Outline

I. Introduction

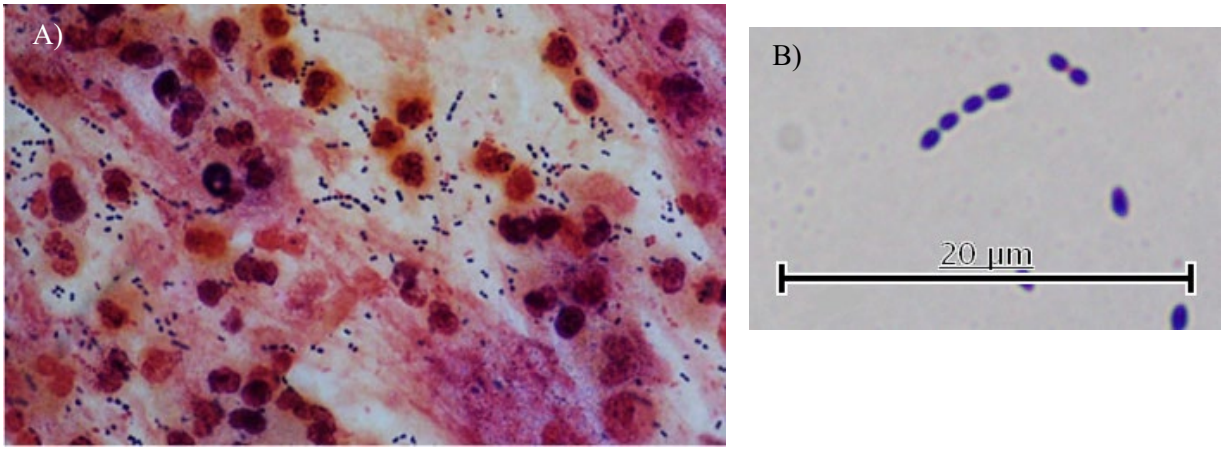


Figure 1: Gram stain of *S. pneumoniae* occurring in pairs and short chains in A) sputum sample with polymorphonuclear leucocytes in the background and B) a pure culture of S. pneumoniae. Image was obtained at 1000X magnification under oil-immersion. Stains kindly provided by Dr Timothy Barkham, Department of Laboratory Medicine, Tan Tock Seng Hospital and Mr Clement Ng, Department of Microbiology and Immunology, National University of Singapore.

S. pneumoniae, or 'pneumococcus', is a Gram-positive coccus (GPC) (Figure 1). About 40-50% of children and 20-30% of adults carry pneumococci asymptomatically in their nasopharynx [1], but it is a common cause of severe disease, traditionally being among the top 3 causes of bacteraemia.

Invasive pneumococcal disease (IPD) is far more common in children, and adults >65yrs (Figure 2). Functional or anatomic asplenia/splenic dysfunction, chronic respiratory, heart, renal and liver disease are also risk factors for infection [4].

In 2017, WHO included penicillin non-susceptible *S. pneumoniae* in its list of antibiotic-resistant "priority pathogens" posing the greatest threat to human health [5].

Virulence of *S. pneumoniae* is due to the highly immunogenic polysaccharide capsule which evades the immune response by blocking phagocytosis. There are 100 known antigenically distinct variants of this capsule, called serotypes [6]: some are more common than others.

Transmission occurs mainly via direct contact with respiratory droplets.

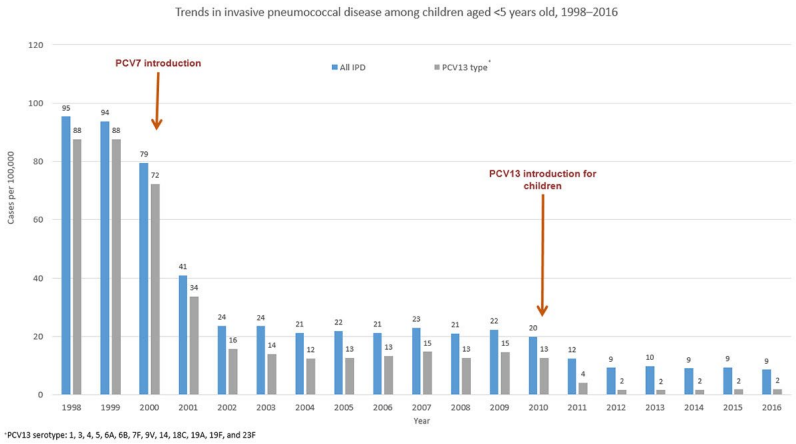
II. Clinical Features

'IPD' refers to invasion into a normally sterile site, and includes pneumonia, meningitis and bacteraemia, while more common and less severe non-invasive disease include otitis media, sinusitis and bronchitis [7-9].

Symptoms depend on the body part affected by infection and can include/not limited to:

Infection	**Symptoms**
Pneumonia (Respiratory)	Fever, cough, shortness of breath, chest pain, chills, sweats, aches and pains, headache
Meningitis (CNS)	Fever, stiff neck, headache, confusion, photophobia (Sensitivity to light), chills, sweats, aches and pains
Bacteraemia (Blood)	Fever, chills, sweats, aches and pains, confusion, headache
Otitis media (Ear)	Ear pain, loss of hearing, fever, ear discharge
Sinusitis (Respiratory)	Fever, facial pain and pressure
Bronchitis (Respiratory)	Cough and chest discomfort

(A)



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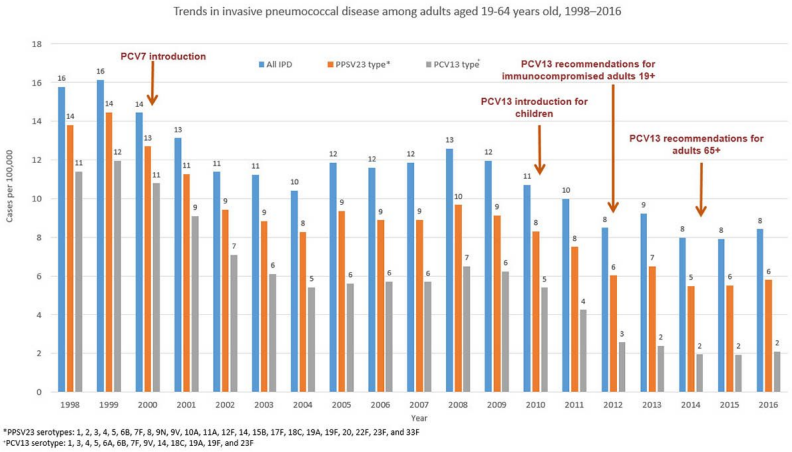

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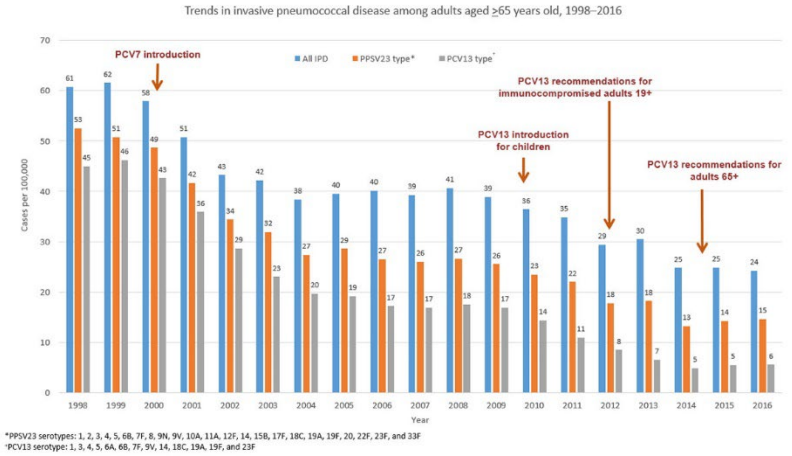

Figure 2: Changes in the incidence of invasive pneumococcal disease (IPD) among (A) children <5 years old, (B) adults 19 through 64 years of age and (C) adults 65 years or older from 1998 through 2016 in the United States. Rates of IPD expressed as cases per 100,000 population are shown on the y-axis, and calendar year of surveillance on the x-axis.

Blue bars represent overall IPD incidence, the orange bars represent IPD incidence caused by serotypes included in 23-valent pneumococcal polysaccharide vaccine (PPSV23) and the grey bars represent IPD incidence caused by serotypes included in the 13-valent pneumococcal conjugate vaccine (PCV13). Source from [10]. This material is in the public domain and may be freely used or reproduced without obtaining copyright permission.

III. Detection and Diagnostic Methods

- **Culture and isolation [Gold standard]; e.g. from blood, CSF, sputum [11]**
  - Allows antibiotic susceptibility testing
  - Colonies are alpha-haemolytic on blood agar, catalase negative, optochin susceptible, bile soluble [12], and positive with latex agglutination assays (Figure 3).
- **Gram stain; lanceolate GPC in pairs and short chains**
  - Diagnostic on sputum or CSF
- **Rapid antigen test for Pneumococcal cell wall polysaccharide using immunochromatographic tests**
  - Rapid, inexpensive and simple.
  - High specificity, but low sensitivity [13].
  - Test urine for pneumonia, or CSF for meningitis.
  - Interpret with caution in young patients because a positive urine test result may simply be the result of nasopharyngeal colonization [13].

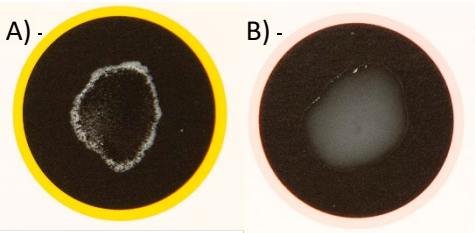

Figure 3: Latex agglutination assay (A) Clumping observed as a positive result (B) No clumping observed, negative result. Figure kindly provided by Ms Chan Chuu Ling, Department of Microbiology and Immunology, National University of Singapore.

IV. Prevention and Control Strategies

Pneumococcal vaccines, targeting the capsule, have been extremely effective in children (Figure 2A). Vaccination of children also reduced invasive disease in adults (Figure 2B-C).

Two types of pneumococcal vaccine are available for clinical use in Singapore

1) Pneumococcal polysaccharide vaccine (PPSV23)
2) Pneumococcal conjugate vaccine (PCV10, PCV13, PCV20 [14, 15])

**The number in the vaccine name refers to the number of Pneumococcal serotypes that each vaccine provides protection against.*

The challenges to effective vaccine use include the huge diversity in pneumococcal capsule types, as well as serotype replacement. Serotype replacement involves the increase in non-vaccine serotypes replacing vaccine serotypes in carriage and invasive disease [15, 16].

Singapore's National Childhood Immunisation Schedule [17]: children should be given two doses of PCV10 or 13 at ages 4 and 6 months, followed by a booster at 12 months.

PPSV23 is not recommended for children younger than 2 years of age [18] as it is poorly immunogenic. In very young children, the developing immune system may not respond as effectively to T-cell independent antigens like the polysaccharides in PPSV23. PPSV23 primarily induces a T-cell-independent immune response and does not elicit immune memory, unlike PCV vaccines which use polysaccharide conjugated to a carrier protein to induce a T-cell-dependent immune response, and are able to establish immunological memory [19].

Adult Immunisation Schedule: ≥65 years, one dose of PCV13 and one dose of PPSV23 [17].

PCV20 only became available in 2023 [14]; it may replace current recommendations cited above.

V. Treatment Options

Antimicrobials: Penicillins, cephalosporins, 'respiratory quinolones', macrolides, or doxycycline, depending on site of infection. Dose is dependent on the site of infection.

For mild infection in the community setting, oral amoxicillin is often used. In more severe respiratory tract infections intravenous penicillin or ceftriaxone, a 3rd generation cephalosporin, is used.

Meningitis is special due to the blood brain barrier, which prevents beta-lactam drugs achieving CSF concentrations necessary to treat strains with reduced penicillin/cephalosporin susceptibility. These strains are common, so for meningitis we use 'ceftriaxone plus vancomycin' as empiric treatment while awaiting laboratory results. If the pneumococcus is confirmed to be sufficiently susceptible to beta-lactams, the vancomycin is cancelled [20].

For pneumococci resistant to beta-lactams, or patients allergic to penicillin – vancomycin, macrolides, quinolones or tetracyclines [4].

For more severe infections, appropriate resuscitation, oxygenation and invasive or supportive care can be prescribed as required [4].

VI. Pathweb Links

Lobar pneumonia case study – Most cases of lobar pneumonia are caused by *S. pneumoniae*

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