STREPTOCOCCI

Streptococci are classified on the basis of:
- Hemolysis on blood agar.
- Biochemical reactions.
- Serologic specificity (most definitively)

1-Serologic grouping

- Hemolytic streptococci are divided into 18 serologic groups (Lancefield groups A – U), based on antigenic differences in cell wall carbohydrates antigens (C antigen).
- The capsular polysaccharides antigens are used to classify group B streptococci & Streptococcus pneumoniae.
- Surface protein antigens as M protein can be used for classification of S. pyogens

GROUP A STREPTOCOCCI

(S. Pyogens)

Morphology
- Gram positive cocci.
- Arranged in long chains (The chains arise because Streptococci divide in one plane).
- Non spore forming, non motile.
- Have a capsule of hyaluronic acid.

Virulence factors of S. pyogenes

1. Adherence to host cells: by M protein.
2. Inhibition of phagocytosis: by hyaluronic acid capsule & M-protein
3. Invasion by production of enzymes & toxins

Antigenic structure of S.pyogens

1- Carbohydrate antigen(c antigen) of group A, has no role in virulence
2- Protein antigens: M proteins: clearly virulence factors.
3- The capsule of S. pyogens: non antigenic, composed of hyaluronic acid, which is chemically similar to that of host connective tissue.

Enzymes produced by S.pyogenes

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptokinase</td>
<td>Lysis of fibrin</td>
</tr>
<tr>
<td>Streptodornase</td>
<td>Lysis of nucleic acid</td>
</tr>
<tr>
<td>Hyaluronidase</td>
<td>Spreading factor which digest hyaluronic acid</td>
</tr>
<tr>
<td>Streptolysins</td>
<td>Streptolysin S is non antigenic hemolysin.</td>
</tr>
<tr>
<td>Antibodies to these enzymes are used in diagnosis of streptococcal diseases</td>
<td>Streptolysin O is antigenic hemolysin.</td>
</tr>
<tr>
<td>Exotoxins: Pyrogenic (Erythrogenic toxin)</td>
<td>Causes rash of scarlet fever &amp; has been associated with a toxic shock-like syndrome.</td>
</tr>
</tbody>
</table>
Diseases caused by *S. pyogenes*

**A) SUPPURATIVE INFECTIONS**

1. Acute streptococcal toxic shock like syndrome - similar in pathogenesis and manifestation to staphylococcal toxic shock syndrome.
2. Scarlet fever (erythrogenic toxin) Usually affects children, characterized by fever, skin rash & stomatitis (Strawberry tongue).
   - The skin rash is due to direct effect of the erythrogenic toxin on the skin.

**B) TOXOGENIC DISEASES**

1- *Streptococcal toxic shock like syndrome* - similar in pathogenesis and manifestation to staphylococcal toxic shock syndrome.
2- *Scarlet fever (erythrogenic toxin)* Usually affects children, characterized by fever, skin rash & stomatitis (Strawberry tongue).
   - The skin rash is due to direct effect of the erythrogenic toxin on the skin.

**C) POST STREPTOCOCCAL SEQUELAE**

Infection with *Streptococcus pyogenes* can give rise to:

1. Acute rheumatic fever
2. Acute glomerulonephritis.

These begin 1-3 weeks after an acute streptococcal illness period.

- Acute rheumatic fever is a sequel only of pharyngeal infections
- Acute glomerulonephritis can follow infections of the pharynx or the skin

- The pathogenesis of acute rheumatic fever & glomerulonephritis is not well understood.
- The mechanism is immune mediated & may be due to:

**Pathogenesis**

1. Some of the antibodies produced during streptococcal infections cross-react with certain host tissues.
2. These can indirectly damage host tissues, even after the organisms have been cleared.
3. This explains the autoimmune responses that develop following some infections.

**Laboratory Diagnosis of *S. pyogenes***

Samples

Differ according to clinical diseases.

<table>
<thead>
<tr>
<th>Throat swab</th>
<th>Blood</th>
<th>Sputum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharyngitis</td>
<td>Puerperal sepsis</td>
<td>Endocarditis</td>
</tr>
<tr>
<td>Scarlet fever</td>
<td>Erysipelas</td>
<td>Bacteremia</td>
</tr>
</tbody>
</table>

Media for culture

- No growth on ordinary media.
- Complete hemolysis on blood agar.
- Colonies are pin point & translucent

Growth can be identified by

1. Film stained by Gram: to show the morphology.
2. Catalase test: negative (Staphylococci are catalase positive).
3. Bacitracin (0.04 µg) sensitivity: sensitive
4. (Other beta hemolytic streptococci are bacitracin resistant)
5. Specific definitive identification: can be done by reaction with specific antibodies.

Samples are examined by:

1- Direct film stained by Gram.
2-Culture

Streptococci are

- Facultative anaerobes.
- Optimum temperature: 37°C
- CO2 5-10% enhances growth.

Clumping of the latex particles is seen in the "A" circle (arrow) indicating that this is a Lancefield group A *Streptococcus (Streptococcus pyogenes)*. A negative test is milky in appearance.
**DIAGNOSIS OF RHEUMATIC FEVER**

Clinical picture & history of preceding streptococcal infections.

**Laboratory diagnosis by:**

1. Non specific tests as C-reactive protein & high ESR
2. Specific tests:
   - by detection of an increase in antibody titer to at least one of the streptococcal antigens including antistreptolysin O (ASO) which is most widely used
     - anti-DNase
     - antihyaluronidase
     - antistreptokinase
3. Detected by agglutination reaction using latex particle

**DIAGNOSIS OF SCARLET FEVER**

Specimen: throat swab examined as mentioned before.

**Schultz Charlton reaction:**
- Injection of the polyvalent antienterythrogenic toxin in the rash lead to disappearance of the rash within 6-12 hours
- due to neutralization of the toxin with specific antitoxin.

**PUERPERAL SEPSIS AND BACTEREMIA**

are diagnosed by blood culture

**PREVENTION OF S. PYOGENS INFECTIONS**

No vaccine is available to combat S. pyogens infections.
- There are many trials to produce vaccine based on the antigenicity of M-protein.
  - Long acting penicillin can be used to prevent recurrent pharyngitis and its immune-mediated sequelae

<table>
<thead>
<tr>
<th>GROUP B STREPTOCOCCI</th>
<th>GROUP D STREPTOCOCCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Streptococcus agalactiae)</td>
<td>(Strept. Faecalis Enterococci)</td>
</tr>
<tr>
<td>They are part of the normal vaginal flora.</td>
<td>Hydrolyse hippurate.</td>
</tr>
<tr>
<td>Capsulated</td>
<td>Positive for CAMP test.</td>
</tr>
<tr>
<td>Produce large mucoid colonies.</td>
<td>S. agalactiae produces a protein called the CAMP factor which acts to amplify the beta hemolytic activity of S. aureus.</td>
</tr>
<tr>
<td>There are at least 5 antigenic capsular types.</td>
<td>Present in gastrointestinal tract.</td>
</tr>
<tr>
<td>Are bacitracin resistant.</td>
<td>Considered as indication of fecal pollution of water</td>
</tr>
<tr>
<td></td>
<td>Causes UTI’s and wound infection.</td>
</tr>
<tr>
<td></td>
<td>particularly resistant to antibiotics.</td>
</tr>
<tr>
<td><strong>Bile Esculin Hydrolysis</strong></td>
<td><strong>Prevention</strong></td>
</tr>
<tr>
<td><strong>Diseases caused by S. agalactiae</strong></td>
<td>By I.V. administration of ampicillin to pregnant mothers who have Group B in vagina.</td>
</tr>
<tr>
<td>1. Neonatal septicemia</td>
<td></td>
</tr>
<tr>
<td>2. Pneumonia</td>
<td></td>
</tr>
<tr>
<td>3. meningitis which occur in babies born to mothers with Group B in vagina</td>
<td></td>
</tr>
</tbody>
</table>

**STREPTOCOCCUS VIRIDANS**

- Gram positive cocci
- arranged in pairs or short chains.
- Non spore forming, non motile & non capsulated
- Produce α hemolytic small colonies.
- Resistant to optochin & not bile soluble.
- Form a major part of normal oral flora.
- Are important etiologic agents of bacterial endocarditis
- Dental manipulation & dental disease with the associated transient bacteremia are the most common predisposing factors in bacterial endocarditis ,especially if heart valves have been damaged by previous rheumatic fever or by congenital heart disease

**ANAEROBIC STREPTOCOCCI**

Are part of the normal flora of the mouth, intestinal tract, upper respiratory & genital tracts

Causes wide variety of serious mixed infections of the female genital tract as well as to brain, pulmonary, and abdominal abscesses.

Thug's
**STREPTOCOCCUS PNEUMONIA**

**MORPHOLOGY**
- Gram positive lancet shaped diplococci
- Non spore forming & Non motile
- Capsulated.

**CLINICAL MANIFESTATIONS**
- S. pneumoniae is the most frequent cause of pneumonia & its complications
- It is common cause of sinusitis, acute bacterial otitis media & conjunctivitis.

**PATHOGENESIS**
1. Polysaccharide capsule: main virulence factor as it resists phagocytosis
2. *S. pneumoniae* can be classified into 80 serotypes according to antigenic structure of the capsule
3. Capsule can be detected by a serological test (Quellung reaction).
4. When the specific polyvalent antibodies are added to bacterial suspension it causes swelling of the capsule (Capsular swelling reaction).

**LABORATORY DIAGNOSIS**
- Sample: Sputum which is rusty
- Direct smear stained by gram
- Culture

**CULTURE**
1. Facultative anaerobe.
2. Optimum temperature is 37°C
3. Can grow on normal co2, but 5-10% co2 enhance growth.
4. No growth on ordinary media.
5. On blood agar produce alpha hemolysis.
6. Colonies are small with depressed centers.

**PREVENTION**
- Vaccine is available
  - Vaccine – contains purified capsular material from 23 of most common serotype causing pneumococcal infections
  - Recommended for young children, elderly, debilitated or immunosuppressed individuals.

**IDENTIFICATION OF GROWTH**
1. Film stained by gram to show the morphology.
2. Biochemical reactions:
   - fermentation of inulin
   - bile solubility
   - sensitivity to optochin (Positive reaction for all)
3. Pathogenicity to mice: intra peritoneal injection of culture in mice causes death in 18-48 hours due to septicaemia.
4. Capsular swelling reaction

All these tests are negative for other viridans streptococci.

**DIFFERENCE OF S.PNEUMONIAE & S.VIRIDANS**

<table>
<thead>
<tr>
<th>S.PNEUMONIAE</th>
<th>S.VIRIDANS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovoid/lanceolate diplococci</td>
<td>Morphology</td>
</tr>
<tr>
<td>Capsulated</td>
<td>Capsule</td>
</tr>
<tr>
<td>Flattened/draughtsman</td>
<td>Colony</td>
</tr>
<tr>
<td>Soluble</td>
<td>Bile solubility</td>
</tr>
<tr>
<td>Sensitive</td>
<td>Optochin sensitivity</td>
</tr>
<tr>
<td>Positive</td>
<td>Quellung reaction</td>
</tr>
<tr>
<td>Pathogenic</td>
<td>Mice pathogenicity</td>
</tr>
<tr>
<td>Alpha hemolysis</td>
<td>Effect on blood agar</td>
</tr>
<tr>
<td>Positive</td>
<td>Inulin fermentation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Short/long chains of rounded cocci</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td></td>
<td>Convex</td>
</tr>
<tr>
<td></td>
<td>Not soluble</td>
</tr>
<tr>
<td></td>
<td>Resistant</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td></td>
<td>Non pathogenic</td>
</tr>
<tr>
<td></td>
<td>Alpha hemolysis</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
</tr>
</tbody>
</table>