Respiratory infections
Atypical pathogens in community acquired pneumonia and Whooping cough

Natalie Neu, MD

Community acquired pneumonia (CAP) and Atypical pathogens

- CAP-<50% of cases have identifiable cause
- Atypical- differ from classic symptoms of pneumococcal pneumonia and clinical picture different, more indolent, longer duration and may involve upper and lower respiratory tract
- Atypicals usually don’t respond to penicillin

Clinical scenario 1

- 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

- 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 multiformes, hemolytic anemia, myocarditis, pericarditis, neurologic abnormalities
- Treatment: erythromycin

Erythema multiforme

Clinical scenario 2

- 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

Chlamydia pneumonia

- Infect non-ciliated columnar cells
- Multiply in alveolar macrophages
- Perivascular and peribronchial 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
- Xray-consolidation, reticular nodular pattern, adenopathy
- Titors: > 1:64 diagnostic
- Treatment: doxy, tetracycline, erythromycin

**Clinical scenario 3**

- 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 4 (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**

**“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**

**Toxin production and disease manifestation**

**G protein and ADP ribosylation**
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

Toxins and pathogenesis

<table>
<thead>
<tr>
<th>Toxin/Pathogenesis</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pertussis toxin- increased CAMP</td>
<td>Increased resp secretions and mucus (paroxysmal stage)</td>
</tr>
<tr>
<td>Adenylate cyclase and hemolysin toxin</td>
<td>Inhibit leukocyte 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 epith 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>
</tr>
</tbody>
</table>

Pertussis clinical symptoms

- 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

Toxins and pathogenesis

<table>
<thead>
<tr>
<th>Toxin/Pathogenesis</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pertussis toxin- increased CAMP</td>
<td>Increased resp secretions and mucus (paroxysmal stage)</td>
</tr>
<tr>
<td>Adenylate cyclase and hemolysin toxin</td>
<td>Inhibit leukocyte 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 epith 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>
</tr>
</tbody>
</table>

Pertussis clinical symptoms

- 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