

Staphylococcus

OBJECTIVES:

- Staphylococci.
- General Characteristics of Staphylococci.
- ***Staphylococcus aureus***
- ***Staphylococcus epidermidis***
- ***Staphylococcus saprophyticus***

Staphylococci with streptococci constitute the main group of medically important gram positive cocci , Ubiquitous in nature.

Staphylococcus aureus

- is the most virulent.
- common cause of bacterial infections.
- Also important cause of intoxications such as:
 - Food poisoning
 - Toxic shock syndrome

Coagulase-negative *staphylococcus*:

Frequently involved in nosocomial and opportunistic infections.

➤ ***Staph. epidermidis***

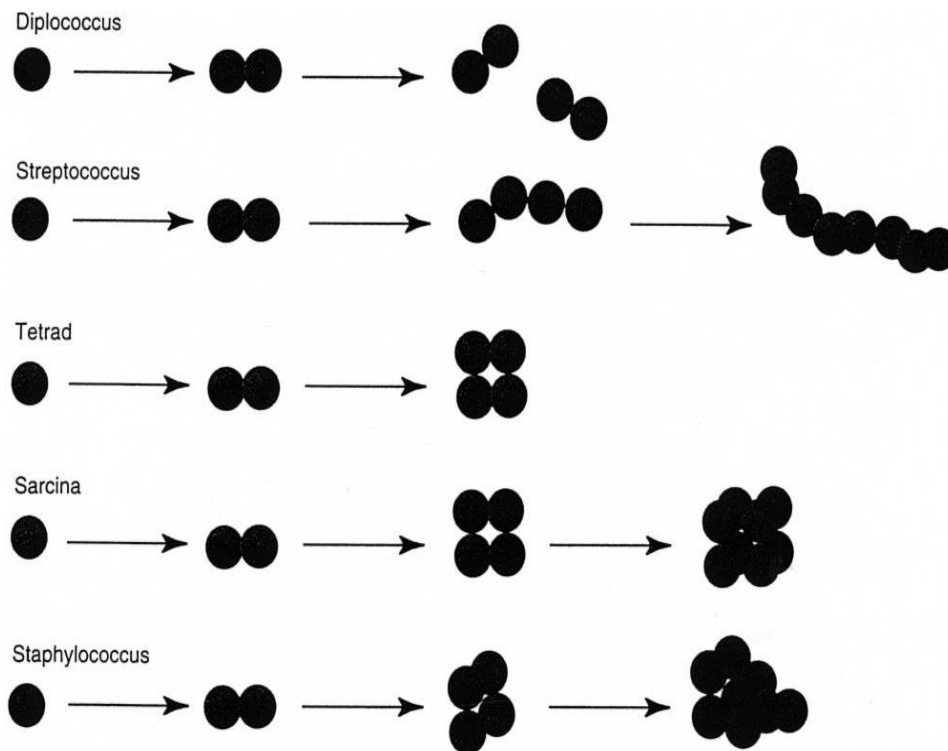
- Present in large numbers as part of the normal flora of the skin.
- Despite its low virulence ,it is common cause of implants infections such as heart valves and catheters.
- Acquired drug resistance by *Staph. epidermidis* is even more than *Staph .aureus*.

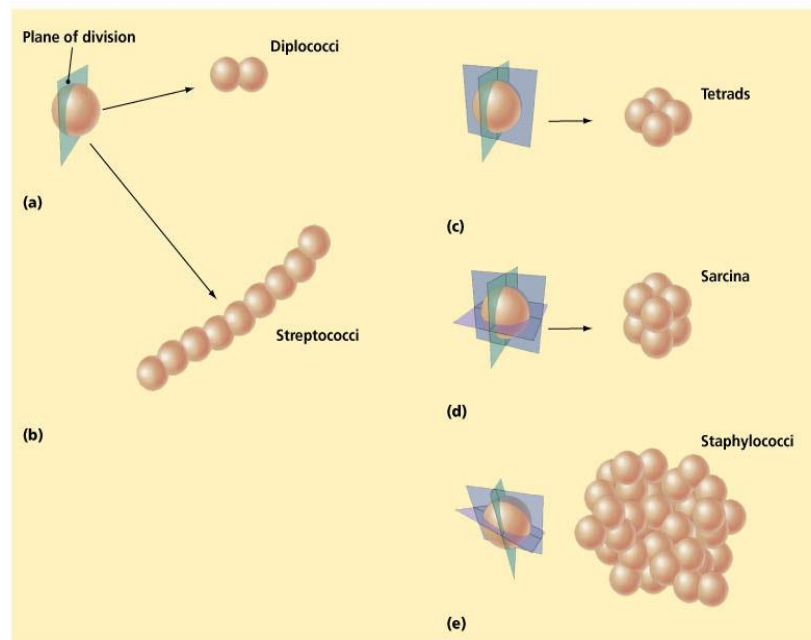
Staph.saprophyticus:

- infrequently lives on skin, intestine, vagina.
- Causes UTI specially cystitis in women.

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.





***Staphylococcus aureus*:**

- Aureus = gold hence “golden Staph”.
- The more virulent strain that can produce a variety of conditions depending on the site of infection.
- 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.

Virulence factors of *Staph. Aureus*:

Enzymes:

- Coagulase: coagulates plasma and blood; produced by 97% of human isolates; diagnostic , **Triggers** blood clotting.
- Hyaluronidase: digests connective tissue.
- Staphylokinase: digests blood clots. Dissolves fibrin threads in blood clots, allowing *Staphylococcus aureus* to free itself from clots.
- DNase: digests DNA.
- Lipases: digest oils; enhances colonization on skin.
- Penicillinase: inactivates penicillin.

Toxins:

- **Hemolysins** (α , β , γ): 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.

Hemolysis (α, β, γ):

TABLE 18.1 Major Virulence Factors of *Staphylococcus aureus*

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

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.

Pathogenicity:

- “Staph’ infections result when staphylococci breach the body’s physical barriers.
- Entry of only a few hundred bacteria can result in disease.
- Pathogenicity results from 3 features:
 - Structures that enable it to evade phagocytosis.
 - Production of enzymes.
 - Production of toxins.

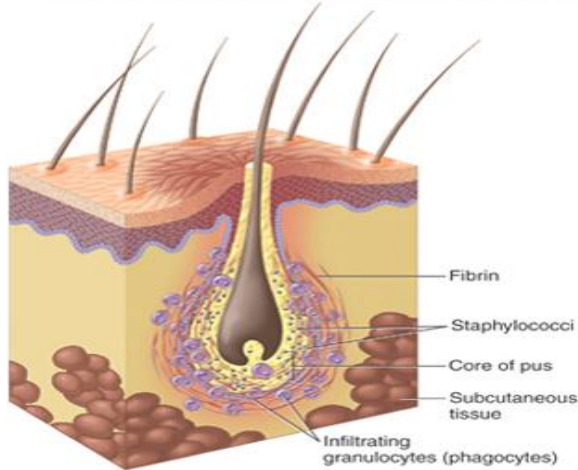
Staphylococcal Disease:

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.

Cutaneous lesions of *Staph. aureus*:

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(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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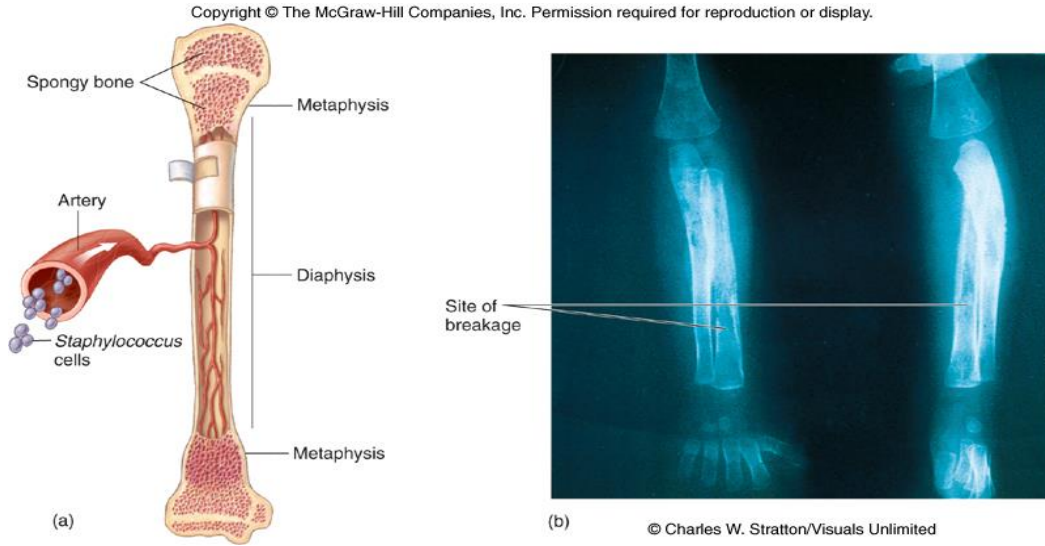


(c) A carbuncle on the back of the neck. Carbuncles are massive deep lesions that result from multiple, interconnecting furuncles. Swelling and rupture into the surrounding tissues can be marked.
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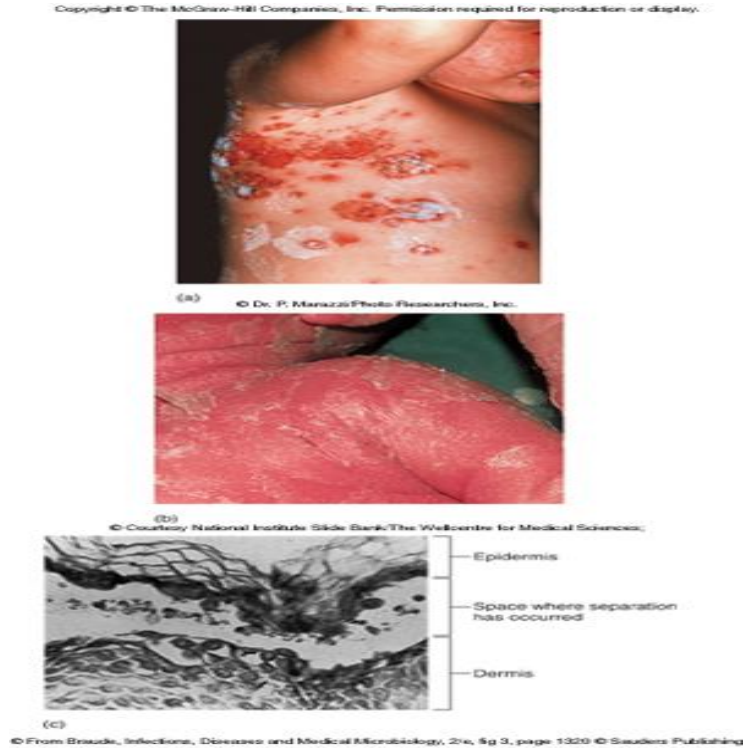
Staphylococcal Diseases: Systemic Disease:

- **Toxic shock syndrome-TSS** toxin is absorbed into the blood and causes shock.
- **Bacteremia:** presence of bacteria in the blood.
- **Endocarditis:** occurs when bacteria attack the lining of the heart.
- **Pneumonia:** inflammation of the lungs in which the alveoli and bronchioles become filled with fluid.
- **Osteomyelitis:** inflammation of the bone marrow and the surrounding bone.
- **Food intoxication:** ingestion of heat stable enterotoxins; gastrointestinal distress.

Staphylococcal osteomyelitis in a long bone:



Effects of staphylococcal toxins on skin:



Toxic Shook Syndrome (TSS)symptoms:

- 8-12 h post infection.
- Fever.
- Susceptibility to Endotoxins.
- Hypotension.
- Diarrhea.
- Multiple Organ System Failure.
- Erythroderma (rash).

Toxic Shook Syndrome (TSS) Treatment :

- Clean any obvious wounds and remove any foreign bodies.
- Prescription of appropriate antibiotics to eliminate bacteria.
- Monitor and manage all other symptoms, e.g. administer IV fluids.
- For severe cases, administer methylprednisone, a corticosteroid inhibitor of TNF- α synthesis.

Identification of *Staphylococcus* in Samples:

- Frequently isolated from pus, tissue exudates, sputum, urine, and blood.
- Cultivation, catalase, biochemical testing, coagulase.

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.

Treatment:

- Drain infected area.
- Deep/metastatic infections:
 - ✓ semi-synthetic penicillins.
 - ✓ Cephalosporins.
 - ✓ Erythromycin.
 - ✓ Clindamycin.
- Endocarditis
 - ✓ semi-synthetic penicillin + an aminoglycoside.

Prevention of Staphylococcal Infections:

- Universal precautions by healthcare providers to prevent nosocomial infections.
- Hygiene and cleansing.
- Also important is the proper cleansing of wounds and surgical openings, aseptic use of catheters or indwelling needles, an appropriate use of antiseptics.

Streptococci

General Characteristics of Streptococci:

- Gram-positive spherical/ovoid cocci arranged in long chains; commonly in pairs.
- Nonspore-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.

Classification of Streptococci:

Streptococci can be classified by several schemes , for example by the:

- Hemolytic properties.
- Serologic groups.
- Metabolic properties.

Hemolytic properties:

- **β-Hemolytic:**
 - β-Hemolytic streptococci cause gross lysis of red blood cells resulting in a clear ring around the colony.
 - Group A Streptococcus.
 - Group B Streptococcus.
- **α or γ –Hemolytic**
 - Group D Streptococcus.
- **α-Hemolytic**
 - α-hemolytic streptococci cause a chemical change in the hemoglobin of RBCs in blood agar, resulting in appearance of a green pigment that forms a ring around the colony .
 - *Streptococcus viridans* and *Streptococcus pneumonia*
- **γ –Hemolytic**
 - Streptococci that cause no color change or lysis of RBCs.

Serologic (Lancefield) grouping:

- Many species of streptococci have in their cell walls a polysaccharide known as the **C-carbohydrate** , which is antigenic .
- Lancefield classification system based on cell wall Ag – 17 groups (A, B, C,.....).
- The lancefield scheme classifies primarily β -hemolytic streptococci.
- The clinically most important groups of β -hemolytic streptococci are types A and B.

Hemolysis patterns on blood agar

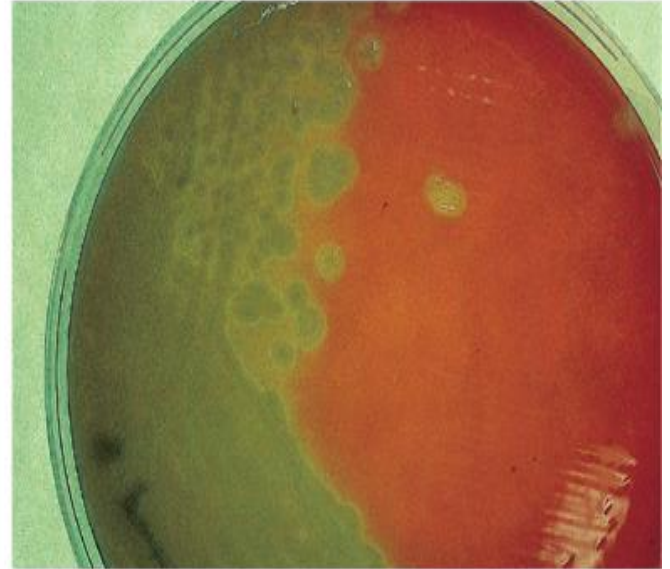
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Streptococcus pyogenes
with zones of β -hemolysis



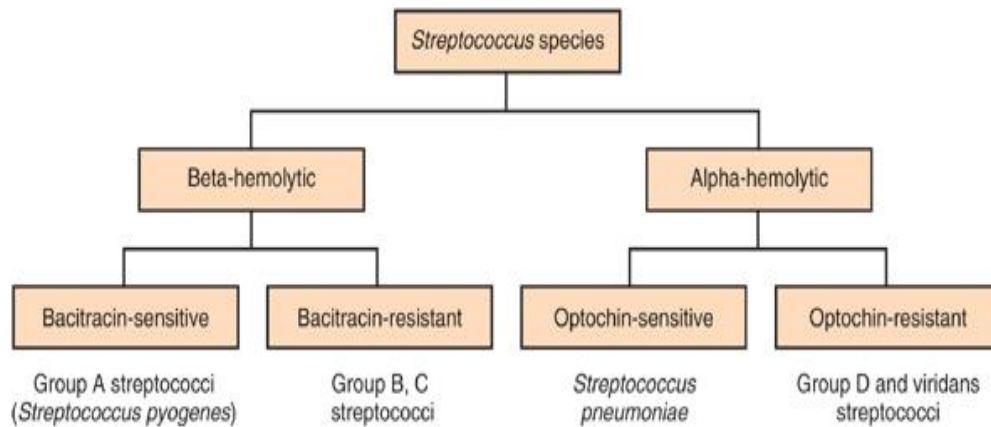
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Human Streptococcal Pathogens:

- *S. pyogenes*
- *S. agalactiae*
- *Viridans streptococci*
- *S. pneumoniae*
- *Enterococcus faecalis*

 β -Hemolytic *S. pyogenes* (group A):

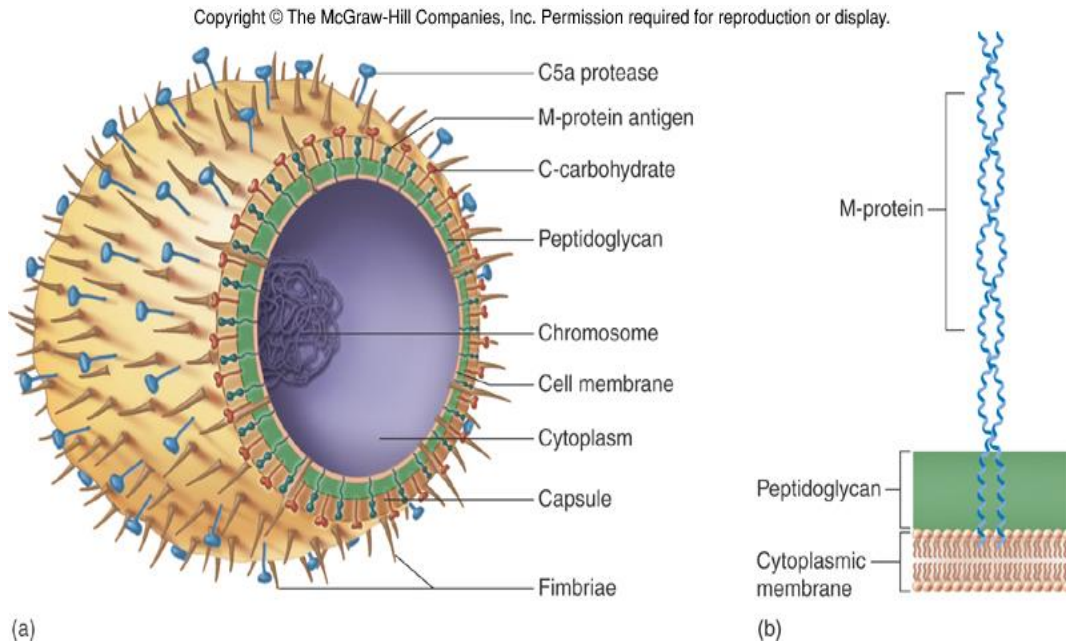
- *Streptococcus pyogenes* is the most virulent member of this gram positive cocci.
- Strict pathogen.
- Inhabits throat, nasopharynx, occasionally skin.
- Low inoculum suffices for infection.
- Etiologic agent in all causes of cellulitis any where in the body.
- Some strains cause post infectious sequelae ,including:
 - **Rheumatic fever.**
 - **Acute glomerulonephritis.**

Transmission of *S.pyogenes*:

- Via aerosol from a nasopharyngeal carrier or someone who has streptococcal pharyngitis.
- Direct contact with a skin carrier or a patient with impetigo.

Virulence Factors of β -Hemolytic *S. Pyogenes*:

- Produces surface antigens:
 - **C-carbohydrates** –(all group A Streptococci contain this antigen).
 - **Fimbriae** – adherence.
 - **M-protein** – has antiphagocytic activity.
 - **Protein F** (fibronectin-binding protein) mediate attachment to fibronectin in the pharyngeal epithelium.
 - **Hyaluronic acid capsule** – provokes no immune response.



- **Extracellular toxins:**
 - **Streptolysins :**
 - Streptolysin O (SLO): Damage mammalian cells , resulting in the release of lysosomal enzymes.
 - Streptolysin S (SLS): lyses erythrocytes, leukocytes and platelets.
- ***Streptococcal pyrogenic* exotoxins , These toxins causes a variety of effects including:**
 - Rash in scarlet fever.
 - Severe streptococcal toxic-like disease.
- **Extracellular enzymes:**
 - **Streptokinase** – digests fibrin clots.
 - **Hyaluronidase** – breaks down connective tissue.
 - **DNase** – hydrolyzes DNA.
 - **C5a protease**-hinders complement and neutrophil response (C5a has chemotactic activity that attract neutrophils).

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** – Affecting all age groups , patients with erysipelas suffer from fiery red, advancing erythema , especially on the face and lower limbs.
- **Throat infections**
 - Acute pharyngitis or pharyngotonsillitis.

Streptococcal skin infections:

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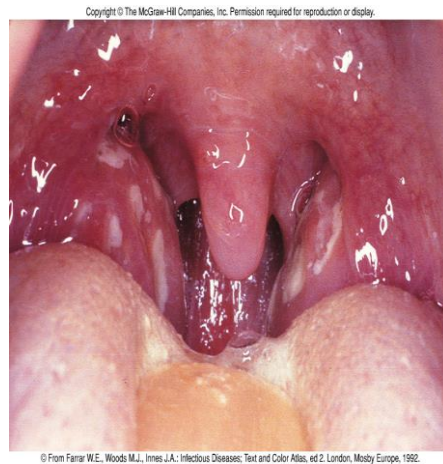
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Pharyngitis and tonsillitis:**Scope of Clinical Disease:**

- **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:

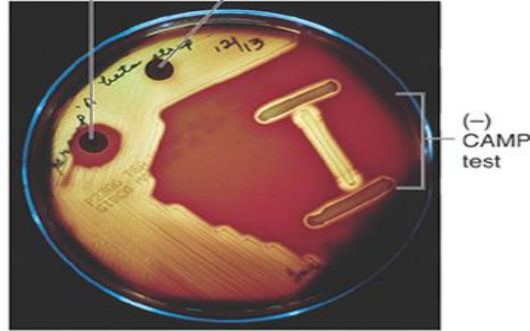
Cultivation and diagnosis ensure proper treatment to prevent possible complications.

- Rapid diagnostic tests based on monoclonal antibodies that react with C-carbohydrates.
- Culture using bacitracin disc test.
- CAMP test.
- Esculin hydrolysis.

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Streptococcal tests:

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Bacitracin disc SXT disc



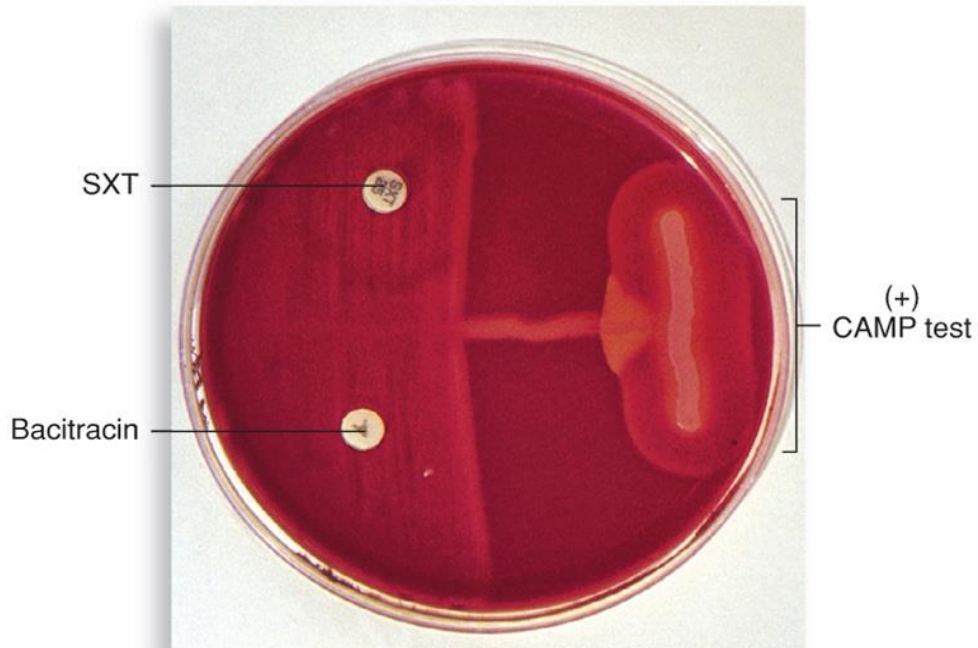
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β -hemolytic streptococci:

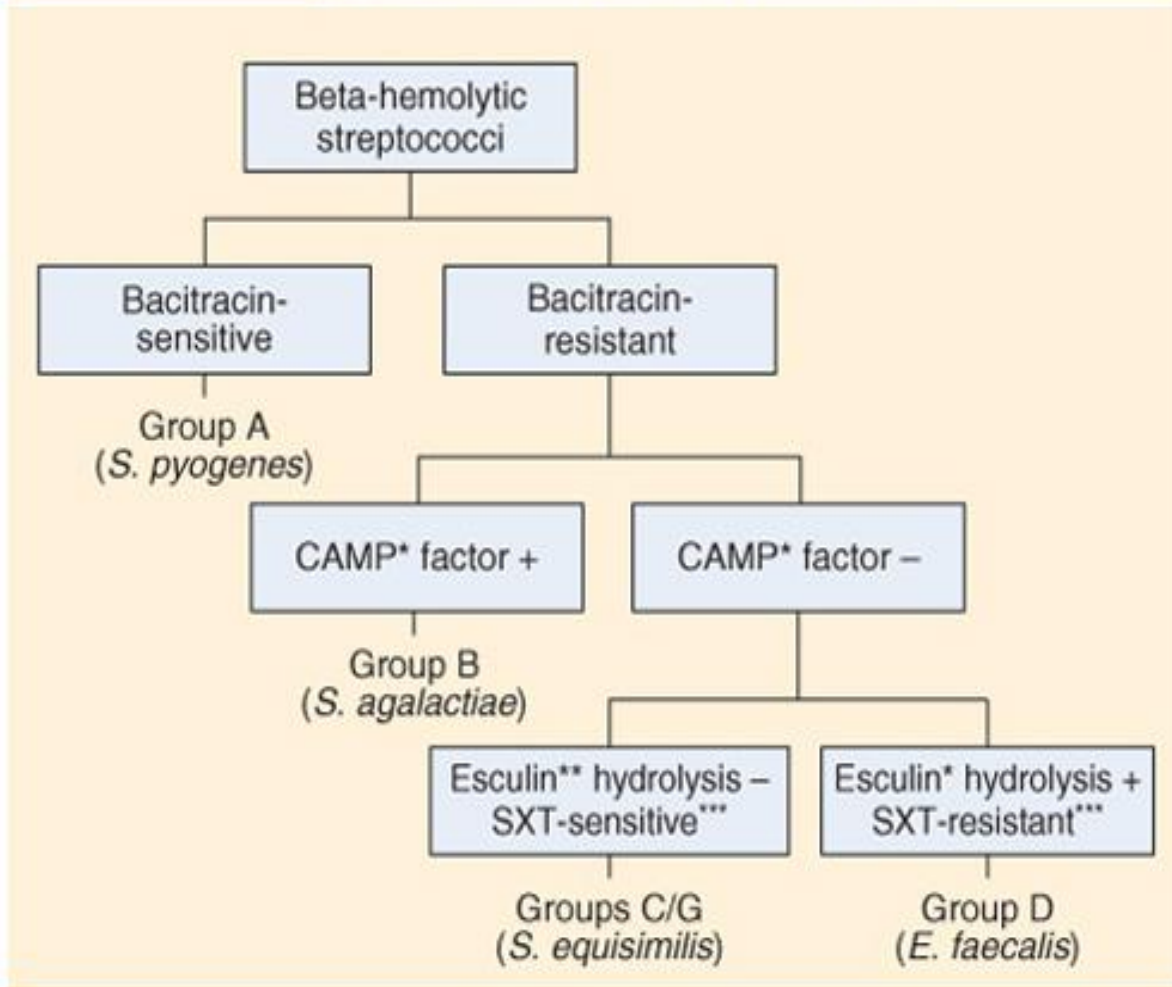
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TABLE 18.4 Scheme for Differentiating Beta-Hemolytic Streptococci



*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 esculetin. 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.
- *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.
- Lack catalase and peroxidases.

Diagnosing *Streptococcus pneumoniae*:

- All pathogenic strains form large capsules – major virulence factor..
- Specific soluble substance (SSS) varies among types.
- 90 different capsular types have been identified.

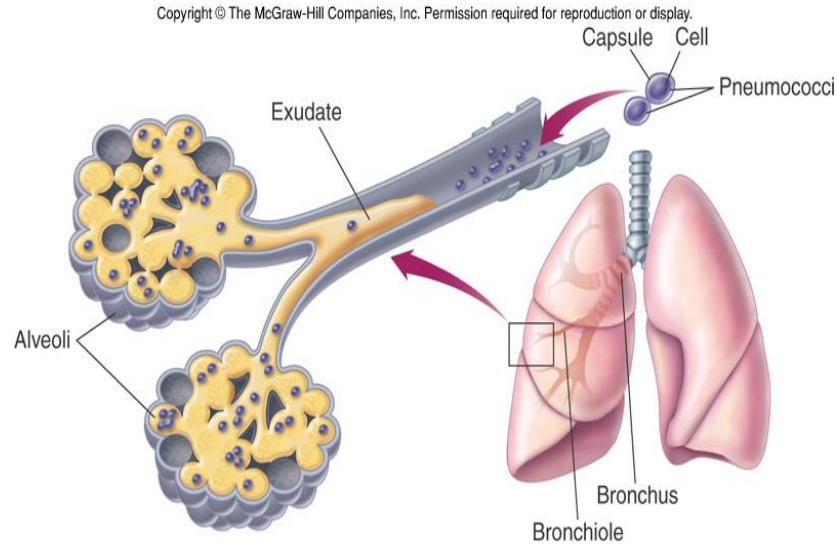
Causes:

- Pneumonia.
- Otitis media.
- Bactermia.
- Meningitis.

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.

The course of bacterial pneumonia:



Cultivation and Diagnosis:

- Gram stain of specimen – presumptive identification.
- Quellung test or capsular swelling reaction.
- α -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.