Respiratory infections
Community acquired pneumonia: a review of common pathogens

Natalie Neu, MD

Respiratory tract anatomy
Community acquired pneumonia: CAP

- 5.6 million cases annually
- #1 cause of death due to infectious diseases in the U.S.
- $9.7 billion dollars annually
- 3 groups for patient management
  - Outpatient, inpatient (non-ICU), ICU
- Etiology:
  - *Streptococcus pneumoniae* (#1)
  - “Atypical organisms”
  - Viral (e.g. RSV, influenza, adenovirus)
  - Gram negative
  - Other

CAP: general principles

- Presentation
- Etiology
- Specific organisms and pneumonia
  - *Streptococcus pneumoniae*
  - Mycoplasma
  - Chlamydia
  - Legionella
  - Pertussis
Pneumonia: presentation and working up the etiology

- **Common complaints**
  - Dyspnea, fever, cough (productive or not), chills, chest pain, myalgia, headache
- **History**
  - Age, co-morbidities, sick contacts, unusual exposures, social situation/support
- **Physical exam findings**
  - Rales, tactile fremitus, decreased breath sounds, rhonchi
- **Radiology**
  - Confirming the diagnosis; may or may not help narrow the diagnosis e.g. *S. pneumoniae*: lobar; *S. aureus*: multilobar/abscess; Mycoplasma- diffuse interstitial

---

**Table 2: Microbiologic Pathogens in Community-Acquired Pneumonia.**

<table>
<thead>
<tr>
<th>Microbial Agent or Cause</th>
<th>Prevalence (%)</th>
<th>North American Sources*</th>
<th>British Sources†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumonia</em></td>
<td>20–60</td>
<td>60–75</td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>3–10</td>
<td>4–5</td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>3–5</td>
<td>1–5</td>
<td></td>
</tr>
<tr>
<td>Other non-penicillin</td>
<td>3–10</td>
<td>Rare</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>3–5</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Atypical agents</td>
<td>10–20</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Legionella</td>
<td>2–5</td>
<td>2–5</td>
<td></td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>1–6</td>
<td>5–18</td>
<td></td>
</tr>
<tr>
<td><em>Coxiella pneumoniae</em></td>
<td>4–5</td>
<td>8–16</td>
<td></td>
</tr>
<tr>
<td>Vicnae</td>
<td>2–15</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Aspiration</td>
<td>6–10</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

*Based on 15 published reports from North America. †Based on 14 published reports from Europe. **Includes respiratory pathogen group A streptococci, and *Mycoplasma pneumoniae*, which account for 1 to 2 percent of cases.

---

Clinical scenario 1

- Francisco is a 2 year previously well
- Presented with URI symptoms and fever to PMD in July
- Respiratory symptoms worsened, cxr revealed right sided pneumonia, WBC 24K with 80% PMN and 3% bands
- Initially treated with IV therapy without resolution in 4 days
- CT scan showed large right sided effusion
Complicated pneumonia with empyema
**Streptococcus pneumoniae**

- Gram-positive; oval or lancet-shaped, occur in pairs or short chains (diplococci)
- Capsular polysaccharide is most important virulence factor; approximately 85 capsular types
- Decreasing incidence but remains the **most commonly isolated pathogen** in patients with pneumonia
- Organism causes pneumonia, meningitis, otitis media, sinusitis, bacteremia, pericarditis, arthritis
Structure, Virulence Factors and Pathogenesis

- Capsular polysaccharide is most important virulence factor; approximately 85 capsular types
- Protein adhesins: allow binding to epithelial cells in the oropharynx
- Secretory IgA protease - inhibits function of secretory IgA which normally binds bacteria to mucin to facilitate clearance from the respiratory tract
- Pneumolysin - creates pores in and destroys ciliated epithelial cells
- Hydrogen peroxide - reactive O2 intermediate causes tissue damage
- Teichoic acid, peptidoglycan and pneumolysin activate complement

S. Pneumoniae
Diagnosis, treatment and prevention

- Diagnosis:
  - Blood culture, urine antigen test, sputum culture
- Treatment: Beta-lactam antibiotics
  - Risk factors resistance in Streptococcus pneumoniae
    - Age >65, receipt of β-lactam therapy within 3 months, alcoholism, immune suppression, multiple medical co-morbidities, exposure to child in daycare
    - PCN Resistance classified by breakpoints
      - Sensitive MIC ≤ 0.6
      - Intermediate MIC 0.1-1 mcg/ml
      - Resistant MIC ≥ 2 mcg/ml
  - Cephalosporins, vancomycin, macrolides, linezolid
- Prevention: Vaccines
  - Conjugated pneumococcal vaccine (Prevnar®)
  - 23 valent pneumococcal vaccine (Pneumovax®)
Clinical scenario 2

- Myra is a 21 year old medical student living in the dorm room studying for exams
- She goes to student health complaining of low grade fever, headache, non-productive cough, sore throat and general malaise
- Her exam reveals mild fine inspiratory rales—nothing impressive
- The Dr sends her for an xray that reveals bilateral infiltrates

Mycoplasma pneumonia
Mycoplasma

- Does not have a cell wall
- Cell membrane contains sterols not present in other bacteria
- Special enriched media needed for growth
- Laboratory cultures rarely done- diagnosis usually by serology (IgG)
- Bedside test- cold agglutinins

Mycoplasma- pathogenesis and immunity

- **P1**- protein attachment factor- facilitates attachment to sialic acid receptors of respiratory epithelium and RBC surface
- Remains extracellular
- Causes local destruction of cilia, interferes with normal airway clearance which leads to mechanical irritation and persistent cough
- Acts as a super antigen stimulating PNM’s and macrophages to release cytokines (TNFα, IL1, and IL 6)
Walking pneumonia

- Lacks seasonal pattern, spread by droplet secretions
- Common in children and young adults
- Mild respiratory symptoms
- Complications: otitis media, erythema multiforme, hemolytic anemia, myocarditis, pericarditis, neurologic abnormalities
- Treatment: erythromycin

Erythema multiforme
Clinical scenario 3

- JM 10 week old infant born to a 16 year old mom
- Pregnancy history limited due to lack of prenatal care but baby born full term, no complications, left hospital 2 days
- Seen by pediatrician at 2 weeks old with eye discharge was given eye drops
- Returned to ER: RR 60, cough but no fever
- Xray done and bloods drawn

Chlamydia trachomatis xray
Chlamydial pneumonias: *trachomatis, pneumoniae, psittaci*

- Intracellular parasites - use host high energy phosphate compounds
- Trilaminar outer membrane which contains LPS
- Two phase life cycle - Elementary body (infectious) and reticulate body (divides by binary fission in the host)

Chlamydial pneumonias

- Infect non-ciliated columnar cells
- Multiply in alveolar macrophages
- Perivascular and peribronchiolar infiltrates
- Clinical symptoms due to host immune response
- Immunity not long-lasting
- Diagnosis by serology - four fold rise in titer
**C. trachomatis pneumonia**

- Neonatal infection presents at 1-3 months of age
- Staccato-like cough, rapid respiratory rate
- NO FEVER
- Evaluation: minimal chest findings, xray hyperinflation and diffuse infiltrates, peripheral eosinophilia
- Associations: atherosclerotic heart disease
- Treatment: erythromycin
- Prevention: maternal screening

**C. pneumoniae**

- Single strain- TWAR
- Prolong incubation period
- Common in school age children
- Indolent course-sore throat, chronic cough, no fever
- Chest xray variable (lobar, diffuse, bilateral)
- Diagnosis: PCR and serology
- Treatment: macrolide, doxycycline, levofloxacin
C. psittaci

- **History:** Parrot exposure
- **Mild clinical respiratory symptoms, fever, rash**
- **Concomitant symptoms:** CNS-headache, confusion, cranial nerve palsy, seizures; hepatitis; pericarditis
- **X-ray:** consolidation, reticular nodular pattern, adenopathy
- **Titers:** > 1:64 diagnostic
- **Treatment:** doxy, tetracycline, erythromycin

Psittacosis
Clinical scenario 4

- Charlie is a 68 year old retired plumber who recently underwent a renal transplantation
- Felt great and was tinkering around his house updating his bathroom fixtures
- Came for follow up visit complaining of high fever, cough, chills and his wife said that he was acting confused at times
- Laboratory studies reveal WBC 35,000 with left shift, LDH >1000
- Chest xray reveals multilobar process
Legionella species

The 1976 Legionnaire’s Convention, Philadelphia, PA

- 29/180 patients died due to pneumonia
- Identification of a gram negative bacilli
- Epidemiologic link to being in the lobby of Hotel A; historical link to 1966 outbreak in a psychiatric hospital
- National panic- worries about biologic and chemical warfare- media frenzy
- 6 months to identify the organism
Legionella pneumophila and micdadei

- 2-6% community acquired pneumonias
- Risk: immunocompromised, hospitalized, and outbreak situations
- Gram negative bacilli- don’t stain with common reagents
- Fastidious and grow on supplemented media
- Organisms contaminate water sources: air conditioning systems and water tanks

Legionella: pathogenesis and immunity

- Intracellular pathogen- multiply in macrophages and monocytes
- Proteolytic enzymes kill the infected respiratory cells leading to formation of microabscesses
- Immunity- Cell mediated immunity (T cells) needed for immune response
Legionnaires disease

- Incubation period up to 10 days
- Clinical- influenza like illness or severe manifestation= pneumonia
- Fever (105), rigors, cough, headache
- Multilobular infiltrates and microabscesses
- Extrapulmonary manifestations: CNS, diarrhea, abdominal pain, nausea
- High white counts, abnormal liver, renal panel
- High mortality-15-20% depending on host

Legionella: Diagnosis, prevention and treatment

- Urine antigen detection assays- EIA for L.pneumophila only
- Serology >1:128 positive however late development of antibodies
- Culture on special media
- Treatment: macrolide or levofloxacin
- Prevention: hyperchlorination, super heating, continuous copper-silver ionization
Clinical scenario 5
(Loyola Univ Medical Center)

- Jerry, a 7 month old child, comes to clinic with a running nose, sneezing and slightly irritable
- Diagnosed with URI
- Returns 2 weeks later because he is turning blue with coughing spells. Spells are worse at night, seems to have spasms and then he “whoops” for air.
- Examination reveals mildly dehydrated, not distressed, clear lung exam
- WBC reveals leucocytosis with lymphocytosis

Bordetella pertussis
Bordetella pertussis
“Whooping cough”

- Fastidious, gram negative coccobacilli
- *Pertussis, parapertussis, and bronchiseptica*
- Spread by respiratory droplets
- Rapid multiplication in mucus membrane
- No bacteremia
- Toxins cause local tissue damage

Binding and uptake by phagocytic cells
Pertussis toxin

G protein and ADP ribosylation
Toxin production and pathophysiology

<table>
<thead>
<tr>
<th>Toxin Type</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pertussis toxin</td>
<td>Activate alternative complement, cytokine release</td>
</tr>
<tr>
<td>Heat-labile toxin</td>
<td>Local tissue destruction</td>
</tr>
<tr>
<td>Tracheal cytotoxin</td>
<td>Destroys ciliated cells, IL-1 (fever), NO (kills epithelial cells)</td>
</tr>
<tr>
<td>Adenylate cyclase and hemolysin toxin</td>
<td>Inhibit WBC chemotaxis, phagocytosis, and killing</td>
</tr>
<tr>
<td>Lipid A and Lipid X</td>
<td>1↑ secretions (paroxysmal stage)</td>
</tr>
<tr>
<td></td>
<td>1↑ secretions (paroxysmal stage)</td>
</tr>
</tbody>
</table>

Pertussis clinical symptoms
Pertussis

- Incidence declined due to vaccine
- Affects children under 1 and adults with waning immunity
- Incubation period 7-10 days
- Three stages of disease: catarrhal, paroxysmal, convalescent
- Diagnosis: special media- Bordet-Gengou- blood, charcoal, and starch. Nasopharyngeal culture
- Serologic testing: acute and convalescent titers
Figure 2. Percent distribution of patients hospitalized for respiratory diseases: United States, 2003

Figure 1. First-listed diagnostic categories with a million or more hospital discharges, with average length of stay: United States, 2003