

## Respiratory infections

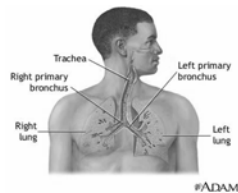
### Community acquired pneumonia: a review of common pathogens

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## CAP: general principles

- Presentation
- Etiology
- Specific organisms and pneumonia
  - *Streptococcus pneumoniae*
  - Mycoplasma
  - Chlamydia
  - Legionella
  - Pertussis

## Respiratory tract anatomy



## 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

## 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

### Bartlett, J. G. et al. N Engl J Med 1995;333:1618-1624

Table 2. Microbiologic Pathogens in Community-Acquired Pneumonia.

Microbial Agent or Cause	Prevalence (%)	
	North American Studies*	British Thoracic Society†
Bacteria		
<i>Streptococcus pneumoniae</i>	20–60	60–75
<i>Haemophilus influenzae</i>	3–10	4–5
<i>Staphylococcus aureus</i>	3–5	1–5
Gram-negative bacilli	3–10	Rare
Miscellaneous	3–5	—
Atypical agents	10–20	—
Legionella	2–8	2–5
<i>Mycoplasma pneumoniae</i>	1–6	5–18
<i>Chlamydia pneumoniae</i>	4–6	—
Viruses	2–15	8–16
Aspiration	6–10	—

\*Based on 15 published reports from North America.<sup>1-15</sup> None of these studies used techniques adequate to detect anaerobes in respiratory secretions; these organisms account for 20 to 30 percent of cases in some reports.<sup>10</sup> *P. carinii* is excluded but may account for up to 15 percent in recent reports from urban centers.<sup>16</sup>

†Based on an analysis of 453 adults in a prospective study of community-acquired pneumonia in 25 British hospitals.<sup>16,17</sup> Dashes indicate that the pathogen was not included in the study. Includes *Moraxella osloensis*, group A streptococci, and *Moraxella meningitidis* (each accounting for 1 to 2 percent of cases).

IDSA guidelines for adult CAP. CID 2000; 31 (Aug).

**Table 7.** Epidemiological conditions related to specific pathogens in patients with selected community-acquired pneumonia.

Condition	Commonly encountered pathogen(s)
Alcoholism	<i>Streptococcus pneumoniae</i> and anaerobes
COPD and/or smoking	<i>S. pneumoniae</i> , <i>Haemophilus influenzae</i> , <i>Moraxella catarrhalis</i> , and <i>Legionella</i> species
Nursing home residency	<i>S. pneumoniae</i> , gram-negative bacilli, <i>H. influenzae</i> , <i>Staphylococcus aureus</i> , anaerobes, and <i>Chlamydia pneumoniae</i>
Poor dental hygiene	Anaerobes
Epidemic legionnaires' disease	<i>Legionella</i> species
Exposure to bats or soil enriched with bird droppings	<i>Histoplasma capsulatum</i>
Exposure to birds	<i>Chlamydia psittaci</i>
Exposure to rabbits	<i>Francisella tularensis</i>
HIV infection (early stage)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , and <i>Mycobacterium tuberculosis</i>
HIV infection (late stage)	Above plus <i>P. carinii</i> , <i>Cryptococcus</i> , and <i>Histoplasma</i> species
Travel to southwestern US	<i>Coccidioides</i> species
Exposure to farm animals or parturient cats	<i>Coxiella burnetii</i> (Q fever)
Influenza active in community	Influenza, <i>S. pneumoniae</i> , <i>S. aureus</i> , <i>Streptococcus pyogenes</i> , and <i>H. influenzae</i>
Suspected large-volume aspiration	Anaerobes (chemical pneumonitis, obstruction)
Structural disease of lung (bronchiectasis, cystic fibrosis, etc.)	<i>Pseudomonas aeruginosa</i> , <i>Burkholderia</i> ( <i>Pseudomonas</i> ) <i>cepacia</i> , and <i>S. aureus</i>
Injection drug use	<i>S. aureus</i> , anaerobes, <i>M. tuberculosis</i> , and <i>S. pneumoniae</i>
Airway obstruction	Anaerobes, <i>S. pneumoniae</i> , <i>H. influenzae</i> , and <i>S. aureus</i>

NOTE. COPD, chronic obstructive pulmonary disease.

Complicated pneumonia with empyema

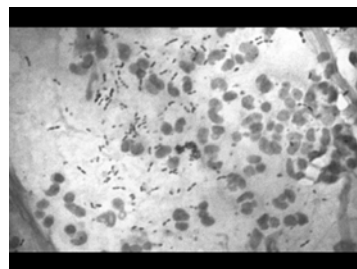


Clinical scenario 1

- 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

*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

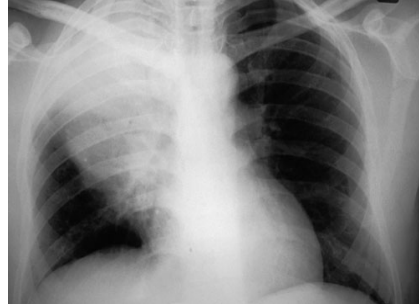


## Structure, Virulence Factors and Pathogenesis

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- 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 O<sub>2</sub> intermediate causes tissue damage
- Teichoic acid, peptidoglycan and pneumolysin activate complement

## Mycoplasma pneumoniae



## *S. Pneumoniae* Diagnosis, treatment and prevention

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

## Mycoplasma

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- 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

## Clinical scenario 2

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- 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- pathogenesis and immunity

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- 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 (TNF $\alpha$ , IL1, and IL 6)

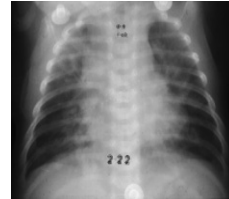
## Walking pneumonia

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- 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

## *Chlamydia trachomatis* xray

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## Erythema multiforme

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## Chlamydial pneumonias: *trachomatis, pneumoniae, psittaci*

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- 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)

## Clinical scenario 3

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- 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

## Chlamydial pneumonias

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- 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

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- 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



### *C. pneumoniae*

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- 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

### Clinical scenario 4

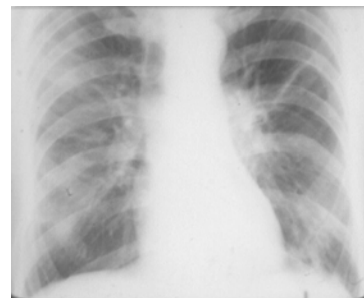
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- Charlie is a 68 year old retired plumber who recently underwent a renal transplantation
- Felt great and was tinkering around his house updating his bathroom fixtures
- Came for follow up visit complaining of high fever, cough, chills and his wife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

### *C. psittaci*

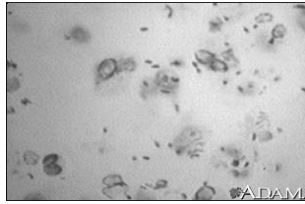
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- History: Parrot exposure
- Mild clinical respiratory symptoms, fever, rash
- Concomitant symptoms: cns- headache, confusion, cranial nerve palsy, seizures; hepatitis; pericarditis
- Xray-consolidation, reticular nodular pattern, adenopathy
- Titers: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



## Legionella species

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## Legionella: pathogenesis and immunity

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- 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

## The 1976 Legionnaire's Convention, Philadelphia, PA

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- 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

## Legionnaires disease

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- 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 pneumophila and micdadei*

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- 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: Diagnosis, prevention and treatment

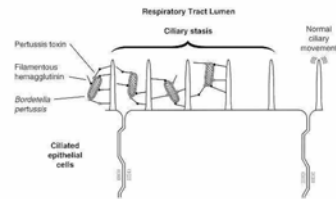
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- Urine antigen detection assays- EIA for *L.pneumophila* only
- Serology >1:128 positive however late development of antibodies
- Culture on special media
- Treatment: macrolide or levofloxacin
- Prevention: hyperchlorination, super heating, continuous copper-silver ionization

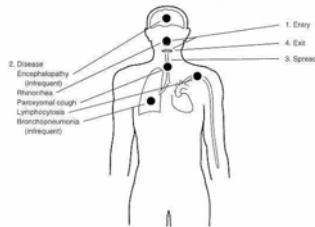
## Clinical scenario 5 (Loyola Univ Medical Center)

- 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

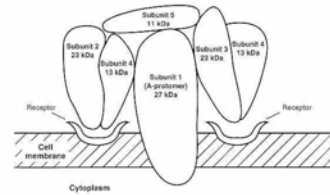
## Binding and uptake by phagocytic cells



## *Bordetella pertussis*



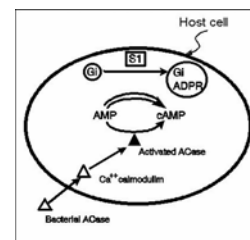
## Pertussis toxin



## *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

## G protein and ADP ribosylation



### Toxin production and pathophysiology

Pertussis toxin- ↑ CAMP	↑ secretions (paroxysmal stage)	
Adenylate cyclase and hemolysin toxin	Inhibit WBC chemotaxis, phagocytosis, and killing	
Heat-labile toxin	Local tissue destruction	
Tracheal cytotoxin	Destroys ciliated cells, IL-1 (fever), NO (kills epithelial cells)	
Lipid A and Lipid X	Activate alternative complement, cytokine release	

- ### 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

