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# Streptococci and *Streptococcus pneumoniae*

key points of the lecture

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# Streptococci

- Facultatively anaerobic
- Catalase negative
- Gram-positive cocci, don't produce spores, non-motile

- Strong fermenters of carbohydrates, resulting in the production of lactic acid - a property responsible for the involvement of some oral streptococci in the decalcification of teeth, i.e. dental caries
- More than 70 species.
- found as part of the normal flora of the human oral cavity and pharynx
- Important human pathogens

# Medical important species

*Streptococcus pyogenes*

*Streptococcus agalactiae*

*Streptococcus pneumoniae*

*Streptococcus salivarius*

# Haemolytic activity

- Beta – the principal marker for potentially pathogenic streptococci
- Pyogenic streptococci are also referred to as haemolytic streptococci

# Haemolytic activity

- Alfa – the principal marker for potentially pathogenic strep
- Most commensal strep give rise to a green discoloration around colonies on BA
  - Collectively, commensal streptococci are often called ‘viridans streptococci’, which refers to their  $\alpha$ -haemolytic property
  - (viridis = green)
  - $\alpha$ -haemolytic property – *S.pneumoniae*

# Lancefield grouping

- An important method of distinguishing between pyogenic streptococci is the serological classification discovered by Rebecca Lancefield, who detected different versions of the major cell wall polysaccharide among the pyogenic streptococci.

# serological groupes Lancefield

- not all streptococci have this groupe specific antigen of cell wall
- Group A (GAS)    *S. pyogenes*            bacitracin    beta hemolysis
- Group B (GBS)    *S. agalactiae*            CAMP            beta hemolysis
- Group C            *S. anginosus*                            beta, alfa
- Group D            *S. bovis*                                alfa, gama
- - *S. pneumoniae*    optochin +    alfa
- - *S. salivarius*        optochin -    alfa



# *STREPTOCOCCUS PYOGENES*

- Lancefield group A streptococci **GAS**
- associated exclusively with human infections
- causes a wide range of suppurative infections:
  - in the respiratory tract
  - skin
  - life-threatening soft tissue infections
  - certain types of toxin-associated reactions
- may result in severe nonsuppurative sequelae due to adverse immunological reactions induced by the infecting streptococci

# Virulence factors

- Adhesion
  - the principal mechanism by which *Str. pyogenes* binds to epithelial cells of the pharynx and skin is interaction with host fibronectin, a matrix protein on eukaryotic cells
- F protein
  - Receptor for fibronectin
  - interaction between the streptococcal F protein and host cell fibronectin mediates internalization of the bacteria into host cells
- M protein
  - involved also in adherence to mucosal and skin epithelial cells
  - protection against phagocytosis and cooperation with complement

- Capsule
  - Inhibits phagocytosis - an antiphagocytic effect
  - The capsule is identical to the hyaluronic acid of the connective tissue of the host and is not immunogenic
- Streptolysins
  - **streptolysins O** (oxygen labile) - found in many pathogenic bacteria, immunogenic - serum antibodies can be demonstrated after streptococcal infection, particularly after severe infections
  - **streptolysins S** (serum soluble) - responsible for the  $\beta$ -haemolysis around colonies on BA - non-immunogenic
  - both of which lyse erythrocytes, polymorphonuclear leucocytes and platelets by forming pores in their cell membrane

- Pyrogenic exotoxins
  - fever generating
- Hyaluronidase
  - degrades hyaluronic acid, the ground substance of host connective tissue
  - may facilitate the spread of infection along fascial planes
- Streptokinase
  - known as fibrinolysin
  - soft tissue infections due to *Str. pyogenes* are more diffuse, and often rapidly spreading
- DNA-ases
  - in pus, declines viscosity of pus

# Clinical manifestation *S.pyogenes*

- suppurative infections in the respiratory tract
- The most common route of entry of *Str. pyogenes* is the upper respiratory tract
- Spread from person to person is by respiratory droplets or by direct contact with infected wounds or sores on the skin

# Non-invasive streptococcal disease

- **Pharyngitis**

- the most common infection caused by *Str. pyogenes*
- Clinical signs: sore throat, fever, malaise and headache generally develop 2–4 days after exposure to the pathogen
- The posterior pharynx is usually diffusely reddened, with enlarged tonsils that may show patches of grey–white exudate on their surface and, sometimes, accumulations of pus in the crypts
- The local inflammation results in swelling of cervical lymph nodes
- Occasionally, tonsillar abscesses develop - very painful and potentially dangerous as the pathogen may spread to the bloodstream

# Non-invasive streptococcal disease

- **Scarlet fever**
- diffuse erythematous rash of the skin and mucous membranes
- Pharyngitis caused by certain pyrogenic exotoxin-producing strains of *Str. pyogenes* may be associated with rash
- known as scarlet fever or scarlatina
- The rash develops within 1–2 days after the first symptoms of pharyngitis, initially appears on the upper chest, then spreading to the extremities
- the tongue becomes red ('strawberry tongue')

# Non-invasive streptococcal disease

## Skin infections

- suppurative infections
- may cause several types of skin infection, sometimes in association with *Staph. aureus*
- **impetigo** or **pyoderma** – mainly in children, primarily affects exposed areas on the face, arms or legs
- Infection after contact with an infected person and the bacteria enter the skin through small defects
- clear vesicles develop, which within a few days become purulent



# Non-invasive streptococcal disease

## Skin infection

- **Erysipelas**
- occurs in the superficial layers of the skin and involves the lymphatics
- characterized by
  - diffuse redness of the skin
  - local pain,
  - enlargement of regional lymph nodes and
  - fever
- Untreated, the infection may spread to the bloodstream, and was often fatal before antibiotics became available

# Invasive soft tissue infections *S.pyogenes*

- Necrotizing fasciitis
  - progresses very rapidly, destroying fat and fascia
  - Systemic shock and general deterioration occur very quickly
- Streptococcal toxic shock syndrome
  - fever, malaise, nausea, vomiting and diarrhoea, confusion and a flat rash over large parts of the body
  - Without treatment, the disease progresses to shock and general organ failure
- Other suppurative infections
  - lymphangitis, pneumonia and meningitis - relatively rare
- Bacteraemia
  - in patients with necrotizing fasciitis and toxic shock syndrome

# Non-suppurative sequelae *S.pyogenes*

- **Rheumatic fever**
- **Acute glomerulonephritis**
- Both are caused by immune reactions induced by the streptococcal infection
- The first clinical signs appear 1–5 weeks after the infection

# *STREPTOCOCCUS AGALACTIAE*

- Lancefield group B streptococci - GBS
- produces several virulence factors, including haemolysins, capsule polysaccharide, peptidase, hyaluronidase, and various surface proteins
- Hemolysin known as the CAMP factor (so-called because it was originally described by Christie, Atkins and Munch-Petersen), plays an important role in the recognition of this species in the laboratory
- The CAMP factor lyses sheep or bovine red blood cells pretreated with the  $\beta$ -toxin of *Staph. aureus*

# Clinical manifestation

- **Infection in the neonate**

- 1. Early-onset disease, most cases of which present at or within 12 h of birth.
- 2. Late-onset disease, presenting more than 7 days and up to 3 months after birth.
- The clinical symptoms include lethargy, cyanosis and apnoea;
- when septicaemia progresses, shock and death will occur if treatment is not instituted quickly.
- Meningitis and pulmonary infection may be associated

- **Infections in the adult**

- amniotic infection may result in
- abortion,
- chorioamnionitis,
- post-partum sepsis (endometritis) and
- other infections (e.g. pneumonia) in the postpartum period in young, previously healthy women

# *STREPTOCOCCUS PNEUMONIAE*

- commonly called the pneumococcus
- In contrast to other streptococci, *Str. pneumoniae* generally occurs as characteristic diplococci

# Virulence factors

- **Capsule**

- capsular polysaccharide, antiphagocytic
- The serotypes are designated by numbers (total of 91 different capsular serotypes have been identified)

- **IgA1 protease**

- cleaves human IgA1 , enables these pathogens to evade the protective functions of the principal immunoglobulin isotype of the upper respiratory tract

- **Pneumolysin**

- inhibits neutrophil chemotaxis, phagocytosis and the respiratory burst



# *STREPTOCOCCUS PNEUMONIAE*

- It primarily causes
  - disease of the airways and associated tissues
  - middle ear,
  - paranasal sinuses,
  - mastoids and
  - lung parenchyma
  - may spread to other sites, such as the meninges, joints, peritoneum, and endocardium

- **Pneumonia**

- the most frequent cause of pneumonia

- **Otitis media and sinusitis**

- Middle ear infections (otitis media) affect children between the ages of 6 months and 3 years
- prevalence is highest among children attending kinder garten or primary school

- **Meningitis**

- invasion arises from the pharynx to the meninges via the bloodstream
- Meningitis may occasionally complicate pneumococcal infection

# Laboratory diagnosis

- Sampling
  - throat or skin swabs, pus, blood cultures, cerebrospinal fluid, expectorates or urine
- Microscopy
- Cultivation on BA – type of hemolysis
- Bacitracin test
- CAMP test
- Bile solubility test
- Optochin test
- Ag detection - diagnostic kits use specific antibodies to detect the group A antigen in the material on the swab
- Ab detection - important means of establishing the diagnosis of poststreptococcal rheumatic fever and glomerulonephritis (ASO)

# Therapy

- *Str. pyogenes* - 100% susceptible for PNC, (in allergies macrolides ERY)
- *Str. agalactiae* - good susceptibility for PNC, macrolides and glycopeptides
- *Str. pneumoniae* - PNC, TTC, CEF, resistance for PNC – multiresistance
  - In patients unable to tolerate penicillin, erythromycin is the most widely used alternative agent for respiratory pneumococcal infections.
  - Sensitivity to penicillins and other antibiotics varies widely, and clinical isolates must be tested for their susceptibility

# Key points

- *Str. pyogenes* (GAS) is among the most prevalent of human bacterial pathogens
- *Str. pyogenes* and group C and G streptococcal infections range from sore throat, scarlet fever and superficial skin infections to invasive soft tissue infections and septicaemia.
- They produce several superantigenic extracellular toxins that are involved in the pathogenesis of the rash associated with scarlet fever and streptococcal toxic shock syndrome.
- Rheumatic fever and acute glomerulonephritis are potential immune-mediated sequelae of infections with *Str. pyogenes*.

# Key points

- *Str. agalactiae* (GBS) causes neonatal septicaemia and meningitis.
- *Str. pneumoniae* is the principal cause of pneumonia, middle ear infections and meningitis.
- Commensal streptococci of the oral cavity.

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