Chapter 15

Gram positive cocci (contd)

Streptococcus pyogenes and related streptococci

Streptococci cause a wide variety of infections.

-- ***Streptococcus pyogenes*** (group A streptococcus) is a leading bacterial cause of **pharyngitis** and **cellulitis**.

-- It is also an important cause of **impetigo**, **necrotizing fasciitis**, and **streptococcal toxic shock syndrome**.

-- It also incites **rheumatic fever** and **acute glomerulonephritis**.

-- ***Strept. agalactiae*** (group B streptococci) is a leading cause of **neonatal sepsis** and **meningitis**.

-- ***Enterococcus faecalis*** is involved in **hospital acquired UTI** and **endocarditis**.

-- **Viridans group streptococci** are the common cause of **endocarditis**.

-- ***Strept. bovis*** also causes **endocarditis**.

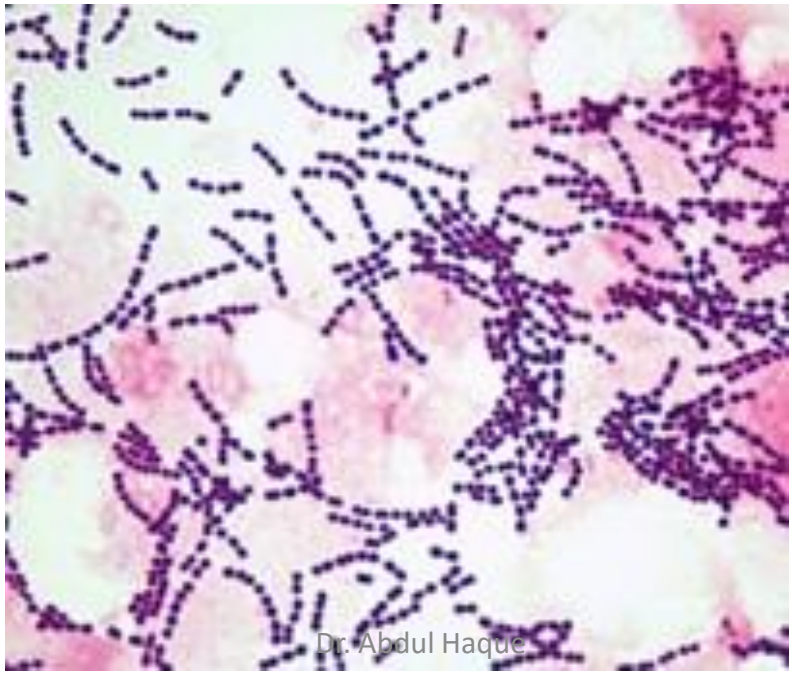
Important properties

-- **Streptococci** are Gram-positive, **non motile**, **non spore forming** cocci.

-- Individual cells are round-to-ovoid cocci, 0.6-1.0 micrometer in diameter.

-- **Streptococci** occur in **pairs** or in **chains** of varying lengths.

-- These are **catalase-negative**.



An important criterion to identify streptococci is **hemolysis on blood agar**.

1. **β-hemolytic streptococci** form a **clear zone** around their colonies due to **complete lysis of RBCs**. It is due to enzymes **streptolysin O** and **S**.

2. **α-hemolytic streptococci** form a **green zone** around the colonies due to **incomplete lysis of RBCs**. Green color is produced by oxidation of hemoglobin to **biliverdin** by H_2O_2.

3. **γ-hemolysis** is term used for non hemolytic streptococci


α
β
γ
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Classification of streptococci

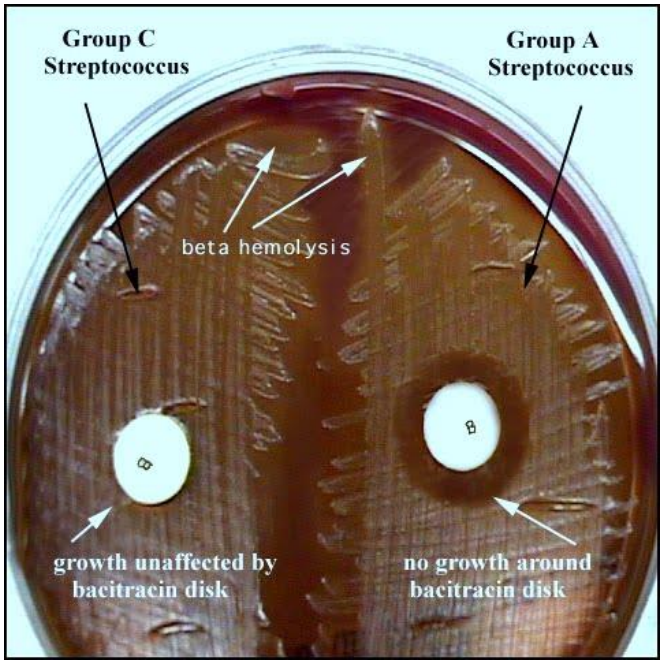
β-hemolytic streptococci

-- These are arranged into **groups A-U** (**Lancefield groups**) on the basis of antigenic differences in **C carbohydrate**.

-- Growth of ***Strept. pyogenes*** (Group A) is **inhibited** by antibiotic **bacitracin**.

-- ***Strept. aglactiae*** (Group B) are usually **bacitracin resistant**.

Hydrolysis of **hippurate** is a unique feature.



-- **Group D streptococci** include ***Enterococcus faecalis*****,** ***Enterococcus faecium*** and ***Strept. bovis***.

-- **Enterococci** can grow in hypertonic (**6.5% saline**) or in **bile** and are not killed by penicillin G.

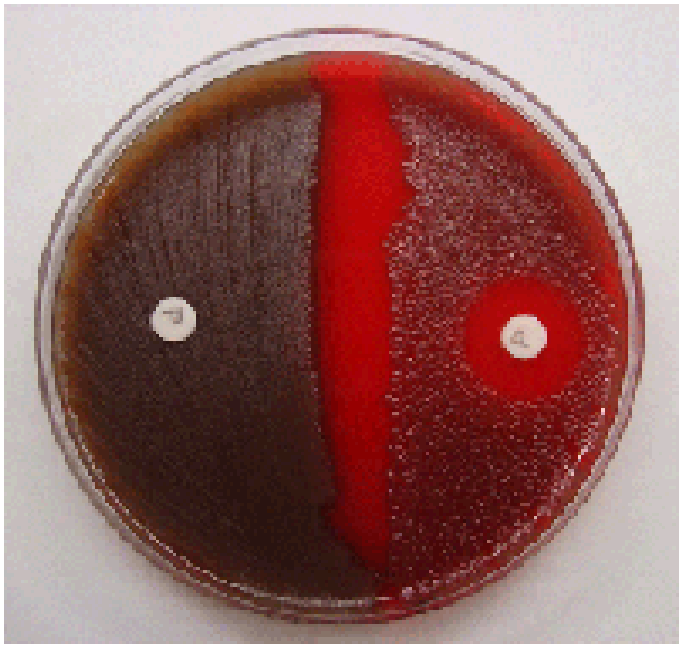
-- ***Strept. bovis*** does not have such resilience. Hemolytic reaction of Group D streptococci is variable.

-- Groups C, E,F,G,H, and K-U can rarely cause human infection.

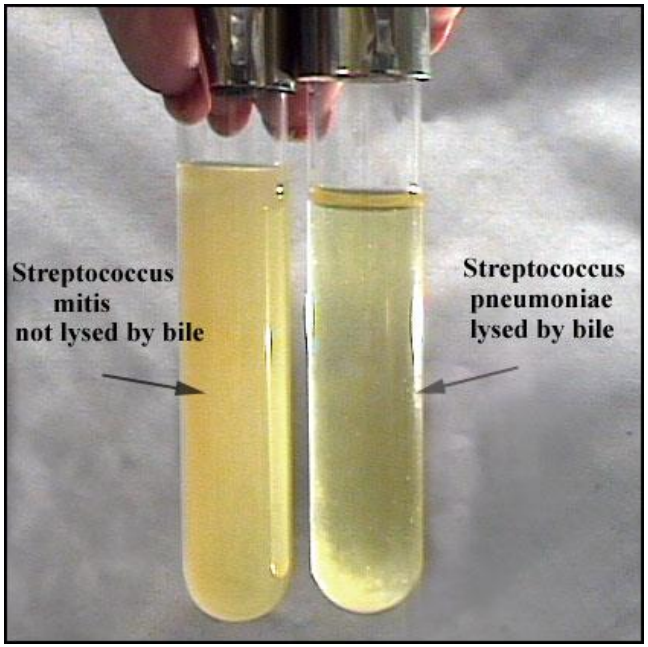
Non-β-hemolytic streptococci

The principal **α-hemolytic streptococci** are ***Strept. pneumonia*** and viridians group (***Strept. mitis, Strept. sanguis,*** and ***Strept. mutans***).

They can be differentiated by **optochin sensitivity** and **bile solubility** of colonies. ***Strept. pneumonia*** is sensitive to both.



Optochin sensitivity



Bile solubility

Peptostreptococci

-- These grow under **anaerobic or microaerophilic** conditions and produce **variable hemolysis**.

-- They are part of **normal flora** of gut, mouth, and female genital tract and participate in mixed anaerobic infections.

-- ***Pepto. magnus*** and ***Pepto. anaerobius*** are frequently isolated from clinical samples.

Transmission

-- Most streptococci are part of **normal flora** of human throat, skin, and intestines but produce disease when they gain access to tissues or blood.

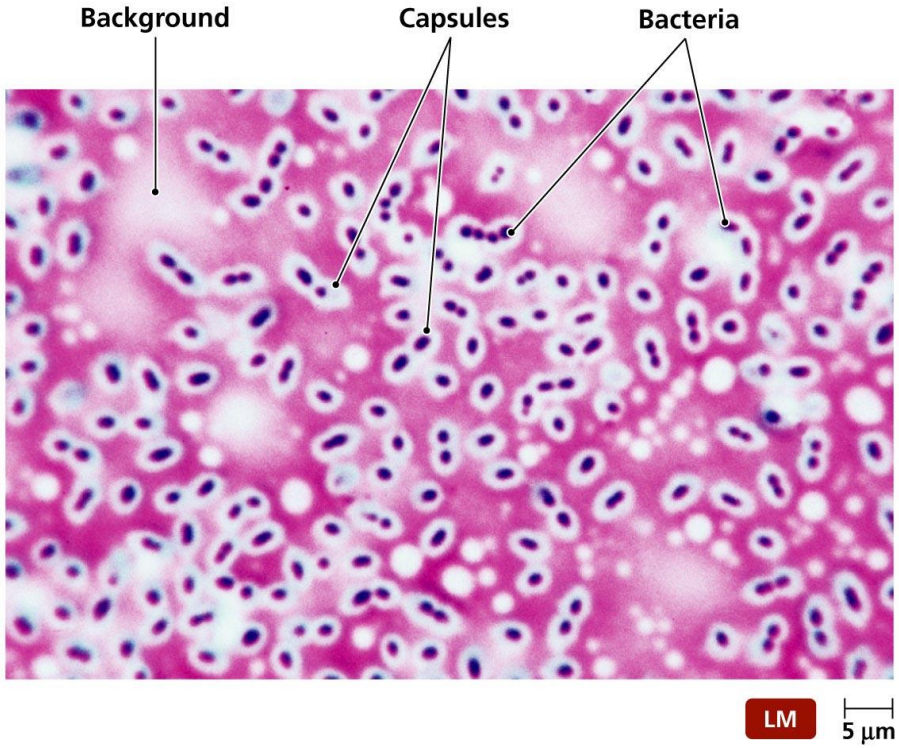
-- **Viridans streptococci** and ***Strept. pneumonia*** are found chiefly in **oropharynx**.

-- ***Strept. pyogenes*** is found on the **skin** and the **oropharynx** in small numbers.

-- ***Strept. agalactiae*** occurs in the **vagina** and **colon**; and both the enterococci and anaerobic streptococci are located in the colon.

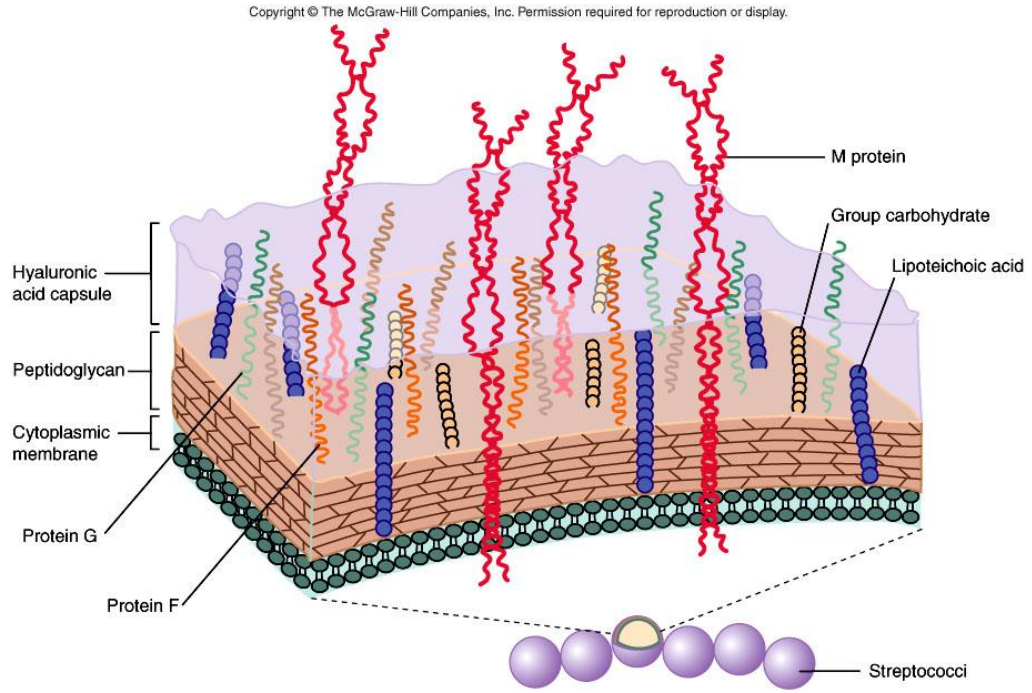
Antigenic components of **β-hemolytic streptococci** include:

1. **Capsular polysaccharide (C-substance)** which determines the group. It is **located in cell wall** and specificity is **determined by amino sugar**.



2. **M proteins** are clearly virulence factors associated with both **colonization** and **resistance to phagocytosis**.

They **protrude** from outer surface of cell and interfere with ingestion by phagocytes.



More than **80 types** of ***S. pyogenes*** M proteins provide different serotypes.

Antibody to M protein provides type-specific immunity.

The M proteins of certain M-types are considered **rheumatogenic** since they contain **antigenic epitopes related to heart muscle**, and thus may lead to **autoimmune rheumatic carditis (rheumatic fever)** following an acute infection.

Some M-types are **nephritogenic** (cause glomerulonephritis).

3. Beside M-proteins there are **microcapsules** that play a role in retarding phagocytosis.

The reason is that they are made up of **hyaluronic acid** which is a normal constituent of human body. Therefore antibodies are not made.

Pathogenesis

Strept. pyogenes cause disease by three mechanisms:

1. **Pyogenic inflammation** which is induced locally at the site of the organisms in tissue.

2. **Exotoxin production** which can cause widespread systemic symptoms in areas of the body where there are no organisms.

3. **Immunologic** which occurs when antibodies against an organism cross reacts with normal tissue causing inflammation without presence of organisms.

Strept. pyogenes produces following **inflammation related enzymes**:

1. **Hyaluronidase** can digest host connective tissue hyaluronic acid, as well as the organism's own capsule. It facilitates rapid spread in skin infections (**cellutlitis**).

2. **Streptokinases** participate in **fibrin lysis**. It activates plasminogen to form plasmin which dissolves fibrin in clots, thrombi and emboli. It can be used to lyse thrombi in the coronary arteries of heart attack patients.

3. **DNase (streptodornase)** which **degrades DNA** in exudates or necrotic tissue. Antibody to DNase B develops during pyoderma and can be used for diagnostic purposes.

Important toxins and hemolysins of *Strept. pyogenes* are:

-- **Erythrogenic toxin** causes the rash of scarlet fever. Its mechanism of action is similar to that of **TSST** of *Staph. aureus*. It acts as a **superantigen.**

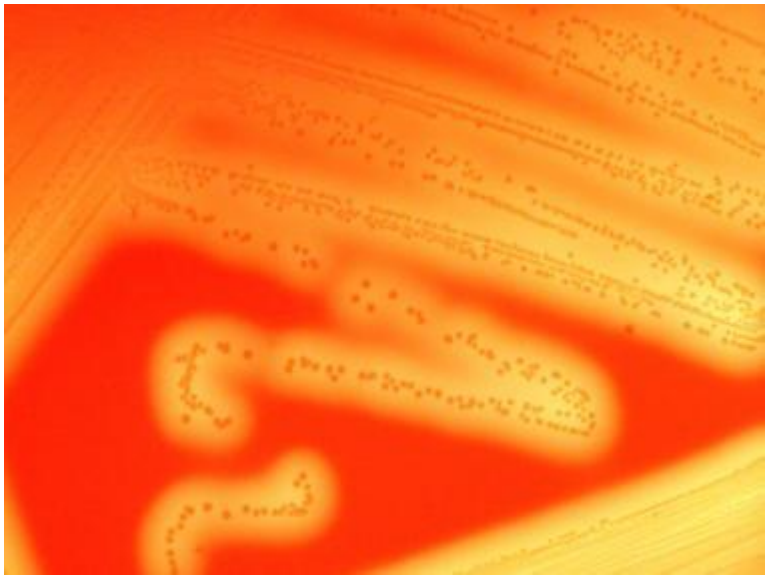
It is produced only by certain strains which carry the relevant genes on a **lysogenic bacteriophage**.

Injection of a skin test dose gives a positive reaction in persons lacking antitoxin (**Dick test**).

-- **Streptolysin O** is an **oxygen-labile** hemolysin/leukocidin. It causes **β-hemolysis** only when colonies **grow beneath** the surface of agar.

It is antigenic and antibody (ASO) develops. **ASO titre** is important for diagnosis of rheumatic fever.

-- **Streptolysin S** is an **oxygen-stable** hemolysin/leukocidin. It is not antigenic but is responsible for **β-hemolysis when colonies grow on the surface of agar.**



-- **Pyrogenic exotoxin A** is the toxin responsible for most cases of **streptococcal toxic shock syndrome**. Its mechanism of action is similar to that of TSST of *Staph. aureus*.

-- **Exotoxin B** is a **protease that rapidly destroys tissue** and is produced in large amounts by so called “flesh-eating” strains causing **necrotizing fasciitis**.

-- **Pathogenesis** by ***Strept. agalactiae*** is based on the ability of organism to produce **inflammatory response**.

-- **No toxic enzymes or exotoxins** are described and there is no evidence of immunological disease.

-- They have a **polysaccharide capsule** that is **antiphagocytic** and **anticapsular antibody** is protective.

-- Similarly **no pathogenic factors** have been described for ***Strept. pneumonia*** and **viridians streptococci.** Their main **virulence factors** are **capsules**.

Clinical findings

Strept. pyogenes

-- ***Strept. pyogenes*** is the most common cause of **pharyngitis** (sore throat) characterized by pain and fever.

-- **Inflamed throat and tonsils**, a **yellow exudate** and **tender cervical lymph nodes** are observed.

-- Spontaneous recovery without treatment occurs after 10 days but **rheumatic fever** may occur.

-- If untreated, it can extend to middle ear (**otitis media**), the sinuses (**sinusitis**), the mastoids (**mastoiditis**) or the meninges (**meningitis**).

-- If **erythrogenic toxin** is produced and host lacks antitoxin, **scarlet fever** is produced with a characteristic **‘strawberry tongue”.**

-- They also cause **streptococcal toxic shock syndrome**, which is clinically similar to that of **Staphylococci**.

-- Difference is that in case of ***Strept. pyogenes*** there is a **recognizable site** of pyogenic inflammation and **blood cultures are often positive**.

Strept. pyogenes can also cause **skin** and **soft tissue infections** such as **cellulitis**, **erysipelas**, **necrotizing faciitis** and **impetigo**.

Lymphangitis can also occur. They also cause **endometritis** (puerperal fever), a serious infection of pregnant women, and sepsis.

Erysipelas

Impetigo

Strept. agalactiae

-- ***Strept. agalactiae*** cause **neonatal sepsis** and **meningitis**.

-- Children born **prior to 37 weeks' gestation** have a greatly increased risk, as well as those whose **mother lack antibody** (and thus not transferred).

-- They are also an important cause of **neonatal pneumonia**.

-- ***Strept. agalactiae*** can cause infections in **adults** as well including pneumonia, endocarditis, arthritis, cellulitis, osteomyelitis, and postpartum endometritis.

-- **Diabetes** is the main predisposing factor for infections in adults.

Viridans streptococci

-- **Viridans streptococci** (e.g., ***Str. mutans, Str. sanguis, Str. salivarius***, and ***Str. mitis***) are the most common cause of **infective endocarditis**.

-- They enter the bloodstream from oropharynx, typically after **dental surgery**. Signs of endocarditis are fever, heart murmur, and anemia.

-- It is **100% fatal** unless treated with antimicrobials. Enterococi may contribute 10% cases.

-- Any of these organisms may settle on deformed valves. At least 3 blood cultures are required in more than 90% cases.

-- **Viridans streptococci** also cause **brain abscesses** often in combination with mouth anaerobes. **Dental surgery** is an important predisposing factor.

-- This combination can cause **abdominal abscesses** as well.

-- ***Strept. bovis*** causes **endocarditis** especially in patients with colon carcinoma.

-- **Peptostreptococci** are one of the most common bacteria found in **brain, lung, abdominal, and pelvic abscess.**

-- **Enterococci** cause **UTI** especially in hospitalized patients.

-- **Indwelling urinary catheters** and urinary tract instrumentation are important predisposing factors.

-- They also cause **endocarditis**, esp. in those who have undergone GIT or UTI surgery or instrumentation.

-- They also cause **intra-abdominal and pelvic infections** typically **in combination with anaerobes.**

Poststreptococcal (nonsuppurative) diseases

-- In these disorders, a local infection with ***Streptococcus pyogenes*** is **followed several weeks later by inflammation in an organ that was not infected by streptococci.**

-- The inflammation is caused by an **immunologic (immune) response to M proteins that cross reacts with human tissue.**

-- The reaction depends on the nature of M proteins – some responses are **nephritogenic (AGN)** and others are **rheumatogenic** causing **acute rheumatic fever.**

Acute glomerulonephritis

-- **AGN** occurs **2-3 weeks after skin infection** in response to **M proteins**, most frequently **type 49**.

-- Striking clinical features are **hypertension, edema** of the face and ankles, and **"smoky"** urine.

-- Most patients recover completely and recurrence with fresh infection is rare.

-- This disease is initiated by **antigen-antibody complexes** on the glomerular basement membrane.

-- Prevention is eradication of streptococcal colonies from skin.

Acute rheumatic fever

-- **Usually app 2 weeks after pharyngitis, rheumatic fever may develop**.

-- **Carditis** damages myocardial and endocardial tissue, **especially the valves.**

-- **ASO titers** and **ESR** are elevated.

-- Mostly age group **5-15 years** is affected.

-- It is an **immunological reaction** between cross reacting antibodies to certain M proteins which **also react with antigens of joint, heart, and brain tissue.**

-- This **autoimmune disease** is greatly worsened by **recurrence** of streptococcal infections.

-- If initial streptococcal infection is treated **within 8 days** of onset, disease is prevented.

-- After a **heart damaging attack** of rheumatic fever, reinfection must be prevented by long term prophylaxis.

-- In **developing countries**, rheumatic fever may develop in up to **5% persons** after streptococcal infection.


Thank You!