

MICROBIOLOGY

Sheet

Slide

Handout

Number

4

Subject

Streptococci

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This sheet was written according to section 3 recording.

Streptococci

General characteristics

- It is a gram-positive cocci.
- Comes in the shape of chains or pairs (*pneumococci* or *streptococci pneumoniae*).
- Usually capsulated
 - Capsule structure in the case of *streptococci pneumoniae* is composed of Polysaccharide
 - Capsule structure in the case of *group A strep. pyogenes* is composed of Hyaluronic acid
 - Capsule structure in the case of *group B strep. pyogenes* is composed of Sialic acid
- Non motile
- Non spore forming
- Facultative anaerobes, which means they can live in both aerobic and anaerobic conditions but they prefer aerobic.
- Catalase negative (Catalase test is used to differentiate between *streptococci* and *staph. Staphylococci* are catalase positive and *streptococci* are catalase negative.)
- Incubation period is usually between 1-4 days.

Classifications

1. Oxygen requirements:

- a. Anaerobic
- b. Aerobic or facultative anaerobic

2. Serology (Lanciefield classification):

Lanciefield is the scientist that discovered a unique structure within the *streptococcus*, he discovered a carbohydrate antigen within the cell wall and that the carbohydrate antigen has different structures, and because of that they were classified into groups A, B, C, D, E, F, G, and W. The most known classification are groups A and B. Group D used to be *streptococcus* but now it is more known as enterococcus. There are certain *streptococci* that don't apply to this classification (don't have a carbohydrate antigen within their cell wall), such as *S. Pneumoniae* and *Viridans streptococci*

3. Hemolysis on blood agar:

Even though blood agar and chocolate agar are partially similar to some extent, blood agar was used because it has RBCs intact within it, unlike chocolate agar what has heated blood (i.e. already lysed blood).

a. α -Hemolysis

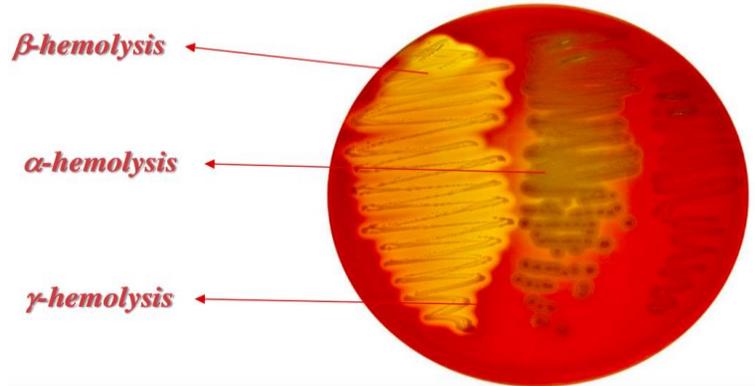
- i. Partial hemolysis
- ii. Green color on plate

b. β -Hemolysis

- i. Complete hemolysis
- ii. Yellow color on plate

c. γ -Hemolysis

- i. No hemolysis
- ii. Red color on plate



Group A Streptococci

Characteristics

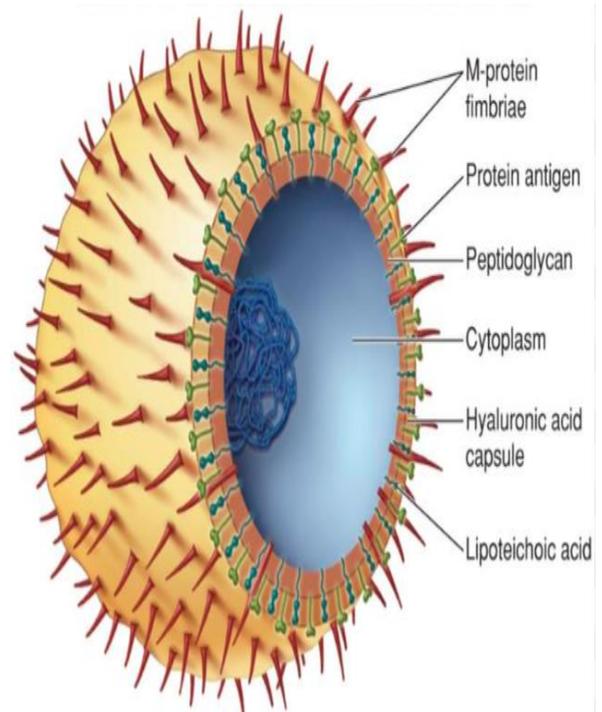
- Also known as *S. Pyogenes*.
- This is the microorganism that is the number one cause of bacterial pharyngitis (remember that Pharyngitis is mainly caused by viral infections), which is 90% of bacterial caused pharyngitis.
- *S. Pyogenes* is most commonly seen in the ages of 5-15 years old. Among those ages (5-15 years old) 15%-40% of pharyngitis cases are caused by *S. Pyogenes*.

Transmission

- Close contact (2-5 feet) in a closed space (e.g. Classroom), through aerosols and droplets.
- During the winter months (late fall and early spring).

Structural components:

- **M protein.** It is an important protein and it has multiple roles to play in the case of *S. Pyogenes*. These roles are:
 - 1) It helps in adhesion and attachment of the bacteria to the cells along with Lipoteichoic acid and F protein
 - 2) Its structure has two parts
 - a. Conserved/stable part. This part is embedded in the cell wall.
 - b. Variable Part. This part is hanging out of the cell wall. ***This part is the antigenic part of the bacteria giving it more than 80 and in some circumstances more than 100 serotypes for S. Pyogenes.***



- 3) Interferes with opsonization and lysis of the bacteria.
- 4) Because it is antigenic, there will be a production of antibodies against the M protein in the bacteria. It also has a similar structure with Myosin, therefore causing molecular mimicry (structural, functional, and immunological similarities between two molecules found on an infectious pathogen and in a host tissue). The result will be that the antibody will target both the bacteria (M protein) and the heart valves (Myosin) in the body.

Note: this is known as immune hypersensitivity, which has four types:

- **Types 1:** Allergy resulting from IgE and Histamine.
- **Type 2:** IgG mediated (Molecular mimicry)
- **Type 3:** Immune complex mediated (antibody-antigen complex), which occurs in *S. Pyogenes* since the antigen is the M protein and the antibody is being produced against it.
- **Type 4:** delayed, cell mediated type hypersensitivity

Note: In untreated cases, a large number of antigen-antibody complexes will be produced, these complexes themselves trigger the complement system, resulting in an excessive amount of complement system activation that can't control the problem, complexes will then deposit in the tissue. In the case of *S. pyogenes*, they deposit in the kidney causing glomerulonephritis (damage to glomeruli of kidney, resulting in the impairment of filtration function, causing a leakage of protein and blood). Clinical features are hypertension, hematuria, proteinuria, and edema, and are mostly seen in children. Patients will come with dark color hazy/opaque urine (dark because of the presence of RBCs and Opaque because of the presence of protein).

- **Lipoteichoic acid & F protein:** adhesion and attachment of the bacteria to the cell.
- **Hyaluronic acid capsule**, which plays a role in camouflage (hiding the bacteria from the immune system).

Enzymes

- **Streptokinase** causes thrombolysis (fibrin in the clot is being lysed to give fibrinogen). Because it is thrombolytic, it is used in the treatment of emergency cases of myocardial infarction.
- **Deoxynucleases**
- **C5a peptidase** it inhibits C5a, which is a complement component. Inhibiting C5a will therefore inhibit chemotaxis.
- **Pyrogenic toxins** are produced because of the *S. Pyogenes* infections, and some of the manifestations that we will talk about will be because of these toxins. Similar toxins are found in *staphylococci*, these antigens are called super antigens.
- **Streptolysins** are pore-forming cytotoxins that attach and enter the target cell. It also plays a role in α -Hemolysis and β -Hemolysis (it is the enzyme that lyses the RBCs). It has two types:
 1. Streptolysin O is oxygen unstable
 2. Streptolysin S is oxygen stable

Note: if the patient is assumed to have *S. Pyogenes* and we take a culture of the swab obtained, we should incubate it aerobically and anaerobically because some *S. Pyogenes* will have Streptolysin AO, some will have Streptolysin O only, and some will have Streptolysin S only. If Streptolysin

O is present in an aerobic condition, it will not work as it will not give us hemolysis and eventually misdiagnose the patient.

Diseases caused by S. Pyogenes

Divided into:

1. Suppurative (pus production)

- a. **Non-invasive** (e.g. pharyngitis, skin infection, and impetigo)

Note: *S. Pyogenes* can be present as normal flora in the respiratory tract and skin. In humid temperate areas where there is multiple insects, when an insect bites a person, the person starts scratching, breaking the barriers and introducing the bacteria, resulting in impetigo.

- b. **Invasive** (e.g. scarlet fever, pyoderma, and necrotizing fasciitis).

Note: scarlet fever, pyoderma, and necrotizing fasciitis are not a direct result from the presence of the bacteria; it's a result from the action of the toxin on the tissue. Scarlet fever in children who are untreated with antibiotics especially under the age of 2 will produce toxins. These toxins will lead to rash on the chest and spread to extremities with characteristics of sand paper consistency, erythema of buccal mucosa, and strawberry tongue appearance. Necrotizing fasciitis is one of the most terrible presentations of a bacteria infection, also known as a "flesh-eating bacteria".

2. Non Suppurative (no pus production)

- Rheumatic fever, which is a life threatening inflammatory disease that leads to damage of heart valve muscle (mechanism is the immune hypersensitivity type 2 - molecular mimicry)
- Glomerulonephritis, which is an immune complex disease of the kidney (mechanism is the type 3 immune hypersensitivity - the antigen-antibody complex).

Note: treatment of antibiotics will prevent Rheumatic fever from occurring but doesn't prevent Glomerulonephritis.

Note: more than 99% of patients with strep throat and not given antibiotics will **not** develop rheumatic fever, but duration of illness and severity of symptoms will become worse. If suspect (not fully diagnose) *S. Pyogenes* is present give antibiotics to treat illness and prevent complications from occurring. The other 1% chance of developing rheumatic fever will be due to reinfection, most probably

from a different serotype causing the infection then what was caused the first time. To prevent this from occurring we give penicillin, and if that didn't work then our last option is tonsillectomy.

Hemolysis on blood agar was used to differentiate between α -Hemolysis and β -Hemolysis. Now we will discuss how to differentiate between β -Hemolytic Streptococci and α -Hemolytic Streptococci.

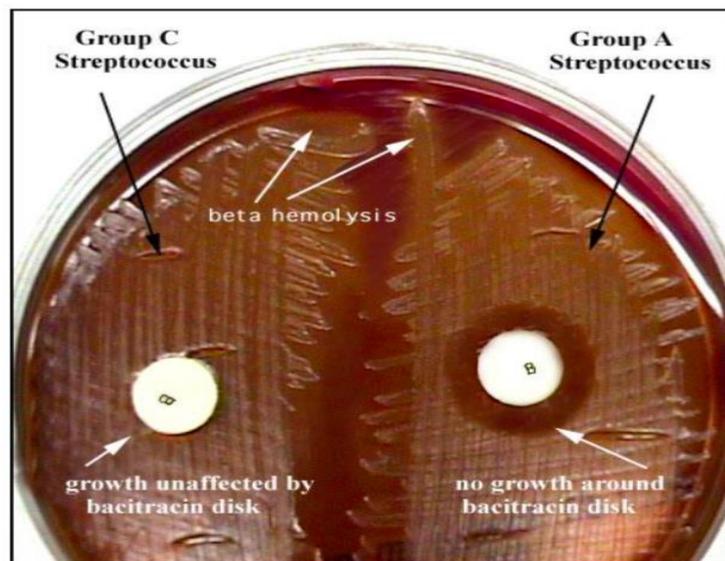
Tests used differentiation between β -Hemolytic Streptococci

1. Lanciafield classification
2. Bacitracin susceptibility test

It is an antibiotic that shows if the bacterium is resistant or susceptible. If susceptible then a zone of inhibition will be shown around the antibiotic disk. If it is resistant then no zone of inhibition will be shown around the antibiotic disk

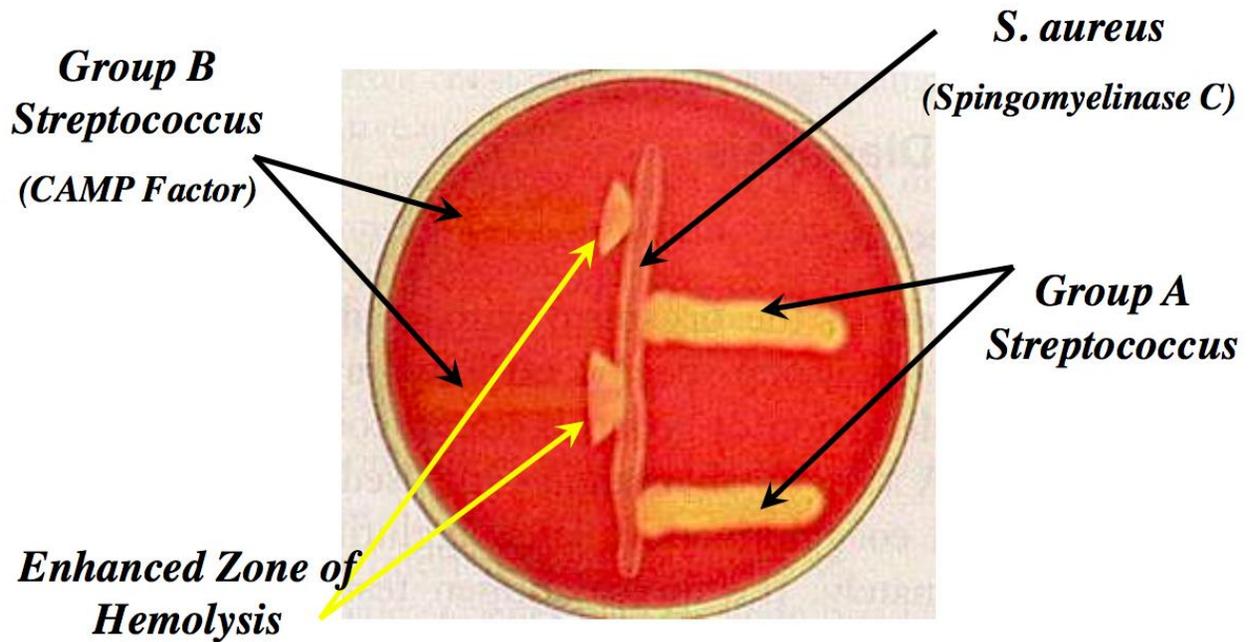
Susceptible \rightarrow **S. Pyogenes** (Group A)

Resistant \rightarrow **S. Agalactiae** (Group B) or others.



3. CAMP test

Used with Staphylococci. Staphylococci is in the middle, and perpendicularly we put two group A's and two group B's. We incubate for 24-48 hours and then see the hemolysis pattern. If enhanced hemolysis in the form of an arrowhead is seen then is a result of **S. Agalactiae** (Group B). If no enhancement of an arrowhead is seen then is indicates **S. Pyogenes** (Group A) (figure in the next page)



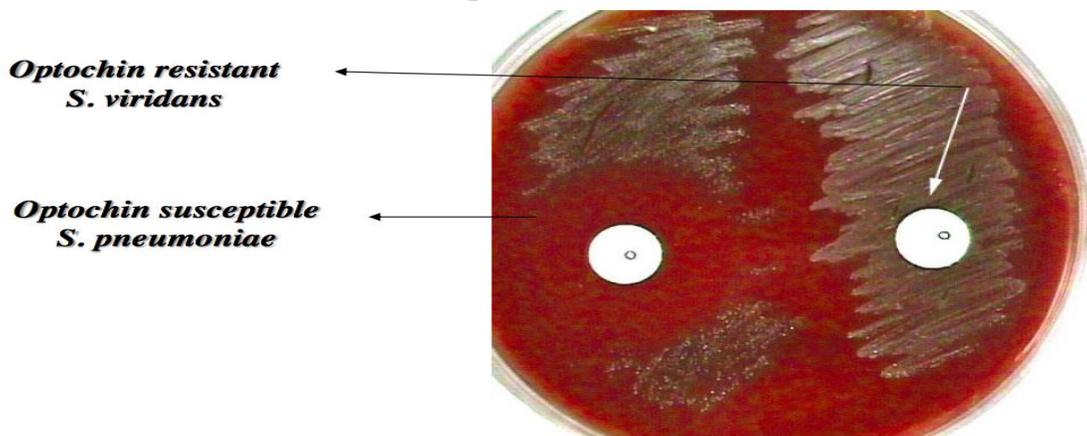
Tests used differentiation between α -Hemolytic Streptococci

1. Optochin Test

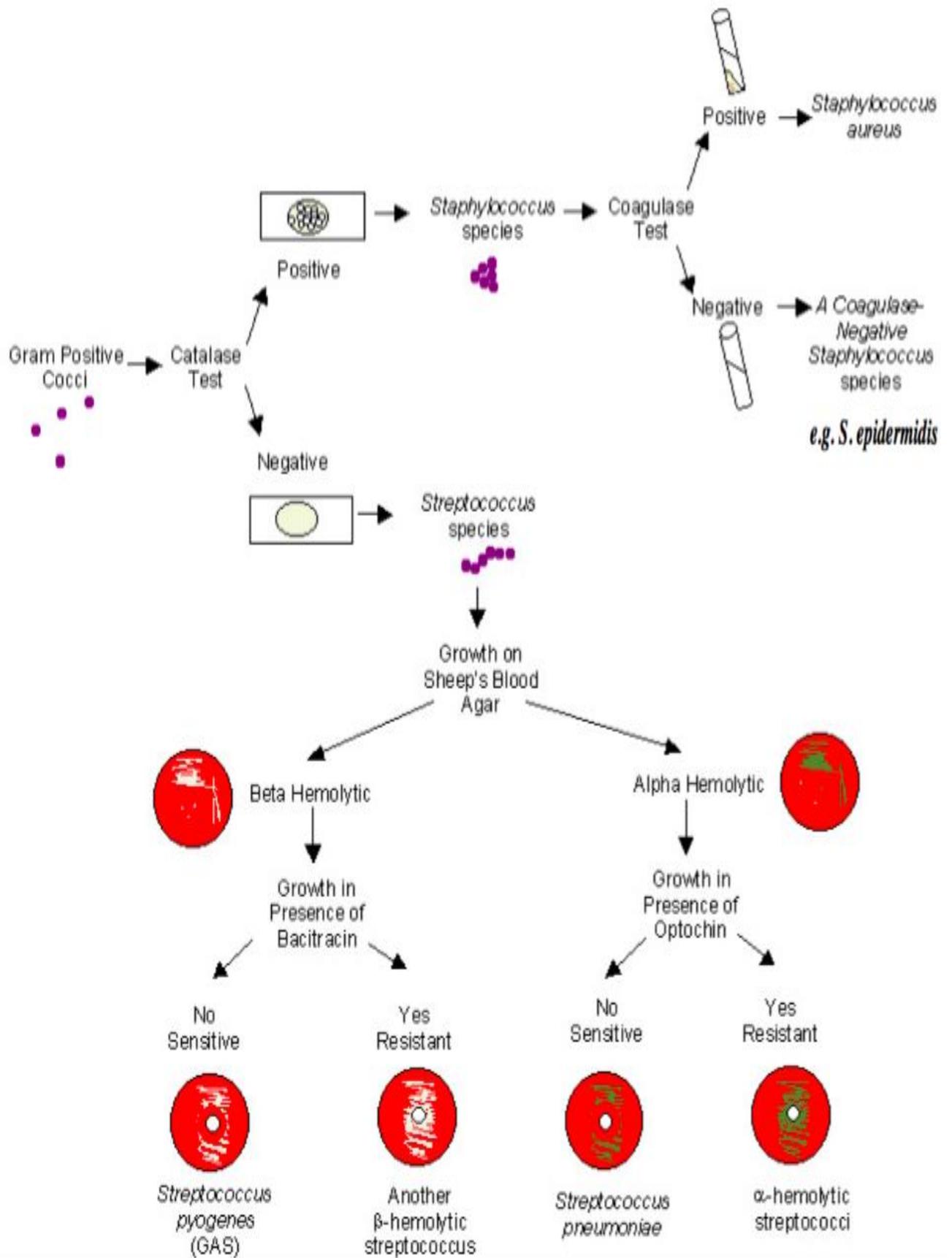
Similar to bacitracin but used to differentiate between α -hemolytic rather than β -hemolytic. Will either show that the bacterium is susceptible (zone of inhibition around the antibiotic disk will be seen) or resistant (no zone of inhibition around the antibiotic disk).

Susceptible \rightarrow **S. Pneumoniae** (Group A)

Resistant \rightarrow **S. Viridans** (Group B).



2. Bile solubility test **NOT INCLUDED**



Skin and soft tissue infections

1. Cellulitis

2. Erysipelas

cutaneous infection with the involvement of the lymphatic system, as a result of the lymphatic system this will lead to edema. Can be presented on the face or leg as a result of untreated *S. Pyogenes* infections.

3. Impetigo

4. Necrotizing fasciitis (Flesh-eating bacteria)

Upper respiratory tract infections

1. Tonsillitis / pharyngitis

most common bacterial cause of tonsillitis

2. Scarlet fever

- Occurs in children below 10 years old.
- Incubation period is 2-3 days.
- Strawberry tongue.
- Rash presented as sand paper consistency.

3. Acute otitis media & sinusitis

Other Suppurative diseases

- **Puerperal (after delivery) sepsis**
- **Neonatal sepsis.** Especially when the women are infected with *S. Agalactiae* (group B)
- **Lymphangitis**
- **Pneumonia**

Systemic disease

- **Streptococcal toxic shock syndrome (TSS)**
 - Caused by super antigens
- **Bacteremia**

Nonsuppurative sequelae of acute *S. pyogenes*

● Acute rheumatic fever

Inflammatory reaction characterized by arthritis, Carditis, erythema marginatum, or subcutaneous nodules.

Is a complication that is caused by *S. Pyogenes* that was caused by only a respiratory tract infection **not** cutaneous infection.

- **Acute glomerulonephritis**

Is a complication that is caused by *S. pyogenes* that was caused by both a respiratory tract infection **and** a cutaneous infection. Differentiated by:
Development of glomerulonephritis caused by a respiratory infection will take 7-10 days.

Development of glomerulonephritis caused by a cutaneous infection will take 4-6 weeks.

Diagnosis

- Clinical presentation (most common one)
- Culture
- Catalase test
- Hemolysis type
- Bacitracin test
- Optochin test
- Fast Step KIT (new)

Take two swabs of the pharynx and tonsils at the same time, insert the swab in a solution found in the KIT. Then place the indicator (similar to a pregnancy test) in the solution with the bacteria. One line will give a negative result and two lines will give a positive result. If the indicator says its positive then give antibiotics. If the indicator says its negative, don't be 100% confident, send the second swab for culturing and sensitivity, then wait 24-48 hours for the results. If you suspect strep even without diagnosis then treat patient with fluid antibiotic. This KIT is 98% specific and 90% sensitive.

Note: 98% specific means 98% of the time the indicator says its positive and the results were actually positive, and 2% of the time the indicator says its positive and the results were negative actually (**false positive**).

Note: 90% sensitive means 90% of the time the indicator says its positive and the results were actually positive, and 10% of the time the indicator says its negative and the results were actually positive (**false negative**).

Treatment

- Penicillin (drug of choice)

- Amoxicillin and amoxicillin clavulanic acid
- Macrolides such as erythromycin, azithromycin, and clarithromycin,

Prevention

- Penicillin prophylactically only in cases of acute rheumatic fever not glomerulonephritis.
- Tonsillectomy

Group B Streptococci

Characteristics

- Also known as S. Agalactiae
- Major cause of neonatal sepsis.
- Pregnant women can either be carriers or infected in the vagina.
- During birth the neonate will be infected. Neonate might be presented with meningitis, pneumonia, and sepsis.
- Associated with high mortality rate.

Sorry for any mistakes.

