Genus *Streptococcus*

Streptococci

- Streptococci are **Gram-positive cocci** that grow in chains or pairs.

- Cell division occurs in a single plane resulting in chains.

- Streptococci are **catalase negative.** The catalase test is the common test used to distinguish *Streptococcus* species from *Staphylococcus* species.

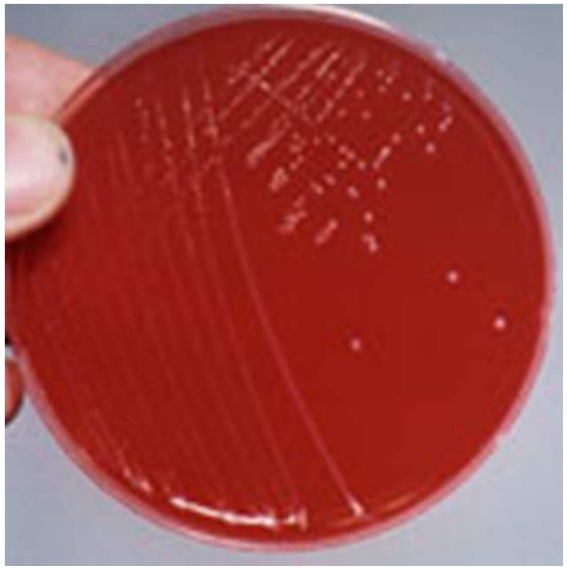
- Streptococci are typically grouped by hemolysis on blood agar plates:
  - **Alpha hemolysis** occurs when the RBCs are intact, but hemoglobin is converted to biliverdin. This causes a greening of the plate.

  - **Beta hemolysis** is true hemolysis due to the actions of a hemolysin, an erythrocyte lysing enzyme. The plate becomes clear where the blood cells have been lysed.

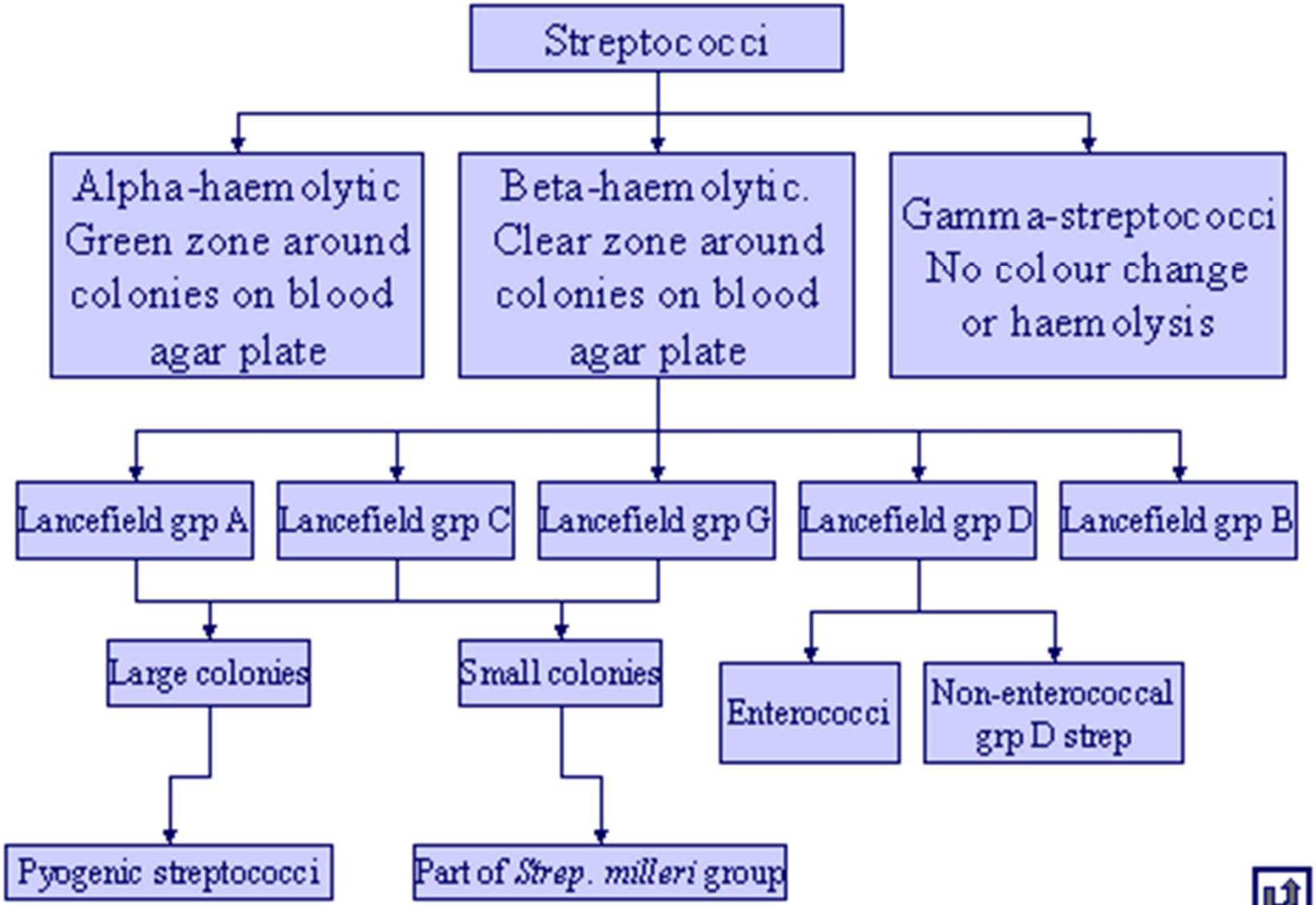
  - **Gamma hemolysis** is a misnomer, there is actually no hemolysis.

alfa hemolysis

beta hemolysis



gamma hemolysis


Streptococci
Alpha-haemolytic
Green zone around colonies on blood agar plate
Beta-haemolytic.
Clear zone around colonies on blood agar plate
Gamma-streptococci
No colour change or haemolysis
Lancefield grp A
Lancefield grp C
Lancefield grp G
Lancefield grp D
Lancefield grp B
Large colonies
Small colonies
Enterococci
Non-enterococcal grp D strep
Pyogenic streptococci
Part of *Strep. milleri* group

THE ALPHA HEMOLYTIC STREPTOCOCCI

The Alpha Hemolytic Streptococci

- Alpha hemolytic streptococci are classified by the results of their culture in the presence of optochin or their solubility in bile (deoxycholate)
  - **Optochin non susceptible** (Bile Salts resistant) **= The Viridans Streptococci**
  - **Optochin susceptible** (Bile Salts susceptible) = ***Streptococcus pneumoniae***

Optochin resistant
viridans streptococci

Optochin susceptible
S. pneumoniae

The Viridans Streptococci

- The viridans streptococci are the part of normal flora.
- ***S. mutans*** participates with other mouth flora to form biofilms ("plaque") - dental carries.
- Other oral streptococci, like ***S. gordonii,*** frequently cause endocarditis.

Streptococcus pneumoniae

- Gram-positive, lancet-shaped diplococci.
- the most autolytic of the pathogens (**the muramidase**, the autolysin)
- only human pathogen
- Up to 40% of children are colonized (the nasopharynx)
- Children less than 5 years of age have a higher rate of carriage; adults without children the lowest rate.

Streptococcus pneumoniae

- the most common cause of bacterial **community-acquired pneumonia, otitis media, sinusitis, bacteremia, and meningitis**.
- Risk factors for severe infection include debilitated state of health and certain diseases, like sickle-cell anemia, Hodgkin's disease, multiple myeloma, HIV, and an absence of spleen.

Virulence Factors of *Streptococcus pneumoniae*

•**Capsula** the most important factor composed of repeating oligosaccharide units. More >100 types, immunity is type specific. Only about 15 types cause majority of the infections. The capsule interferes with the opsonizing activity of the alternative complement pathway.

•**teichoic acid** stimulates production of platelet activating factor (PAF), and mimics PAF activity.

•**Peptidoglycan** binds to CD14 on macrophages and induces the secretion of cytokines.

•**Pneumolysin** is a cytolysin that forms pores when inserted into eukaryotic membranes.

•**Neuraminidase** may unmask cell-surface binding receptors

•**Hyaluronidase** may facilitate tissue spread.

•**IgA1 proteases** may prevent IgA-mediated immune clearance.

Treatment

- **Penicillin**
- Macrolides (erythromycin, clarithromycin) in patient with allergy to penicillin
- In severe infections (endocarditis) in combination with aminoglykosides (gentamicin) – synergic effect
- **Prevention**: vaccines – capsule antigens
  - polysaccharide vaccine (23 serotypes) – poorly immunogenic in infants

Conjugate vaccines – 10- or 13-PCV (pneumococcal conjugate vaccine) – antigen is conjugated to protein to increase a stimulation of immune system

THE BETA HEMOLYTIC STREPTOCOCCI

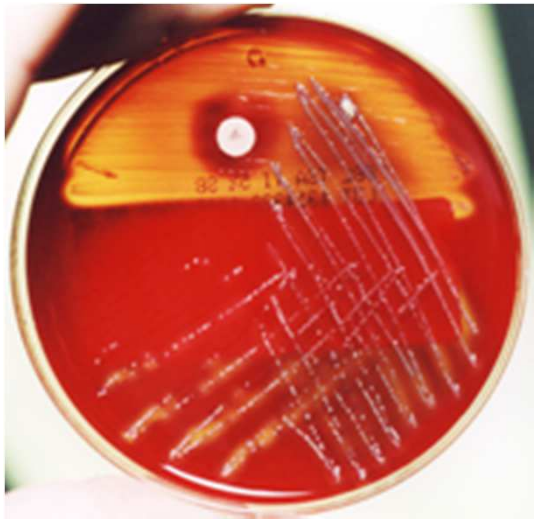
The beta Hemolytic Streptococci

- The **ß-hemolytic streptococci** are further divided into groups based on their **Lancefield antigen**-a cell wall carbohydrate that is characteristic of that particular Group of ß-hemolytic streptococci.

The beta Hemolytic Streptococci – group A

- **Group A *Streptococcus pyogenes***
  - Among the beta-hemolytic streptococci, *Streptococcus pyogenes* is the most virulent for humans.
  - an obligate human pathogen.
  - *Streptococcus pyogenes* is susceptible to **bacitracin (99%) -** diagnostic test, all other ß-hemolytic streptococci are resistant (95%).

Bacitracin susceptible *S. pyogenes*



The beta Hemolytic Streptococci – group A

- Diseases caused by *Streptococcus pyogenes*:
    - **Upper Respiratory Tract:** Tonsillitis
    - **Skin**: Impetigo, Cellulitis, Erysipelas, Necrotizing Fasciitis
    - **Toxin Mediated Disease:** Scarlet Fever, Streptococcal Toxic Shock Syndrome
    - **Post Streptococcal sequelae**:
        - Rheumatic fever
        - Glomerulonephritis

Virulence factors of *Streptococcus pyogenes*

A. Surface Constituents

M protein

- **M protein is the most important virulence factor- 80+ types!**
- Certain M protein types are associated with pharyngitis or with skin infections. Shared epitopes between M protein and host tissues may contribute to the pathogenesis of rheumatic fever
- M protein prevents phagocytosis by inhibiting C3b deposition on the bacterial surface.
- M protein adheres to epithelial cells.
- Antibody to a specific N terminus provides immunity to that M type, but not to others.

F protein

- F protein allows binding to fibronectin.
- F protein may or may not bind respiratory epithelial cells.

Virulence factors of *Streptococcus pyogenes*

A. Surface Constituents

Hyaluronic acid capsule

- The capsule inhibits phagocytosis

C5a protease

- C5a protease cleaves the C5a component of complement, inhibits neutrophil chemotaxis *in vitro*.

Lipoteichoic acid (LTA) or fibronectin binding molecule

- LTA is attached to M protein.
- It may allow binding to fibronectin.

Virulence factors of *Streptococcus pyogenes*

B. Secreted Virulence Factors

Hyaluronidase

- destroys hyaluronic acid.

Streptolysin O

- This oxygen labile (inhibited by oxygen) hemolysin that is only active in its reduced form.
- Streptolysin O works by inserting directly into the host cell membrane forming transmembrane pores.
- It is antigenic, and can be used to test for evidence of recent streptococcal infection.

Streptolysin S

- Streptolysin S is oxygen stable, and made in the presence of serum.
- It is a hemolysin causing the beta-hemolysis seen on blood agar plates.
- is nonantigenic.
- is one of the most potent cytotoxins
- is a virulence factor in the pathogenesis of invasive infections such as necrotizing fasciitis.

Virulence factors of *Streptococcus pyogenes*

B. Secreted Virulence Factors

Streptokinase

- Streptokinase hydrolyzes fibrin and other host proteins helping the organism spread through tissues.
- The purified enzyme is used clinically to dissolve blood clots.

Streptococcal Pyrogenic Exotoxins and Related Superantigens

- Various strains of *Streptococcus pyogenes* can produce a large number of potential superantigens.
- the streptococcal pyrogenic exotoxins (SPE-A, SPE-C, SPE-F, etc.)
- SPE-A is the cause of scarlet fever, and streptococcal toxic shock syndrome complicating invasive infections such as necrotizing fasciitis.

ß-Hemolytic Streptococcus Group B *Streptococcus agalactiae*

- GBS is part of the normal vaginal and/or intestinal flora in 20-30% of adults.

- Children are more susceptible to GBS infection than adults.

- Babies aspirates the organism in the infected amniotic fluid.

- **Identification**
  - Culture and CAMP test, agglutination (B group)

ß-Hemolytic Streptococcus Group B *Streptococcus agalactiae*

- **Diseases causes by GBS**
  - **GBS cause a pneumonia, septicemia and meningitis in newborns.** (2-3 cases /1000 births)
    - GBS can easily be detected by doing vaginal culture (35 week)
    - **Early Onset Infections:** Pneumonia and Septicemia
      - These infection occur in first days of life
    - **Late Onset Infections:** Bacteremia and Meningitis
      - GBS is the most common agent of meningitis in 5-30 day olds.
  - Foot ulcers in diabetics
  - Bovine mastitis in cows. GBS is a very important bovine pathogen.

Therapy of streptococcal infection

- **Penicillin** (erythromycin in allergic person)