S. pneumoniae
Optochin sensitive

Quellung reaction (swelling reaction)
Structure and physiology:

- **Streptococcus pneumoniae**: These are Gram-positive, lancet-shaped cocci (elongated cocci with a slightly pointed outer curvature). Usually, they are seen as pairs of cocci (diplococci), but they may also occur singly and in short chains. When cultured on blood agar, they are alpha hemolytic.

- They are non spore forming, and nonmotile.

- Like other streptococci, they lack catalase and ferment glucose to lactic acid.

- Unlike other streptococci, they do not display an M protein, and their cell wall composition is characteristic both in terms of their peptidoglycan and their teichoic acid.
S. pneumoniae

- α hemolytic
- pneumolysin
  - degrades red blood cells under aerobic conditions
- grows well on sheep blood agar
- no group antigen
fastidious bacterium, growing best in 5% carbon dioxide. Nearly 20% of fresh clinical isolates require fully anaerobic conditions.

On agar, pneumococci grow as glistening colonies, about 1 mm in diameter. Two serotypes, types 3 and 37, are mucoid. Pneumococci spontaneously undergo a genetically determined, phase variation from opaque to transparent colonies.

The transparent colony type is adapted to colonization of the nasopharynx, whereas the opaque variant is suited for survival in blood. The chemical basis for the difference in colony appearance is not known, but significant difference in surface protein expression between the two types has been shown.
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<th>Biologic Effect</th>
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<td>Surface protein adhesions</td>
<td>Bind to epithelial cells</td>
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<td>Secretory IgA protease</td>
<td>Disrupts secretory IgA–mediated clearance</td>
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<td>Pneumolysin</td>
<td>Possibly destroys ciliated epithelial cells</td>
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<td>Tissue Destruction</td>
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<td>Teichoic acid</td>
<td>Activates alternative complement pathway</td>
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<td>Peptidoglycan fragments</td>
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<td>Pneumolysin</td>
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<td>Hydrogen peroxide</td>
<td>Allows reactive oxygen intermediates to cause damage</td>
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<td>Phosphorylcholine</td>
<td>Binds phosphodiesterase-activating factor, allowing bacteria to enter host cells</td>
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<td>Phagocytic Survival</td>
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<td>Capsule</td>
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<td>Pneumolysin</td>
<td>Suppresses phagocytic oxidative burst</td>
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The brain. The initial colonization of the oropharynx is...
DISEASES CAUSED BY STREPTOCOCCUS PNEUMONIAE

Non-invasive disease
- Sinusitis (sinuses)
- Otitis media (middle ear)
- Pneumonia (lungs)

Invasive disease
- Bacteraemia (blood)
- Meningitis (CNS)
- Endocarditis (heart)
- Peritonitis (body cavity)
- Septic arthritis (bones and joints)
- Others (appendicitis, salpingitis, soft-tissue infections)

Musher, in Principles and Practice of Infectious Diseases, 1995
Nasopharyngeal carriage may occur in up to 60% of healthy pre-school children and up to 30% of healthy older children and adults.
Electron micrograph of pneumococcus

Surface capsular polysaccharide
Polysaccharide capsule

- Capsular polysaccharides: hydrophilic gels on organism surface
- Most important virulence factor
- Protects against phagocytosis by granulocytes and macrophages
- Elicits a T-cell–independent (not boostable) immune response
The optochin test is a presumptive test that is used to identify strains of *Streptococcus pneumoniae*. Optochin (ethyl hydrocupreine) disks are placed on inoculated blood agar plates. Because *S. pneumoniae* is not optochin resistant, a zone of inhibition will develop around the disk where the bacteria have been lysed. This zone is typically 14mm from the disk or greater.
Pathogenesis

- Colonisation of mucous membranes in respiratory tracts
- Adhesion (bacterial adhesins)
- Invasion of tissues if not defeated
  - Middle ear
  - Sinuses
  - Bronchi
Important for modelling:

**Pneumococcal serotypes**

- Based on properties of capsular polysaccharides
- Immunologically distinct and basis for classification
  - > 40 serogroups (e.g. group 19)
  - > 90 serotypes (e.g. types 19A, 19C, 19F)
- No immunologic cross-reactivity between serogroups
- Some cross-reactivity within some serogroups and some cross-protection
- Geographical and temporal variation
- Some more immunogenic than others
Important for modelling:

Pneumococcal serotypes (II)

- Children <5 y lack ability to mount antibody response to several serotypes
- Such types (6B, 9V, 14, 19F, 23F) more dominating among young children = child serotypes
  - Account for the majority of carriage and disease in children
  - Explains high incidences of carriage and disease in the youngest
- Child serotypes heavily linked to antibiotic resistance
- Limited number of very successful international clones
About the disease

- A major cause of morbidity and mortality worldwide
  - Over 1 million deaths annually due to pneumonia
  - Causes more deaths in young children in US than any other single microorganism
- Incidence of infection varies globally
- Age groups at highest risk for disease:
  - Infants and children < 2 years of age
  - Adults > 65 years of age
- Pneumococcal disease frequently observed in children up to 5 years of age
PNEUMOCOCCUS: DIVERSITY OF SEROTYPES

- There are at least 90 different serotypes of *S. pneumoniae*.
  - Each has a capsule of a different chemical composition.
  - Each stimulates the production of a different antibody.

- Only a minority of serotypes cause most cases of human disease.
  - 8–10 cause two-thirds of serious pneumococcal infections in adults.

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1 Fedson, Mushar, in Vaccines, 1994
2 Henrichsen, J Clin Microbiol, 1995
3 UK DoH, Immunisation Against Infectious Disease, 1996
PNEUMOCOCCAL VACCINES: ANTIGEN COMPOSITION

- 23-valent pneumococcal vaccine contains purified capsular polysaccharides derived from 23 S. pneumoniae serotypes
  - 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F

- Serotype coverage
  - 85–90% of serotypes responsible for all cases of invasive pneumococcal disease
  - Vaccine includes major serotypes that have developed antimicrobial resistance

- Cross protection within some serotypes
  - For example, antibody response to serotype 6B protects against serotype 6A, which is not in the vaccine

1 CDC, MMWR, 1989
2 Fedson, Musher, in Vaccines, 1994
3 Geslin et al., Méd Mal Infect, 1992