Streptococci

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Review questions on Streptococci

1. What are salient features of streptococci? How they look like in Gram stained smear and why?
2. Compare Staphylococci and streptococci.
3. How can you classify Streptococci?
4. Clinical significance of S.pyogenes?
5. Enumerate Toxins and enzymes of S. Pyogenes?
6. Enumerate diseases caused by S. pyogenes
7. Write down pathogenesis of AGN & ARF? How can you prevent them? Role of penicillin?
8. Lab Diagnosis of ARF & AGN
10. Clinical significance of Str Grr B G,Gr C& Gr D
11. Clinical significance of Str pneumoniae and Str viridians
The Streptococci

- Gram positive, spherical, or ovoid, non-motile bacteria.
- Grow in pairs or chains of varying length.
  - Divide in a plane perpendicular to the long axis of the chain
- Over 30 identified species
- Members of this genus cause a variety of diseases but they are also quite common as members of the normal flora.

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Each year ...

- 610 million (61 crores) cases of pharyngitis due to GAS
- 110 million cases of soft tissue infection
- At least 18 million people suffer the consequences of serious GAS diseases
- At least 500,000 deaths
History

- Hipocrates - 5th century BC
- Billroth 1874 – Erysepalas and wound infection
- Pasteur – 1884 – puerperal sepsis
- Rosenbach – named it
- 1919 – Brown – hemolysis
- 1930- Rebeca lancefield – grouping
- 1935 – Griffith - typing
Classification

Classification is Complex. Following are some important classifications.

- **Based on Oxygen requirement:**
  - Obligate anaerobe: *Peptostreptococcus*
  - Facultative anaerobe: Most of the streptococci

- **Based on Hemolysis in BA**: (Brown 1919)
  - Beta hemolytic: Most pathogenic spp. eg. *Str. pyogenes*
  - Alpha hemolytic: *Str. viridans, Str. pneumoniae*
  - Gamma hemolytic: *Str. fecalis, Enterococci*, etc.

- **Based on Group and Type specific cell wall antigen**
  - Grouping based on cell wall CHO antigen: (Lancefield 1933)
    - There 19 Groups – A B C D E F G H K L M N O P Q R S T U V of which Group A, B, C, D, & G are human pathogens
  - Typing based on cell wall M protein antigen: (Griffith)

- **Strains of *Strep. Gr A*** are further typed into >80 serotypes, Some are rheumatogenic and some are nephrotigenic.
Classification based on Hemolysis on Blood Agar

- **α-Hemolytic**: Partial hemolysis which gives a “greenish” appearance.
  - Ex. Viridans Streptococci

- **β-Hemolytic**: Clear zone indicating lysis of red blood cells.
  - *Ex. Streptococcus pyogenes*

- **γ-Hemolytic**: No hemolysis is observed.
Alpha hemolytic streptococcus
Beta hemolysis by *Streptococcus pyogenes*
Lancefield’s Grouping system

- Differentiates streptococci into serogroups by means of antigenic differences in cell wall carbohydrates
- 18 Groups: A-H, K-T
- Some species “non-typable”
  - *Streptococcus pneumonia*, Viridans streptococci
Lancefield Classification

Serogroup

- A (Strep. pyogenes)
- B (S. agalactiae)

Usual Clinical Features

- Pharyngitis, scarlet fever, rheumatic fever, cellulitis, AGN
- Neonatal sepsis and meningitis, chorioamnionitis
Lancefield Classification

Serogroup

- C (S. equi)
- D (Enterococcus, Strep bovis)
- G (S. canis)

Usual Clinical Features

- Upper Respiratory Infections
- Genitourinary and wound infections, endocarditis
- Upper resp. infections, cellulitis, sepsis
Serology: Lanciefield Classification

- Streptococci classified into many groups from A-K & H-V
- One or more species per group
- Classification based on C-carbohydrate antigen of cell wall
  - Groupable streptococci
    - A, B and D (more frequent)
    - C, G and F (Less frequent)
  - Non-groupable streptococci
    - S. pneumoniae (pneumonia)
    - viridans streptococci
      - S. mitis
      - S. salivarius
      - S. sanguinis
      - S. mutans
        - Causing dental carries

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Clinical Important Streptococci

- *S. pyogenes*
  - Group A Beta Hemolytic Strep
- *S. agalactiae*
  - Group B Strep
- Enterococci
- Viridens Streptococci
- *S. pneumonia*
<table>
<thead>
<tr>
<th>Type species</th>
<th>Lancefield serogroup</th>
<th>Normal habitat</th>
<th>Significant human disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pyogenes</em></td>
<td>A</td>
<td>Humans; cattle, humans</td>
<td>Acute pharyngitis and others, Neonatal meningitis and sepsis and infections in adults</td>
</tr>
<tr>
<td><em>S. agalactiae</em></td>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>S. equisimilis</em></td>
<td>C</td>
<td>Wide human and animal distribution</td>
<td>Endocarditis, bacteremia, pneumonia, meningitis, mild upper respiratory infection</td>
</tr>
<tr>
<td><em>E. faecalis</em></td>
<td>D</td>
<td>Human and animal intestinal tracts, dairy products, bacteremia</td>
<td>Biliary or urinary tract infection, endocarditis,</td>
</tr>
<tr>
<td><em>S. bovis (nonenterococcus)</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>S. anginosus</em></td>
<td>F, G</td>
<td>Humans, animals</td>
<td>Subcutaneous or organ abscesses, endocarditis, mild upper respiratory infection</td>
</tr>
<tr>
<td><em>S. sanguis</em></td>
<td>H</td>
<td>Humans</td>
<td>Endocarditis, caries</td>
</tr>
<tr>
<td><em>S. salivarius</em></td>
<td>K</td>
<td>Humans</td>
<td>Endocarditis, caries</td>
</tr>
<tr>
<td>None</td>
<td>O</td>
<td>Humans</td>
<td>Endocarditis</td>
</tr>
<tr>
<td><em>S. suis</em></td>
<td>R</td>
<td>Swine</td>
<td>Meningitis</td>
</tr>
<tr>
<td>&quot;Viridans&quot; <em>S. mitis, S. mutans</em></td>
<td>None identified</td>
<td>Humans</td>
<td>Caries, endocarditis</td>
</tr>
<tr>
<td>Anaerobic or micro-aerophilic</td>
<td>None identified</td>
<td>Wide human and animal distribution</td>
<td>Brain and pulmonary abscesses, gynecologic infections</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>None identified</td>
<td>Humans</td>
<td>Lobar pneumonia and others</td>
</tr>
</tbody>
</table>

*a* Strains of the “S. milleri” group (*S. constellatus, S. intermedius, S. anginosus, minute strains*) may possess antigens of groups A, C, F, or G, or no identifiable Lancefield group antigens; a heterogeneous group, genetically related but with a wide variety of phenotypic and biochemical characteristics.

*b* Disparate grouping undergoing further definition.

*c* Other viridans streptococci (*S. sanguis, S. salivarius “S. milleri,” S. bovis*) have identified group antigens(s); nutritionally variant streptococci may be included in this diverse category.
**Streptococcus pyogenes**

- **Morphology / Culture / Biochemical properties**
  - GPC in chains, Aerobic and FA, grow in BA with clear zone of hemolysis, Catalase negative, Bacitracin sensitive.
  - First described in 1879 by Pasteur in a sample from patient dying of puerpural sepsis.
Streptococcus pyogenes:
Microscopic appearance & colonial morphology
Determinants of Pathogenicity

- Toxins
- Enzymes
- Other factors
Toxins

- **Streptolysin ‘O’** – Oxygen labile, has antigenicity. Destructs RBCs, ASO rises following streptococcal sore throat but not skin infections.

- **Streptolysin ‘S’** – Oxygen stable, Not antigenic.

- **Pyrogenic toxin (Erythogrnic toxin) A** – Present in few strains which are lyosogenic and responsible for scarlet fever.

- **Pyrogenic toxin (Erythogrnic toxin) B** - Rapidly destroys tissue and responsible for necrotizing fascitis.
Enzymes

1. **Hyaluronidase (Spreading factor)** - Breaks down proteoglycans of Connective tissue.

2. **Streptokinase (Fibrinolysin)** – activates plasminogen to plasmin that breaks fibrin clot.

3. **DNase (Streptodornase)** – depolymerizes DNA in exudates or necrotic tissue. Antigenic.

4. **C5-a peptidase** - degrades complement component of C5a, which attracts phagocytes to the sites of complement deposition. Prevents chemotaxis of neutrophils and mononuclear phagocytes.
Other Virulence Factors

1. Capsule - antiphagocytic
2. Fc Binding Protein - antiphagocytic
3. M Protein - antiphagocytic, adhesion
4. Plasmin Binding Protein
S. Pyogenes – Patterns of Disease

1. Direct Bacterial Invasion
2. Toxin Mediated
   - Streptococcal Toxic Shock Syndrome
   - Scarlet Fever
3. Delayed Disease Caused by Host Response
   - Acute Rheumatic Fever
   - Acute Glomerulonephritis
Due to local invasion

- Streptococcal pharyngitis, Tonsillitis, Sinusitis, Adenitis, Otitis media and mastoiditis.
- Skin infections – Folliculitis, Cellulitis, impetigo
- Sepsis – Infections of wounds, burns and chronic skin lesions
- Pulmonary abscess, empyema
- Septicaemia, acute endocarditis
- Purperal sepsis
Due to Exotoxin release

- Scarlet fever-
- Toxic shock syndrome –
- Necrotizing fascitis
Delayed antibody mediated

- Rheumatic fever
  - Following Pharyngitis due to type II hypersensitivity
- Acute glomerulonephritis
  - Following skin infections due to type III hypersensitivity
How common is invasive group A streptococcal disease?

- About 9,400 cases of invasive GAS disease occurred in the United States in 1999.
- About 300 were STSS and 600 were necrotizing fasciitis.
- In contrast, there are several million cases of strep throat and impetigo each year.
- About 20% of patients with necrotizing fasciitis and more than half with STSS die.
- About 10%-15% of patients with other forms of invasive group A streptococcal disease die.
Diagnosis Supporative infections

- **Specimen**: According to site of infection. eg. T/S, Pus, Sputum
- **Microscopy**: Gram positive cocci in chains
- **Isolation and Identification**: Culture in BA, Small colonies with clear zone of hemolysis which are confirmed by Catalase and Bacitracin sensitivity test. **Grouping** and **Typing** is done by serological test.
- **Antigen Detection from T/S**: ELISA and Agglutination test are available.
- **Immunological test**: Dick test for Scarlet fever.
Poststreptococcal Sequelae: Acute Rheumatic Fever

- Nonsuppurative inflammatory lesions involving the:
  - Heart
  - Joints
  - Subcutaneous Tissues
  - Central Nervous System

- Usually follows an upper respiratory infection with Group A Strep
  - Latency 1-5 weeks (Average 19 days)
  - Risk after untreated pharyngitis → <3%
  - Cutaneous infections do not lead to ARF
Poststreptococcal Sequelae: **Acute Rheumatic Fever**

- Associated with Group A streptococci of certain M protein serotypes
  - 1, 3, 5, 6, 14, 18, 19, 24
- Role of M protein in the pathogenesis is unclear. Two hypotheses:
  1. Due to structural features, M protein elicits the production of antibodies cross reactive with host myosin
  2. Due to its *superantigenic* properties, M protein elicit the production of antibodies against host components.
Diagnosis of Rheumatic Fever - Jones Criteria

- **Major Criteria**
  - Carditis (60%)
    - Endocardium, myocardium, pericardium
    - Tachycardia, mitral regurgitation, friction rub
  - Polyarthritis (70%)
    - Migratory, large joints
  - Chorea (10%)
    - Emotional lability, weakness, involuntary movements
  - Erythema Marginatum (10%)
  - Subcutaneous nodules (10%)
Rheumatic fever: chronic valvar disease

- Repeated bouts of valve inflammation may heal with:
  - fibrosis of valve cusps
  - fusion between valve commissures
  - Shortening, thickening of chordae tendinae

- Valves Involved
  - Mitral 70%
  - Mitral + aortic 25%
  - Tricuspid, Pulmonic rarely
Diagnosis of Rheumatic Fever - Jones Criteria

- **Minor Criteria**
  - Clinical
    - Arthralgias
    - Fever
  - Laboratory
    - Elevated acute-phase reactants
    - Elevated erythrocyte sedimentation rate
    - Elevated C-reactive protein
    - Prolonged PR interval

- **Supportive evidence of antecedent group A strep infection**
  - Positive throat culture or rapid streptococcal antigen test
  - Elevated or rising streptococcal antibody titer (ASO)
Prevention and Treatment of Acute Rheumatic Fever

- **Primary Prevention**
  - Adequate therapy of Strep. Pharyngitis
    - Ex. Penicillin for 10 days

- **Treatment of ARF**
  - Penicillin to eradicate Strep.
  - Anti-inflammatory drugs

- **Prevention of Relapse**
  - Daily PCN ≥ 5 years
Poststreptococcal Sequelae: Acute Glomerulonephritis

- Follows infection with a limited number of Group A streptococci serotypes
- More frequently associated with skin infections
  - M types 12, 4, 2, 49
  - Incidence of nephritis:
    - Any Group A Strep infection $\Rightarrow$ <0.5%
    - M type 49 $\Rightarrow$ 23%
Poststreptococcal Sequelae: Acute Glomerulonephritis

- **Precise mechanism?**
  - Immune mediated
    - Antibodies elicited by nephritogenic streptococci react with renal tissues to produce glomerular injury
    - M protein may be the streptococcal trigger
  - Light microscopy reveal a marked increase in glomerular intracapillary cellularity (endothelial and mesangial proliferation)

- **Recurrences rare**
  - Limited number of nephritogenic strains?
  - Acquisition of type-specific antibody?
Any Questions?