(5) Streptococcus

**Classification**
Based on their haemolytic properties, streptococci can be classified into 3 groups:
- **β-hemolytic** e.g. Streptococcus pyogenes
- **α-hemolytic** e.g. Streptococcus viridans
- **γ-hemolytic** e.g. Enterococcus faecalis

**Types of Haemolysis on blood agar**
- **α-haemolysis** "Incomplete"
- **β-haemolysis** "Complete"
- **γ-haemolysis** "No haemolysis"

**Streptococcus pyogenes**
- Morphology: They are gram positive spherical cocci
- They occur in chains of varying length
- Chain formation is due to the cocci dividing in one plane only
- They are non-motile, non-spore forming and some strains produce a capsule of hyaluronic acid

**Cultural characteristics**
- They are aerobic and facultative anaerobic
- Optimum temperature is 37°C
- They can grow on blood agar, and after 24 hrs incubation, colonies are small and surrounded by a wide zone of B-hemolysis

**Lancefield Classification**
- On the bases of group specific carbohydrate antigen contained in the cell wall, haemolytic streptococci have been divided into 21 groups (A to W except I and J)
- S.pyogenes belongs to Lancefield group A

**Determinants of pathogenicity**
- S.pyogenes produces several exotoxins and enzymes which contributes to its pathogenicity and identification
- M protein: it plays a great role in adhesion to pharyngeal epithelial cells, inhibits phagocytosis and intracellular killing by leukocytes. It is the major virulence factor Gp A streptococci
- Hyaluronic acid capsule: protects streptococci against immunological attacks from the infected host
Erythrogenic toxin (Streptococcal pyrogenic exotin)
- There are 3 antigenically distinct erythrogenic toxins A, B and C.
- These exotoxins have been associated with streptococcal toxic shock syndrome and scarlet fever.

Haemolysins
- It produces 2 types of haemolysins: one is O2 labile and called streptolysin O (SLO), the other is O2 stable and called streptolysin S (SLS).
  - SLO: it is produced by Gp A, and also by Gp C and G.
  - SLO: it has toxic effect on the heart and leucocytes.
    → It is strongly antigenic and its antibody will be formed 10-14 days after infection.
  - ASO: it is very important in diagnosis of late complications of streptococcal infections, which occurs after elimination of the organism from the host.
  - SLS: It is non-antigenic. Beside B-haemolysis, it inhibits phagocytosis and has cytotoxic effect on various types of cells.

Streptokinase
- It is produced by Gp A, C and G.
- It is actively fibrinolytic for human fibrin (blood clot).
- It is thought to be at least partially responsible for the rapid spread of streptococcal infection by preventing the formation of a fibrin barrier around the infected site.
- It is given IV for the treatment of early myocardial infarction and other thromboembolic disorders.

Deoxyribonucleases (Streptodornases)
- S pyogenes also elaborates enzymes that degrade DNA.
- Anti-DNase is important in diagnosis of post streptococcal complications due to skin infection.

Hyaluronidase
- It is enzyme which splits hyaluronic acid binding tissue cells together.
- It plays a part in virulence of S.pyogenes by facilitating its spread.

Pathogenicity
- S.pyogenes is intrinsically much more dangerous than S.aureus and has a much greater tendency to spread in the tissues.
- It is more likely to give rise to septicaemia.
- *S. pyogenes* are carried normally in the RT, mouth and skin of about 5% of general population
- *S. pyogenes* causes:
  → Suppurative diseases
  → non-suppurative sequelae

**Suppurative diseases**
- Tonsilitis and pharyngitis
- Scarlet fever
- Impetigo
- Erysipelas
- Others, e.g. puerperal sepsis

- Tonsilitis and pharyngitis: the main site of streptococcal infection is the throat where purulent tonsillitis is the most typical lesion
- Scarlet fever: the disease consists of a combination of sore throat, generalize erythema
- Impetigo: it is a skin infection that occurs most often in young children, particularly those living in crowded, low socioeconomic conditions
- Erysipelas: it is an acute spreading, erythematous skin lesion
- Others: puerperal sepsis, wound and burn infections

**Non suppurative sequelae**
- Acute rheumatic fever
- Acute glomerulonephritis

**Acute rheumatic fever**
- ARF develops in a small percentage (3%) of individuals, 2-3 weeks after the onset of acute streptococcal
- Recovery from ARF occurs without residual injury to the joints, but permanent damage to the heart may occur
- The mechanism by which streptococci produce rheumatic fever is still obscure
- Various theories have been postulate:
  → Antigenic cross reactivity:
    A common cross reacting antigens exists in some Gp A streptococci and the heart
  → Direct toxicity:
    It is due to streptococcal exotoxins
Acute Glomerulonephritis (AGN)
- less frequently than ARF
- AGN occur one week after Gp A streptococcal infection
- S.pyogenes associated with ARF is isolated from the upper respiratory tract only
- S.pyogenes associated with AGN may be isolated from the upper respiratory tract or from skin lesions such as impetigo

Laboratory diagnosis
- In acute suppurative infections, diagnosis is established by identification of β-haemolytic streptococci that have been isolated from the patient
- Specimens: according to the site of infection, throat swab, pus, vaginal swab, blood, etc
- In non suppurative complications, diagnosis is based on the demonstration of rising titer of antibody to one or more of streptococcal antigens
- Microscopic examination: by visualization of gram positive cocci arranged in chains
- Culture and isolatin: on blood agar, incubate at 37C, for 24hrs, observe β haemolytic colonies of streptococci
- Identification:
  - Lancefield grouping
  - Sensitivity to bacitracin disc: the inhibition of growth around the disk is seen with S.pyogenes but not with other streptococci
- ASO: titers > Todd units/nl are indicative of prior streptococcal infection (in ARF)
- Anti-DNAse: titers > 300 or 350 (in AGN)

Treatment
- Penicillin is highly effective in the treatment of all acute infections
- Adequate treatment during acute infection prevents complication of ARF
- Those person who have recovered from ARF are given oral penicillin for many years to prevent recurrence
- In AGN, recurrence is low, so no prophylactic penicillin
- In patients allergic to penicillin, erythromycin, cephalexin may be used
Other groups of Streptococci
B,C,G,D

Group B streptococci
(S.agalactiae)
- They are major pathogens in neonates and young children
- Infection in the neonates is divided into early onset type and late onset
  Early onset type:
  - within the first 5 days of life, the neonate develops septicaemia, pneumonia and meningitis
  - Gp B streptococci are present on the vaginal flora of about 25% of all women
  - Early rupture of the membranes, prolonged labour, prematurity, low birth weight and heavy colonization of mother's vagina lead to early onset infection
  Late-onset type:
  - develops between second to fourth week of life
  - Baby acquires infection from the hospital personnel during nurse procedures
  - Baby to baby spread may also occur
  - This infection is not as severe as early onset type
  - Gp B may also cause adult infections, including septicaemia, endocarditis, meningitis, female genital tract, UTI, surgical wound, pneumonia, arthritis osteomyelitis

Groups C, G and D streptococci
- Group C and G can cause sore throat, pneumonia, septicaemia, meningitis, endocarditis, bone, joint, wound infection
- Group D may cause UTI, wound infection, infective endocarditis, biliary tract infection, peritonitis, suppurative abdominal lesions and septicaemia

Viridans streptococci (Oral streptococci)
- These organisms produce α or no haemolysis on blood agar
- They are constantly present as commensals in the mouth and oropharynx
- Five species include: S.salivarius, S.sangius, S.mutans, S.mitis (mitis), S.milleri
- S.mutans and S.sanguis are involved in the production of dental plaques and caries
- In persons with PF such as valvular disease of the heart, viridians streptococci may cause infective endocarditis.
- Tooth extraction in such individuals should be done under antibiotic cover.

**Diagnosis and treatment of infective endocarditis**
- Repeated blood culture for isolation of α–haemolytic streptococci.
- These streptococci are generally susceptible to penicillin, though some strains are resistant.
- Therefore antibiotic sensitivity should be carried out.

**Key Facts**
- Streptococci are gram positive, non motile, catalase negative cocci.
- They are arranged in chains (S.pyogenes) or pairs (S.pneumoniae).
- Blood enriched media is used for their isolation.
- There is considerable evidence that S.pyogenes is in some way the cause of ARF and AGN.

**Important Questions**
1. Mention classification of streptococci according to haemolytic properties and give examples.
2. Give short account on Lancefield classification.
3. Enumerate determinants of pathogenicity of Strept.pyogenes.
4. What is the major virulence factor for Group A streptococcus and its role?
5. Write short note on strept.pyogenes exotoxins.
6. Which enzyme produced by strept.pyogenes that can be used for treatment of early myocardial infarction?
7. Enumerate suppurative diseases caused by Strept.pyogenes.
8. Give Short account on ARF.
9. Give short account on AGN.
10. What are the theories of ARF caused by strept.pyogenes?
11. Give short account on serological test used for diagnosis of non suppurative sequelae of strept.pyogenes.
13. State True or False.
   a. strept.pyogenes belongs to lancefield Gp b.
   b. streptokinase splits hyaluronic acid in the C.T.
   c. Scarlet fever is one of the non suppurative diseases of strept.pyogenes.
15-Complete
a-... plays great role in adhesion of Strept pyogenes to pharyngeal epithelial cells
b-SLO has toxic effect on ...&...
c-...is very important in diagnosis of ARF
d-... is given IV for treatment of myocardial infarction

Answers
1--β-hemolytic  e.g Streptococcus pyogenes
-α-hemolytic  e.g Streptococcus viridians
-γ-hemolytic  e.g Enterococcus faecalis
2--on the bases of group specific carbohydrate antigen contained in the cell wall, haemolytic streptococci have been divided into 21 groups (A to W except I and J)
-S.pyogenes belongs to Lancefield group A
3--S.pyogenes produces several exotoxins and enzymes which contributes to its pathogenicity and identififcation
-M protein
-Hyaluronic acid capsule
-Hemolysins
-Streptokinase
-Deoxyribonucleases
-hyluarindase
4--M protein : it plays great role in adhesion to pharyngeal epithelial cells, inhibits phagocytosis and intracellular killing by leukocytes. It is the major virulence factor Gp A streptococci
5--There are 3 antigenically distinct erythrogenic toxins A,B and C
-These exotoxins have been associated with streptococcal toxic shock syndrome and scarlet fever
6-Streptokinase
7- Tonsilitis and pharyngitis
Scarlet fever
Impetigo
Erysipelas
Others,e.g.puerperal sepsis
8- Acute rheumatic fever
-ARF develops in a small percentage (3%) of individuals, 2-3 weeks after the onset of acute streptococcal
-Recver from ARF occurs without residual injury to the joints, but permanent damage to the heart may occur
The mechanism by which streptococci produce rheumatic fever is still obscure.

Various theories have been postulate:

→ Antigenic cross reactivity:
A common cross reacting antigens exists in some Gp A streptococci and the heart.

→ Direct toxicity:
It is due to streptococcal exotoxins.

9-Acute Glomerulonephritis (AGN)
- Less frequently than ARF.
- AGN occur one week after Gp A streptococcal infection.
- S.pyogenes associated with ARF is isolated from the upper respiratory tract only.
- S.pyogenes associated with AGN may be isolated from the upper respiratory tract or from skin lesions such as impetigo.

10—Antigenic cross reactivity:
A common cross reacting antigens exists in some Gp A streptococci and the heart.

→ Direct toxicity:
It is due to streptococcal exotoxins.

11—In non supurative complications, diagnosis is based on the demonstration of rising titer of antibody to one or more of streptococcal antigens.

13—

Diagnosis and treatment of infective endocarditis
- Repeated blood culture for isolation of α – haemolytic streptococci.
- These streptococci are generally susceptible to penicillin, though some strains are resistant.
- Therefore antibiotic sensitivity should be carried out.

14-a-F  b-F  c-F
15-a-Mprotein
b-heart and leucocytes
c-ASO
d-St kinase