Pneumococcal Infections

Section 5 Diseases Caused by Gram-Positive Bacteria · Part 5 – Infectious Diseases: Bacterial

KEY CLINICAL POINTS

1. S. pneumoniae is a gram-positive, α-hemolytic, optochin-sensitive, bile-soluble diplococcus.
2. The polysaccharide capsule is the primary virulence factor and basis for serotyping (100 serotypes).
3. Invasive pneumococcal disease (IPD) rates are highest in children <2 years and adults ≥65 years.
4. Pneumococcal pneumonia classically presents as lobar consolidation; 'round pneumonia' is a specific pediatric finding.
5. Elderly patients may present with confusion or malaise without fever or cough (atypical presentation in 30-50% of cases).
6. Asplenia or splenic dysfunction is a critical risk factor for overwhelming pneumococcal disease.
7. Urinary antigen testing is confounded by nasopharyngeal colonization and has modest sensitivity in adults (60-70%).
8. Empyema is the most common focal complication, occurring in <5% of cases.
9. Vancomycin resistance has not yet been observed in clinical pneumococcal strains.
10. PCV introduction has reduced vaccine-serotype IPD by 80-90% but non-vaccine serotypes (e.g., 19A) are emerging.

1. DEFINITION & OVERVIEW

Pneumococci are gram-positive, α-hemolytic diplococci of the genus Streptococcus.

- **Identification:** Optochin sensitivity and bile solubility distinguish S. pneumoniae from other streptococci.
- **Structure:** Capsule composition determines serotype (100 recognized, grouped into 21 serogroups).
- **Growth:** Requires a catalase source (blood) and produces mucoid colonies on blood agar.
- **Morphology:** Absence of capsule results in rough colony morphology; Gram stain shows lancet-shaped diplococci.

Definition (Harrison's 22e): *Pneumococci are divided into serogroups or serotypes based on capsular polysaccharide structure, as distinguished with rabbit polyclonal antisera; capsules swell in the presence of specific antiserum (the Quellung reaction).*

1.1 Microbiology & Classification

- **Classification:** S. pneumoniae belongs to the alpha-hemolytic group (greenish blood agar colonies).
- **Morphology:** Characterized as gram-positive diplococci.

2. EPIDEMIOLOGY

Global burden and risk factors:

- **IPD Prevalence:** Rates are highest in children <2 years and adults ≥65 years.
- **Vaccination Impact:** PCV7/10/13 reduced vaccine-serotype IPD by 80-90%, but non-vaccine serotypes (e.g., 19A) now cause 25-30% of IPD in some regions.
- **Carriage Dynamics:** Nasopharyngeal carriage rates are 20-50% in children and 10-40% in adults. Children serve as primary vectors; daycare attendance increases carriage by 2x.

Reference Figure 151-3: Illustrates the significantly higher prevalence of pneumococcal carriage in children aged 0-4 compared to older cohorts.

Reference Figure 151-4: Demonstrates the bimodal (U-shaped) distribution of IPD before PCV, highlighting high risk in infants and the elderly.

2.1 Risk Groups

High-risk populations include:

- **Immunocompromised:** HIV, chemotherapy, primary immunodeficiencies (B cell, T cell, complement, or phagocytic disorders).
- **Asplenia/Splenic Dysfunction:** Sickle cell disease and other hemoglobinopathies, celiac disease.
- **Chronic Disease:** Chronic heart disease (ischemic, congenital, heart failure), chronic liver disease (cirrhosis, biliary atresia), and chronic respiratory disease (COPD, cystic fibrosis).
- **Other Factors:** Diabetes requiring insulin, cochlear implants, CSF leaks, and age extremes (<2 years or ≥65 years).

Reference Table 151-1: Lists specific conditions including heart failure, cirrhosis, and systemic glucocorticoid treatment for >1 month at doses ≥20 mg/d (children) or ≥1 mg/kg per day.

3. ETIOLOGY & PATHOPHYSIOLOGY

Virulence mechanisms and molecular epidemiology:

- **Primary Virulence:** Polysaccharide capsule (serotype-specific).
- **Enzymes & Proteins:**
  - Pneumolysin (PLY): Causes cell lysis.
  - LytA: Enhances pathogenesis via cell wall lysis.
  - Pili: Inhibit phagocytosis and promote invasion.
  - Neuramidases (NanA, NanB): Remove sialic acid from host glycolipids to facilitate adherence.
- **Immune Evasion:**
  - Hic: Inhibits C3 convertase.
  - PspC: Binds factor H.
  - ZmpA: Cleaves IgA to evade mucociliary clearance.
- **Adhesion Factors:** PsaA, NanA, and BgaA deglycosylate host proteins for receptor exposure.

Reference Figure 151-2: Illustrates the complex cell surface including PBP (penicillin-binding proteins), Hyal (hyaluronidase), and other factors like PsrA.

3.1 Genomic Typing

- **Methods:** MLST (7 loci), cgMLST (>1300 core genes), and GPSC clustering via PopPUNK.
- **Databases:** >50,000 genomes available in PubMLST and GPS; Pathogenwatch for rapid analysis of serotype and resistance profiles.

---

4. CLINICAL FEATURES

Clinical presentations vary by age and comorbidities:

- **Typical Pneumonia:** Lobar consolidation, abrupt onset with chills, and pleuritic chest pain.
- **Pediatric Presentation:** 'Round pneumonia' (perihilar opacities).
- **Elderly Presentation:** Atypical presentation in 30-50% of cases; may present with confusion or malaise without fever or cough.

Reference Figure 151-5: Shows classic lobar consolidation in the right lower lobe.

4.1 Physical Examination

- **Typical:** Fever, tachypnea, crackles on auscultation.
- **Severe/Elderly:** Altered mental status, signs of sepsis (hypotension, oliguria).

---

5. DIFFERENTIAL DIAGNOSIS

Key differentials for pneumococcal syndromes:

- **Pneumonia:** Legionella, Mycoplasma, influenza virus.
- **Meningitis:** Neisseria meningitidis, Haemophilus influenzae type b.
- **Sepsis:** Gram-negative sepsis, fungal infections.
- **Otitis media:** Viral upper respiratory infections, other bacterial pathogens.

---

6. INVESTIGATIONS & DIAGNOSIS

Diagnostic approach for pneumococcal infection:

1. **Blood Cultures:** Gold standard for IPD; positive in 20-30% of cases.
2. **Urinary Antigen Testing:** Used for nonbacteremic pneumonia; sensitivity 60-70% in adults (lower in children).
3. **Molecular Tests (PCR):** Rapid detection from respiratory samples with >95% sensitivity.
4. **Sputum Gram Stain:** Identifies gram-positive diplococci in nonbacteremic cases.

Diagnostic Criteria:

- **Invasive Disease (IPD):** Positive blood culture OR CSF culture.
- **Nonbacteremic Pneumonia:** Clinical suspicion + positive urinary antigen OR PCR.

6.1 Diagnostic Steps

Stepwise approach for nonbacteremic pneumonia:

1. Clinical suspicion of infection → 2. Sputum Gram stain (identify gram-positive diplococci) → 3. Urinary antigen test (confirm if positive, sensitivity 60-70% in adults) → 4. PCR for rapid detection (>95%

sensitivity).

7. MANAGEMENT & TREATMENT

Antibiotic therapy and complication management:

1. **Adult Therapy:** Ceftriaxone 2g IV q24h OR Penicillin G 24 million units IV q4h.
2. **Pediatric Therapy:** Amoxicillin 90 mg/kg/day in divided doses.
3. **Severe Cases (MRSA risk):** Vancomycin 15-20 mg/kg IV q12h (Note: No clinical vancomycin resistance reported).
4. **Alternative Therapy:** Levofloxacin 750 mg PO q24h (for adults without contraindications).
5. **Meningitis Management:** Dexamethasone 0.15 mg/kg IV administered BEFORE antibiotic administration.
6. **Complication Management (Empyema):** Image-guided drainage preferred; surgical thoracotomy for loculated collections.

7.1 Antibiotic Regimens

Reference Table 151-2:

- **Adults (community-acquired):** Ceftriaxone 2g IV q24h (Duration: 5-7 days).
- **Children (<5 years):** Amoxicillin 90 mg/kg/day in 3 doses (Duration: 10 days).
- **Severe sepsis:** Vancomycin 15-20 mg/kg IV q12h (Until culture results).
- **Meningitis:** Ceftriaxone 2g IV q24h + dexamethasone 0.15 mg/kg IV (Duration: 14 days).

8. PROGNOSIS & COMPLICATIONS

Mortality and complications:

- **IPD Case Fatality:** 12% in elderly; 5-10% in children.
- **Focal Complications:**
  - Empyema: Most common focal complication, occurring in <5% of cases.
  - Meningitis: Occurs in 1-2% of cases; results in hearing loss in 20-30% of patients.
  - Septic shock: Occurs in 5-8% of cases.

9. SPECIAL CONSIDERATIONS

Vaccination and prevention:

- **Adults ≥65 years:** PCV13 + PPSV23.
- **High-risk children:** PCV13 at 2, 4, 6, 12-15 months with booster at 18 months.
- **Post-vaccine era:** Non-vaccine serotypes now cause 25-30% of IPD in some regions.

10. KEY PEARLS & CLINICAL TRAPS

Critical clinical pearls:

- **Elderly Presentation:** Often atypical (confusion, malaise) without fever or cough.

- **Urinary Antigen:** Sensitivity is limited in adults (<70%) and even lower in children.
- **Nonbacteremic Pneumonia:** Accounts for 80-90% of all pneumococcal cases.
- **Vancomycin:** No clinical resistance currently observed in pneumococcal strains.

REFERENCE TABLES

TABLE 151-1

Clinical Risk Groups for Pneumococcal Infection

CLINICAL RISK GROUP	EXAMPLES
Asplenia or splenic dysfunction	Sickle cell disease and other hemoglobinopathies, celiac disease
Chronic heart disease	Ischemic heart disease, congenital heart disease, hypertension with cardiac complications, chronic heart failure
Chronic liver disease	Cirrhosis, biliary atresia, chronic hepatitis
Immunocompromise/ immunosuppression	HIV infection, primary immunodeficiency (including B cell, T cell, complement, and some phagocytic disorders), leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chemotherapy, organ or bone marrow transplantation, systemic glucocorticoid treatment for >1 month at a dose equivalent to ≥20 mg/d (children, ≥1 mg/kg per day)
Cerebrospinal fluid leaks	…