Lecture PowerPoint to accompany

Foundations in Microbiology
Seventh Edition

Talaro

Chapter 18
The Cocci of Medical Importance

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18.1 General Characteristics of the Staphylococci

- Common inhabitant of the skin and mucous membranes
- Spherical cells arranged in irregular clusters
- Gram-positive
- Lack spores and flagella
- May have capsules
- 31 species
Figure 18.1 Views of *S. aureus* shape and arrangements
Staphylococcus aureus

- Grows in large, round, opaque colonies
- Optimum temperature of 37°C
- Facultative anaerobe
- Withstands high salt, extremes in pH, and high temperatures
- Produces many virulence factors
Figure 18.2 Blood agar plate, *S. aureus*
Virulence factors of *S. aureus*

**Enzymes:**

- **Coagulase** – coagulates plasma and blood; produced by 97% of human isolates; diagnostic
- **Hyaluronidase** – digests connective tissue
- **Staphylokinase** – digests blood clots
- **DNase** – digests DNA
- **Lipases** – digest oils; enhances colonization on skin
- **Penicillinase** – inactivates penicillin
Virulence factors of *S. aureus*

**Toxins:**

- **Hemolysins** (α, β, γ, δ) – lyse red blood cells
- **Leukocidin** – lyses neutrophils and macrophages
- **Enterotoxin** – induce gastrointestinal distress
- **Exfoliative toxin** – separates the epidermis from the dermis
- **Toxic shock syndrome toxin** (TSST) – induces fever, vomiting, shock, systemic organ damage
TABLE 18.1  Major Virulence Factors of *Staphylococcus aureus*

<table>
<thead>
<tr>
<th>Name</th>
<th>Enzyme/Toxin</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulase</td>
<td>Enzyme</td>
<td>Coagulates blood plasma</td>
</tr>
<tr>
<td>Hyaluronidase</td>
<td>Enzyme</td>
<td>Digests connective tissue of the host</td>
</tr>
<tr>
<td>Staphylokinase</td>
<td>Enzyme</td>
<td>Digests blood clots</td>
</tr>
<tr>
<td>Lipase</td>
<td>Enzyme</td>
<td>Digests oils, allowing bacteria to more easily colonize the skin</td>
</tr>
<tr>
<td>Penicillinase</td>
<td>Enzyme</td>
<td>Inactivates penicillin, rendering the bacterium resistant</td>
</tr>
<tr>
<td>Hemolysins (α, β, γ, δ)</td>
<td>Toxin</td>
<td>Lyse red blood cells</td>
</tr>
<tr>
<td>Leukocidin</td>
<td>Toxin</td>
<td>Lyses neutrophils and macrophages</td>
</tr>
<tr>
<td>Enterotoxins</td>
<td>Toxin</td>
<td>Induce nausea, vomiting, and diarrhea</td>
</tr>
<tr>
<td>Exfoliative toxins (A, B)</td>
<td>Toxin</td>
<td>Cause desquamation of the skin</td>
</tr>
<tr>
<td>Toxic shock syndrome toxin</td>
<td>Toxin</td>
<td>Induces fever, vomiting, rash, organ damage</td>
</tr>
</tbody>
</table>
Epidemiology and Pathogenesis

- Present in most environments frequented by humans
- Readily isolated from fomites
- Carriage rate for healthy adults is 20-60%
- Carriage is mostly in anterior nares, skin, nasopharynx, intestine
- Predisposition to infection include: poor hygiene and nutrition, tissue injury, preexisting primary infection, diabetes, immunodeficiency
- Increase in community acquired methicillin resistance - MRSA
Staphylococcal Disease

Range from localized to systemic

• **Localized cutaneous infections** – invade skin through wounds, follicles, or glands
  
  – **Folliculitis** – superficial inflammation of hair follicle; usually resolved with no complications but can progress  
  
  – **Furuncle** – boil; inflammation of hair follicle or sebaceous gland progresses into abscess or pustule  
  
  – **Carbuncle** – larger and deeper lesion created by aggregation and interconnection of a cluster of furuncles  
  
  – **Impetigo** – bubble-like swellings that can break and peel away; most common in newborns
Figure 18.3 Cutaneous lesions of *S. aureus*

(a) Sectional view of a boil or furuncle, a single pustule that develops in a hair follicle or gland and is the classic lesion of the species. The inflamed infection site becomes abscessed when masses of phagocytes, bacteria, and fluid are walled off by fibrin.

(b) A furuncle on the back of the hand. This lesion forms in a single follicle.

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(c) A carbuncle on the back of the neck. Carbuncles are massive deep lesions that result from multiple, interconnected furuncles. Swelling and rupture into the surrounding tissues can be marked.

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Staphylococcal Disease

• Systemic infections
  – Osteomyelitis – infection is established in the metaphysis; abscess forms
  – Bacteremia – primary origin is bacteria from another infected site or medical devices; endocarditis possible
Figure 18.4 Staphylococcal osteomyelitis in a long bone
Staphylococcal Disease

• Toxigenic disease
  – Food intoxication – ingestion of heat stable enterotoxins; gastrointestinal distress
  – Staphylococcal scalded skin syndrome – toxin induces bright red flush, blisters, then desquamation of the epidermis
  – Toxic shock syndrome – toxemia leading to shock and organ failure
Figure 18.5
Effects of staphylococcal toxins on skin
Other Staphylococci

Coagulase-negative staphylococcus; frequently involved in nosocomial and opportunistic infections

- *S. epidermidis* – lives on skin and mucous membranes; endocarditis, bacteremia, UTI
- *S. hominis* – lives around apocrine sweat glands
- *S. capitis* – live on scalp, face, external ear
- All 3 may cause wound infections by penetrating through broken skin
- *S. saprophyticus* – infrequently lives on skin, intestine, vagina; UTI
Identification of *Staphylococcus* in Samples

- Frequently isolated from pus, tissue exudates, sputum, urine, and blood
- Cultivation, catalase, biochemical testing, coagulase
Figure 18.6 Catalase test
Figure 18.7 Test system to identify *Staphylococcus*
TABLE 18.2 Separation of Clinically Important Species of *Staphylococcus*

1. **Staphylococcus species**
   - **Coagulase-positive** (beta-hemolysis)
     - *Staphylococcus aureus*
       - **Urease production**
         - Ferments mannose: *Staphylococcus epidermidis*
         - Does not ferment mannose: *Staphylococcus saprophyticus*
     - **No urease production**: *Staphylococcus hominis*
   - **Coagulase-negative** (no beta-hemolysis)
     - **Anaerobic growth**
     - **No anaerobic growth**
       - *Staphylococcus capitis*

*A few strains of *S. aureus* are coagulase-negative.*
Clinical Concerns and Treatment

• 95% have penicillinase and are resistant to penicillin and ampicillin
• MRSA – methicillin-resistant *S. aureus* – carry multiple resistance
  – Some strains have resistance to all major drug groups except vancomycin
• Abscesses have to be surgically perforated
• Systemic infections require intensive lengthy therapy
Prevention of Staphylococcal Infections

• Universal precautions by healthcare providers to prevent nosocomial infections
• Hygiene and cleansing
18.2 General Characteristics of Streptococci

- Gram-positive spherical/ovoid cocci arranged in long chains; commonly in pairs
- Non-spore-forming, nonmotile
- Can form capsules and slime layers
- Facultative anaerobes
- Do not form catalase, but have a peroxidase system
- Most parasitic forms are fastidious and require enriched media
- Small, nonpigmented colonies
- Sensitive to drying, heat, and disinfectants
Figure 18.8 Freshly isolated *Streptococcus*
Streptococci

- Lancefield classification system based on cell wall Ag – 17 groups (A, B, C,....)
- Another classification system is based on hemolysis reactions
  - β-hemolysis – A, B, C, G and some D strains
  - α-hemolysis – *S. pneumoniae* and others collectively called *viridans*
Figure 18.9 Hemolysis patterns on blood agar

Streptococcus pyogenes with zones of β-hemolysis

Streptococcus pneumoniae

Group A streptococci (Streptococcus pyogenes)

Group B, C streptococci

Group D and viridans streptococci
Human Streptococcal Pathogens

- *S. pyogenes*
- *S. agalactiae*
- Viridans streptococci
- *S. pneumoniae*
- *Enterococcus faecalis*
<table>
<thead>
<tr>
<th>Species</th>
<th>Lancefield Group</th>
<th>Hemolysis Type</th>
<th>Habitat</th>
<th>Pathogenicity to Humans</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pyogenes</em></td>
<td>A</td>
<td>Beta (β)</td>
<td>Human throat</td>
<td>Skin, throat infections, scarlet fever</td>
</tr>
<tr>
<td><em>S. agalactiae</em></td>
<td>B</td>
<td>β</td>
<td>Human vagina, cow udder</td>
<td>Neonatal, wound infections</td>
</tr>
<tr>
<td><em>S. equisimilis</em></td>
<td>C</td>
<td>β</td>
<td>Swine, cows, horses</td>
<td>Pharyngitis, endocarditis</td>
</tr>
<tr>
<td><em>S. equi, S. zooepidemicus</em></td>
<td>C</td>
<td>β</td>
<td>Various mammals</td>
<td>Rare, in abscesses</td>
</tr>
<tr>
<td><em>S. dysgalactiae</em></td>
<td>C</td>
<td>β</td>
<td>Cattle</td>
<td>Rare</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>D</td>
<td>α, β, N</td>
<td>Human, animal intestine</td>
<td>Endocarditis, UTI*</td>
</tr>
<tr>
<td><em>E. faecium, E. durans</em></td>
<td>D</td>
<td>Alpha (α)</td>
<td>Human, animal intestine</td>
<td>Similar to <em>E. faecalis</em></td>
</tr>
<tr>
<td><em>S. bovis</em></td>
<td>D</td>
<td>N</td>
<td>Cattle</td>
<td>Subacute endocarditis, bacteremia</td>
</tr>
<tr>
<td><em>S. anginosus</em></td>
<td>F, G, L</td>
<td>β</td>
<td>Humans, dogs</td>
<td>Endocarditis, URT** infections</td>
</tr>
<tr>
<td><em>S. sanguis</em></td>
<td>H</td>
<td>α</td>
<td>Human oral cavity</td>
<td>Endocarditis</td>
</tr>
<tr>
<td><em>S. salivarius</em></td>
<td>K</td>
<td>N</td>
<td>Human saliva</td>
<td>Endocarditis</td>
</tr>
<tr>
<td><em>Lactococcus lactis</em></td>
<td>N</td>
<td>V</td>
<td>Dairy products</td>
<td>Very rare</td>
</tr>
<tr>
<td><em>S. mutans</em></td>
<td>NI***</td>
<td>N</td>
<td>Human oral cavity</td>
<td>Dental caries</td>
</tr>
<tr>
<td><em>S. uberis, S. acidominimus</em></td>
<td>NI</td>
<td>V</td>
<td>Domestic mammals</td>
<td>Rare</td>
</tr>
<tr>
<td><em>S. mitior</em></td>
<td>O, M</td>
<td>α</td>
<td>Human oral cavity</td>
<td>Tooth abscess, endocarditis</td>
</tr>
<tr>
<td><em>S. milleri</em></td>
<td>F</td>
<td>N</td>
<td>URT</td>
<td>Endocarditis, organ abscess</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>NI</td>
<td>α</td>
<td>Human RT</td>
<td>Bacterial pneumonia</td>
</tr>
</tbody>
</table>

Note: Species in bold type are the most significant sources of human infection and disease.
N = none; V = varies
*Urinary tract infection
**Upper respiratory tract
***No group C carbohydrate identified
β-hemolytic *S. pyogenes*

- Most serious streptococcal pathogen
- Strict parasite
- Inhabits throat, nasopharynx, occasionally skin
Virulence Factors of β-Hemolytic S. Pyogenes

Produces surface antigens:

- **C-carbohydrates** – protect against lysozyme
- **Fimbriae** – adherence
- **M-protein** – contributes to resistance to phagocytosis
- Hyaluronic acid **capsule** – provokes no immune response
- **C5a protease** hinders complement and neutrophil response
Figure 18.10 View of group A Streptococcus
Virulence Factors of β-Hemolytic 
*S. Pyogenes*

Extracellular toxins:

**Streptolysins** – hemolysins; streptolysin O (SLO) and streptolysin S (SLS) – both cause cell and tissue injury

**Erythrogenic toxin (pyrogenic)** – induces fever and typical red rash

**Superantigens** – strong monocyte and lymphocyte stimulants; cause the release of tissue necrotic factor
Virulence Factors of β-Hemolytic
*S. Pyogenes*

**Extracellular enzymes**
- Streptokinase – digests fibrin clots
- Hyaluronidase – breaks down connective tissue
- DNase – hydrolyzes DNA
Epidemiology and Pathogenesis

• Humans only reservoir
• Inapparent carriers
• Transmission – contact, droplets, food, fomites
• Portal of entry generally skin or pharynx
• Children predominant group affected for cutaneous and throat infections
• Systemic infections and progressive sequelae possible if untreated
Scope of Clinical Disease

Skin infections

- **Impetigo (pyoderma)** – superficial lesions that break and form highly contagious crust; often occurs in epidemics in school children; also associated with insect bites, poor hygiene, and crowded living conditions

- **Erysipelas** – pathogen enters through a break in the skin and eventually spreads to the dermis and subcutaneous tissues; can remain superficial or become systemic

Throat infections

- **Streptococcal pharyngitis** – strep throat
Figure 18.11 Streptococcal skin infections
Figure 18.12 Pharyngitis and tonsillitis
Scope of Clinical Disease

Systemic infections

- **Scarlet fever** – strain of *S. pyogenes* carrying a prophage that codes for erythrogenic toxin; can lead to sequelae
- Septicemia
- Pneumonia
- Streptococcal toxic shock syndrome
Long-Term Complications of Group A Infections

- **Rheumatic fever** – follows overt or subclinical pharyngitis in children; carditis with extensive valve damage possible, arthritis, chorea, fever

- **Acute glomerulonephritis** – nephritis, increased blood pressure, occasionally heart failure; can become chronic leading to kidney failure
Group B: *Streptococcus Agalactiae*

- Regularly resides in human vagina, pharynx, and large intestine
- Can be transferred to infant during delivery and cause severe infection
  - Most prevalent cause of neonatal pneumonia, sepsis, and meningitis
  - Pregnant women should be screened and treated
- Wound and skin infections and endocarditis in debilitated people
Group D Enterococci and Groups C and G Streptococci

• Group D:
  – *Enterococcus faecalis, E. faecium, E. durans*
  – Normal colonists of human large intestine
  – Cause opportunistic urinary, wound, and skin infections, particularly in debilitated persons

• Groups C and G:
  – Common animal flora, frequently isolated from upper respiratory; pharyngitis, glomerulonephritis, bacteremia
Identification

- Cultivation and diagnosis ensure proper treatment to prevent possible complications
- Rapid diagnostic tests based on monoclonal antibodies that react with C-carbohydrates
- Culture using bacitracin disc test, CAMP test, Esculin hydrolysis
Figure 18.14 Streptococcal tests
Figure 18.15
β-hemolytic streptococci
**TABLE 18.4** Scheme for Differentiating Beta-Hemolytic Streptococci

![Flowchart diagram](chart.png)

- **Beta-hemolytic streptococci**
  - Bacitracin-sensitive
    - **Group A** (*S. pyogenes*)
      - **CAMP** factor +
        - **Group B** (*S. agalactiae*)
          - **Esulin** hydrolysis – SXT-sensitive
            - Groups C/G (*S. equisimilis*)
            - **Group D** (*E. faecalis*)
          - **Esulin** hydrolysis + SXT-resistant
    - Bacitracin-resistant

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*Name is derived from the first letters of the names of its discoverers. CAMP is a diffusible substance of group B, which lyses sheep red blood cells in the presence of staphylococcal hemolysin.*

**A sugar that can be split into glucose and esculin. Group D streptococci can accomplish this in the presence of 40% bile.**

***Sulfa and trimethoprim. The test is performed (like bacitracin) with discs containing this combination drug.*
Treatment and Prevention

• Groups A and B are treated with penicillin
• Long-term penicillin prophylaxis for people with a history of rheumatic fever or recurrent strep throat
• Enterococcal treatment usually requires combined therapy
α-Hemolytic Streptococci: Viridans Group

• Large complex group
  – *Streptococcus mutans*, *S. oralis*, *S. salivarius*,
    *S. sanguis*, *S. milleri*, *S. mitis*

• Most numerous and widespread residents of the gums and teeth, oral cavity, and also found in nasopharynx, genital tract, skin

• Not very invasive; dental or surgical procedures facilitate entrance
Viridans Group

• Bacteremia, meningitis, abdominal infection, tooth abscesses
• Most serious infection – subacute endocarditis – Blood-borne bacteria settle and grow on heart lining or valves
• Persons with preexisting heart disease are at high risk
• Colonization of heart by forming biofilms
Viridans Group

- *S. mutans* produce slime layers that adhere to teeth, basis for plaque
- Involved in dental caries
- Persons with preexisting heart conditions should receive prophylactic antibiotics before surgery or dental procedures
**Streptococcus Pneumoniae: The Pneumococcus**

- Causes 60-70% of all bacterial pneumonias
- Small, lancet-shaped cells arranged in pairs and short chains
- Culture requires blood or chocolate agar
- Growth improved by 5-10% CO$_2$
- Lack catalase and peroxidases – cultures die in O$_2$
Figure 18.16 Two effects of streptococcal colonization
Figure 18.17 Diagnosing *Streptococcus pneumoniae*
**S. Pneumoniae**

- All pathogenic strains form large capsules – major virulence factor
- Specific soluble substance (SSS) varies among types
- 90 different capsular types have been identified
- Causes pneumonia and otitis media
Epidemiology and Pathology

- 5-50% of all people carry it as normal flora in the nasopharynx; infections are usually endogenous
- Very delicate, does not survive long outside of its habitat
- Young children, elderly, immune compromised, those with other lung diseases or viral infections, persons living in close quarters are predisposed to pneumonia
- Pneumonia occurs when cells are aspirated into the lungs of susceptible individuals
- Pneumococci multiply and induce an overwhelming inflammatory response
- Gains access to middle ear by way of eustachian tube
Figure 18.18 The course of bacterial pneumonia
Figure 18.19 View of ear anatomy indicating route of infection
Cultivation and Diagnosis

• Gram stain of specimen – presumptive identification
• Quellung test or capsular swelling reaction
• $\alpha$-hemolytic; optochin sensitivity, bile solubility, inulin fermentation
Treatment and Prevention

• Traditionally treated with penicillin G or V
• Increased drug resistance
• Two vaccines available for high risk individuals:
  – Capsular antigen vaccine for older adults and other high risk individuals – effective 5 years
  – Conjugate vaccine for children 2 to 23 months
18.3 Family Neisseriaceae

• Gram-negative cocci
• Residents of mucous membranes of warm-blooded animals
• Genera include *Neisseria, Branhamella, Moraxella*
• 2 primary human pathogens:
  – *Neisseria gonorrhoeae*
  – *Neisseria meningitidis*
Figure 18.21 *Neisseria*
Genus *Neisseria*

- Gram-negative, bean-shaped, diplococci
- None develop flagella or spores
- Capsules on pathogens
- Pili
- Strict parasites, do not survive long outside of the host
- Aerobic or microaerophilic
- Oxidative metabolism
- Produce catalase and cytochrome oxidase
- Pathogenic species require enriched complex media and CO₂
Neisseria Gonorrhoeae: The Gonococcus

• Causes gonorrhea, an STD
• Virulence factors:
  – Fimbriae, other surface molecules for attachment; slows phagocytosis
  – IgA protease – cleaves secretory IgA
Epidemiology and Pathology

• Strictly a human infection
• In top 5 STDs
• Infectious dose 100-1,000
• Does not survive more than 1-2 hours on fomites
Figure 18.22 Comparative incidence of reportable infectious STDs
Gonorrhea

Infection is asymptomatic in 10% of males and 50% of females

- Males – urethritis, yellowish discharge, scarring, and infertility
- Females – vaginitis, urethritis, salpingitis (PID) mixed anaerobic abdominal infection, common cause of sterility and ectopic tubal pregnancies
- Extragenital infections – anal, pharyngeal, conjunctivitis, septicemia, arthritis
Figure 18.23 Gonorrheal damage to the male reproductive tract
Figure 18.24 Ascending gonorrhea in women
Gonorrhea in Newborns

• Infected as they pass through birth canal
• Eye inflammation, blindness
• Prevented by prophylaxis immediately after birth
Diagnosis and Control

• Gram stain – Gram-negative intracellular (neutrophils) diplococci from urethral, vaginal, cervical, or eye exudate – presumptive identification

• 20-30% of new cases are penicillinase-producing PPNG or tetracycline resistant TRNG

• Combined therapies indicated

• Recurrent infections can occur

• Reportable infectious disease
Figure 18.26 Gram stain of urethral pus
Neisseria Meningitidis: The Meningococcus

Virulence factors:
- Capsule
- Adhesive fimbriae
- IgA protease
- Endotoxin

• 12 strains; serotypes A, B, C cause most cases
Epidemiology and Pathogenesis

• Prevalent cause of meningitis; sporadic or epidemic
• Human reservoir – nasopharynx; 3-30% of adult population; higher in institutional settings
• High risk individuals are those living in close quarters, children 6 months-3 years, children and young adults 10-20 years
• Disease begins when bacteria enter bloodstream, cross the blood-brain barrier, permeate the meninges, and grow in the cerebrospinal fluid
• Very rapid onset; neurological symptoms; endotoxin causes hemorrhage and shock; can be fatal
Figure 18.27 Dissemination of the meningococcus from a nasopharyngeal infection
Figure 18.28 One clinical sign of meningococcemia
Clinical Diagnosis

- Gram stain CSF, blood, or nasopharyngeal sample
- Culture for differentiation
- Rapid tests for capsular polysaccharide
Treatment and Prevention

• Treated with IV penicillin G, cephalosporin
• Prophylactic treatment of family members, medical personnel, or children in close contact with patient
• Primary vaccine contains specific purified capsular antigens
**TABLE 18.5** Scheme for Differentiating Gram-Negative Cocci and Coccobacilli

- **Gram-negative cocci and coccobacilli**
  - **Oxidase −**
    - Acinetobacter spp.*
      - Ferments maltose
        - Does not ferment sucrose or lactose
          - Neisseria meningitidis
        - Ferments sucrose; does not ferment lactose
          - Neisseria sicca
        - Ferments lactose; does not ferment sucrose
          - Neisseria lactamica**
      - **Does not ferment maltose**
        - Grows on nutrient agar
          - Reduces nitrite
            - Branhamella catarrhalis
          - Does not reduce nitrite
            - Moraxella spp.
        - Does not grow on nutrient agar
          - N. gonorrhoeae

*See chapter 20.

**A weak pathogen, found in the nasopharynx of children and easily mistaken for N. meningitidis.
Other Gram-Negative Cocci and Coccobacilli

• Genus *Branhamella*
  – *Branhamella catarrhalis* – found in nasopharynx: significant opportunistic in cancer, diabetes, alcoholism

• Genus *Moraxella*
  – Bacilli – found on mucous membranes

• *Genus Acinetobacter*