococcal exotoxins (PSE): A, B, C
- Streptokinase
- Hyaluronidase
Streptococcus

Source of infection:

- Carriers, infected individuals - direct/close contact
- Streptococci are very susceptible to drying and antimicrobial agents
Streptococcus - types of infections

INFECTION

INVASIVE acute
- Skin and mucous membranes infections
- Scarlet fever
- Necrotizing fasciitis
- Septic infections
- Erysipelas

SEQUELAE
- Glomerulonephritis
- Acute rheumatic fever
Streptococcus pyogenes

The most common cause of bacterial pharyngitis or pharyngotonsilitis

Scarlet fever (pyrogenic exotoxin in non-immunized individuals)

Acute rhumatic fever

Glomerulonephritis

Impetigo

Cellulitis (diffuse spreading inflammation)

Puerperal sepsis (disease of uterine endometrium)

Invasive infections: necrotizing fasciitis/myositis
Streptococcus pyogenes

• Erysipelas
• Streptococcal toxic shock syndrome (PSE)
• Bacteremia
• Pneumonia
**Streptococcus pyogenes Infections**

*S. pyogenes* (M protein, PSE, other pathogenicity factors)

- Invasion via skin or mucosa

  - Host organism
    - Anti-M antibody (+)
      - Silent infection
    - Anti-M antibody (-)
      - Local infection:
        - impetigo, erysipelas, cellulitis, lymphangitis, sinusitis, otitis media, tonsillitis
      - Generalized invasive infection:
        - Anti-PSE antibodies (-) and high-risk MHC II allotype
          - sepsis, septic shock, necrotizing fasciitis
        - or
          - scarlet fever (tonsillitis)
Other streptococci

**Streptococcus agalactiae**
- Meningitis and septicemia in neonates
- Infections in adults: endometritis in postpartum women, septicemia, pneumonias in immunosuppressed individuals

**Streptococcus pneumoniae** -
Capsule - antiphagocytic (90 serotypes)
Hyaluronidase
IgA protease
STREPTOCOCCUS PNEUMONIAE

Infections

Purulent:
- Otitis media
- sinusitis
- pneumonia

INVASIVE:
- meningitis
- bakteremia, sepsis
- endocarditis
- peritonitis

Serotypes: 2, 3, 5, 8, 14

Mortality: 15-25%

Vaccine for children
**ENTEROCOCCI**

► **Enterococcus faecalis &**

*E. faecium* cause >90% infections in human

► normal intestinal flora of humans and animals

► resistant to environmental factors and many antimicrobial agents

Source of infections: **endogenous**

Indirect: contaminated surfaces & medical equipment
ENTEROCOCCI: virulence factors

- proteins binding ECM = colonization
- lipoteichoic acid = fibronectin binding, induction of cytokines
- hyaluronidase = invasion into tissue

Most common infections: UTI, endocarditis, catheter-related infections
Other: intraabdominal and pelvic infections, bacteremia, sepsis, postoperative wounds infections, meningitis - uncommon (neurosurgical procedures)
Streptococci in oral cavity

Streptococcus: mitis, mutans, salivarius, sanguis, milleri

- normal flora: oral cavity, intestines, urethra
- endogenous infections: dental carries, endocarditis, mixed infections within oral cavity (e.g. abscesses)