Respiratory infections
Community acquired pneumonia:
a review of common pathogens
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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 (NI)
  - “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
  - Oxygen saturation
  - Rales, tactile fremitus, decreased breath sounds, rhonchi
- Radiology
  - Confirming the diagnosis; may or may not help narrow the diagnosis e.g. S. pneumonia: lobar; S. aureus: multilobar/abscess; Mycoplasma: diffuse interstitial


Table 2: Microbiologic Pathogens in Community-Acquired Pneumonia

<table>
<thead>
<tr>
<th>Microbiologic Pathogen</th>
<th>Percentage (%)</th>
<th>Presence of Lobar Infiltrates</th>
<th>Presence of Multilobar Infiltrates</th>
<th>Presence of Abscess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumonia</td>
<td>25-50</td>
<td>40-75</td>
<td>0-15</td>
<td>0-15</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>10-30</td>
<td>40-75</td>
<td>0-15</td>
<td>0-15</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>10-30</td>
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</tr>
<tr>
<td>Legionella pneumoniae</td>
<td>5-15</td>
<td>40-75</td>
<td>0-15</td>
<td>0-15</td>
</tr>
<tr>
<td>Viruses</td>
<td>10-15</td>
<td>40-75</td>
<td>0-15</td>
<td>0-15</td>
</tr>
</tbody>
</table>

*Data from the study by Bartlett et al.*
Clinical scenario 1

- Francisco is a 2 year old, 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

Microbial causes of CAP in childhood

<table>
<thead>
<tr>
<th>Age</th>
<th>Organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 3 weeks</td>
<td>Group B Streptococcal, Gram negative enteric bacilli, Cytomegalovirus, Listeria monocytogenes, HSV</td>
</tr>
<tr>
<td>3 weeks - 3 months</td>
<td>Chlamydia trachomatis, Respiratory syncyial virus (RSV), Parainfluenza virus type 3 (PIV), Streptococcus pneumoniae, Bordetella pertussis, Staphylococcus aureus</td>
</tr>
<tr>
<td>3 months - 5 years</td>
<td>RSV, PIV, influenza, adenovirus, thymivirus, Streptococcus pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>5-15 years</td>
<td>Mycoplasma pneumoniae, Chlamydia pneumoniae, Streptococcus pneumoniae, Mycobacterium tuberculosis</td>
</tr>
</tbody>
</table>

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 PMS’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. 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
- Xray - consolidation, reticular nodular pattern, adenopathy
- Titors: > 1:64 diagnostic
- Treatment: doxy, tetracycline, erythromycin

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

Psittacosis

- 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
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

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 species

- 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

Bordetella pertussis

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

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

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

Binding and uptake by phagocytic cells
**Pertussis toxin**

- Activate alternative complement, cytokine release

**Pertussis clinical symptoms**

- Incubation period 7-10 days
- Three stages of disease: catarhal, paroxysmal, convalescent
- Diagnosis: special media- Bordet-Gengou- blood, charcoal, and starch. Nasopharyngeal culture
- Serologic testing: acute and convalescent titers

**G protein and ADP ribosylation**

**Toxin production and pathophysiology**

<table>
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<tr>
<th>Toxin Type</th>
<th>Effect</th>
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<tr>
<td>Pertussis toxin-↑CAMP</td>
<td>↑ secretions (paroxysmal stage)</td>
</tr>
<tr>
<td>Adenylate cyclase and hemolysin toxin</td>
<td>Inhibit WBC chemotaxis, phagocytosis, and killing</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>Lipid A and Lipid X</td>
<td>Activate alternative complement, cytokine release</td>
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- Incidence declined due to vaccine
- Affects children under 1 and adults with waning immunity
- New recommendations for booster vaccine for children 11-18 years of age
- Incubation period 7-10 days
- Three stages of disease: catarhal, paroxysmal, convalescent
- Diagnosis: special media- Bordet-Gengou- blood, charcoal, and starch. Nasopharyngeal culture
- Serologic testing: acute and convalescent titers
Figure 3. Percent distribution of patients hospitalized for respiratory diseases: United States, 2003

CAP guidelines: Implementing CAP guidelines locally

Table 2. Elements important for local community-acquired pneumonia guidelines.

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<tr>
<td>Antibiotic resistance</td>
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<td>Antimicrobial resistance assessment (level 1 evidence)</td>
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<td>Antimicrobial resistance assessment (level 2 evidence)</td>
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<td>Patient management</td>
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<td>Early mobilization</td>
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<td>Discharge follow-up</td>
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<td>Discharge support</td>
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CID 2007:44

Treatment recommendations for CAP

1. Patient management
   - Admission decision
   - Antimicrobial selection
   - Antibiotic resistance assessment
   - Antimicrobial resistance assessment (level 1 evidence)
   - Antimicrobial resistance assessment (level 2 evidence)
   - Patient management
   - Early mobilization
   - Discharge follow-up
   - Discharge support

2. Early mobilization
   - Administration of antibiotics
   - Early mobilization
   - Discharge follow-up

3. Discharge support
   - Discharge follow-up
   - Discharge support

4. Discharge support
   - Discharge support

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