PNEUMONIA

DEFINITION

✓ It is acute inflammation of the lung parenchyma. The cause may be infectious or non infectious.
✓ It may be acquired in the community or in the hospital.
✓ Pneumonia affects 450 million/yr, 7% of population and result in 4 million deaths.

Community Acquired Pneumonia (CAP)
- an acute infection of the lung parenchyma
- associated with at least some symptoms of acute infection
- accompanied by the presence of an acute infiltrate on a chest radiograph
- or auscultatory findings consistent with pneumonia, in a patient not hospitalized or residing in a long term care facility for ≥14 days before onset of symptoms.

HAP is a pneumonia that occurs ≥ 48 hrs after hospital admission.

VAP is a pneumonia that occurs ≥ 48 - 72hrs after tracheal intubation.

HCAP is a pneumonia that occurs in any patient who was:
- hospitalized in an acute care hospital for 2 or more days within 90 days of infection,
- received recent IV antibiotics therapy, chemotherapy, or wound care within the last 30 days of the current infection
- or attended a hospital or hemodialysis clinic.

PATHOGENESIS

Inhalation, aspiration and hematogenous spread are the 3 main mechanisms by which bacteria reaches the lungs.

Other
- Inoculation
- Colonization
- Direct spread

Primary inhalation
- when organisms bypass normal respiratory defense mechanisms
- or when the Pt inhales aerobic GN organisms that colonize the URT/ respiratory support equipment

Aspiration
- occurs when the Pt aspirates colonized upper respiratory tract secretions

Stomach:
- reservoir of GNR that can ascend, colonizing the respiratory tract.

Hematogenous
- originate from a distant source & reach the lungs via the blood stream.

PATHOLOGY

<table>
<thead>
<tr>
<th>Initial Phase</th>
<th>Second Stage</th>
<th>Third Phase</th>
<th>Final Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage Of Congestion</td>
<td>Red Hepatization</td>
<td>Gray Hepatization</td>
<td>Resolution</td>
</tr>
<tr>
<td>proteinaceous exudate often of bacteria in the alveoli</td>
<td>Erythrocytes in the cellular intraalveolar exudate neutrophils are also present</td>
<td>no new erythrocytes are extravasating those already present have been lysed and degraded</td>
<td>- macrophage is the dominant cell type in the alveolar space</td>
</tr>
<tr>
<td>This phase is rarely evident in clinical or autopsy specimens because it is so rapidly followed by a red hepatization</td>
<td>Important from the standpoint of host defense Bacteria are occasionally seen in cultures of alveolar specimens</td>
<td>Neutrophil: predominant cell. Fibrin deposition is abundant. Bacteria disappeared</td>
<td>- the debris of neutrophils, bacteria, and fibrin has been cleared, as has the inflammatory response</td>
</tr>
<tr>
<td></td>
<td></td>
<td>This phase is successful containment of the infection &amp; improvement in gas exchange</td>
<td></td>
</tr>
</tbody>
</table>

† macrophage is the dominant cell type in the alveolar space
† the debris of neutrophils, bacteria, and fibrin has been cleared, as has the inflammatory response

CAP – CLASSIFICATION

<table>
<thead>
<tr>
<th>Anatomical</th>
<th>Etiological</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobar</td>
<td>Infective, and non infective</td>
<td>Typical and atypical CAP and HAP</td>
</tr>
<tr>
<td>Bronchopneumonia Interstitial</td>
<td></td>
<td>Pneumonia in Immunocompromized</td>
</tr>
</tbody>
</table>
INFECTIONOUS CAUSES OF CAP

Pneumonia is due to infections caused primarily by **bacteria** or **viruses** and less commonly by **fungi** and **parasites**.

<table>
<thead>
<tr>
<th>Typical</th>
<th>Atypical</th>
<th>Other</th>
<th>Viral</th>
<th>Fungal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumonia 35%</td>
<td>Mycoplasma pneumoniae</td>
<td>An aerobic organisms</td>
<td>Influenza</td>
<td>Aspergillus</td>
</tr>
<tr>
<td>Staph aureus pneumonia</td>
<td>Chlamydophila pneumoniae</td>
<td>TB pneumonia</td>
<td>Parainfluenza pneumonia</td>
<td>Histoplasmosis</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>Legionella pneumophila</td>
<td></td>
<td>Measles</td>
<td>Candidiasis</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>Coxiella burnetii</td>
<td></td>
<td>Adenoviruses</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td></td>
<td></td>
<td>Corona viruses</td>
<td>Parasitic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Toxoplasma</td>
</tr>
</tbody>
</table>

**Clinical Presentation**

- **Lung physical exam**
  - Sensitivity 47-69%; Specificity 58-75%
  - Acute cough (>90%)
  - Fevers/chills (80%)
  - Sputum production (66%)
  - Dyspnea (66%)
  - Pleuritic chest pain (50%)
  - Tachypnea (RR > 24)
  - Egophony
  - Bronchial breath sounds
  - Percussion dullness
  - Diminished breath sounds

**Laboratory Tests**

- CXR / CT
- CBC with differential
- BUN/Cr
- Glucose
- Liver enzymes
- Electrolytes
- Gram stain/culture of sputum
- Pre-treatment blood cultures
- Oxygen saturation

**Diagnostic Evaluation**

- CXR: usually needed to establish diagnosis
- Prognostic indicator
- Rule out other disorders
- May help in etiological diagnosis

**Diagnostic: Cultures**

- Pre-abx Blood Cultures
  - Yield 5-15%
  - Stronger indication for severe CAP
  - Host factors: cirrhosis, asplenia, complement deficiencies, leukopenia
- Pre-abx expectorated sputum Gs & Cx
  - Yield can be variable
  - Depends on multiple factors: specimen collection, transport, speed of processing, use of cytologic criteria
  - Adequate sample w/ predominant morphotype seen in only 14% of 1669 hospitalized CAP pts (Garcia-Vasquez, Arch Intern Med 2004)
- Pre-abx endotracheal aspirate Gs & Cx
- Pleural effusions >5 cm on lateral upright CXR

**Risk Factors for Multidrug Resistance (MDR)**

1. Antibiotics in the past 90 days
2. High frequency of antibiotic resistance in community
3. Immunosuppressive disease or medications
4. HCAP Risk Factors:
   - Hospitalization for at least 2 days in the past 90 days
   - Residence in a SNF
   - Home infusion therapy
   - Dialysis within 30 days
   - Family member with MDR infection

**To Admit or Not?**

**Pneumonia Severity & Deciding Site of Care**

- Using objective criteria to risk stratify & assist in decision re outpatient vs inpatient management
- CURB-65
- PSI
- Caveats
  - Other reasons to admit apart from risk of death
  - Not validated for ward vs ICU
  - Labs/vitals dynamic

**Applying the CURB-65 Rule**

- Group 1: Mortality low (1.5%)
  - (n = 324, died = 3)
- Group 2: Mortality intermediate (0.3%)
  - (n = 184, died = 17)
- Group 3: Mortality high (72%)
  - (n = 216, died = 47)
- Group 4: Mortality very high (100%)
  - (n = 213, died = 213)

**Treatment Options**

- Likely suitable for home treatment
- Consider hospital-supervised treatment
- Options may include: respiratory therapies, hospice, palliative care, outpatient

**Managing in hospital as severe pneumonia**

- Assess for ICU admission: especially if CURB-65 score > 4 of 5

**DBP = diastolic blood pressure**

### Criteria for Severe CAP (Admit to ICU)

<table>
<thead>
<tr>
<th>Minor criteria</th>
<th>Major criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Respiratory rate ≥30 breaths/min</td>
<td>6. Leukopenia (WBC &lt;4000 cells/mm³)</td>
</tr>
<tr>
<td>2. PaO2/FiO2 ratio ≥ 250</td>
<td>7. Thrombocytopenia (platelets &lt;100,000 cells/mm³)</td>
</tr>
<tr>
<td>3. Multilobar infiltrates</td>
<td>• Invasive mechanical ventilation</td>
</tr>
<tr>
<td>4. Confusion/disorientation</td>
<td>• Septic shock with the need for vasopressors</td>
</tr>
<tr>
<td>5. Uremia (BUN ≥20 mg/dL)</td>
<td>8. Hypothermia (core T &lt;36°C)</td>
</tr>
<tr>
<td>9. Hypotension requiring aggressive fluid resuscitation</td>
<td></td>
</tr>
</tbody>
</table>

### Management

1. Rational use of microbiology laboratory
2. Pathogen directed antimicrobial therapy whenever possible
3. Prompt initiation of therapy
4. Decision to hospitalize based on prognostic criteria

- **American Thoracic Society (ATS)**
  - Guidelines - Management of Adults with CAP (2001)
- **Infectious Diseases Society of America (IDSA)**
- **ATS and IDSA joint effort (we will follow this)**
  - IDSA/ATS Consensus Guidelines on the Management of CAP in Adults (March 2007)

### Group 1

- <60 years & Healthy
- no risk factors for DR *S.pneumoniae*
- Macrolide or Doxycycline

### Group 2

- >65 yrs & Presence of co-morbidities
- use of antimicrobials within prev 3 mths
- regions with a high rate (>25%) of infection with Macrolide resistant *S. pneumoniae*
- Respiratory FQ – Levofox, Gemifloxacin or Moxiflox
- 1. Beta-lactam (High dose Amoxicillin, Amoxicillin- Clavulanate is preferred; Ceftriaxone, Cefodoxime, Cefuroxime)
- plus
- Macrolide / Doxycycline

### Group 3

- hospitalization
- Not severely ill
  - (i.e., medical word)
- Respiratory Fluoroquinolone (FQ) Levo. 750 mg/day, Moxi. 400 mg, Gemiflox. Or IV Beta-lactam plus a Macrolide (or Doxycycline)
- (Here Beta-lactam agents are 3 Generation: Cefotaxime, Ceftriaxone, or ampicillin-sulbactam or aztereonam if pseudomonas suspected)

### Group 4

- severely ill, ICU treatment
- No Rs Double drugs (piperacillin-tazobactam, cefepime, imipenem, or meropenem ) plus a fluoroquinolone (levofoxacin, or ciprofoxacin= level one evidence or azithromycin level 2 evidence)
- With Rs (for pseudomonas infection) Triple (A ps. (piperacillin-tazobactam, cefepime, imipenem, or meropenem ), aminoglycoside plus a M or Q(cipro. or levofoxacin)
- 3. For CA-MRSA Add (vancomycin or targocid)

### (Walking Pneumonia) Called Mycoplasma Atypical pneumonia

<table>
<thead>
<tr>
<th>Definition</th>
<th>Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>a mildest form of pneumonia.</td>
<td>• Fever, muscle aches, headaches</td>
<td>– Antibiotic course lasts up to 2 weeks</td>
</tr>
<tr>
<td>• Contagious disease</td>
<td>• Running nose and cold</td>
<td>– Macrolides or Quinolones</td>
</tr>
<tr>
<td>• Caused by mycopl., Legionella, and even Chlamydia.</td>
<td>• Sudden chills</td>
<td>– Antipyretic and hydration</td>
</tr>
<tr>
<td>• Affect 2 million / year in USA</td>
<td>• Sore throat developed by constant cough</td>
<td></td>
</tr>
<tr>
<td>• Common in school-going children and below 40 yrs</td>
<td>• May experience low and rapid breathing at times</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Severe pain in ears, eyes, chest and abdominal muscles</td>
<td></td>
</tr>
</tbody>
</table>

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Thugs
### Influenza pneumonia Treatment

First-line Tx is neuraminidase inhibitors for both influenza A and B:
- **Oseltamivir** 75-150* mg PO BID x 5+ days
- **Zanamavir** 10 mg INH BID x 5+ days

*NOTE:* influenza A resistant to adamantanes (amantadine, rimantadine)

* There is limited data in support of double dosing. But we do it anyway.

### Antiviral Therapy for Influenza

Should be started ASAP in:
- Anyone hospitalized with suspected or confirmed influenza
- Anyone with severe, complicated or progressive respiratory illness
- Anyone at higher risk of complications from influenza

### Individuals at Higher Risk for Influenza Complications

- Extremes of age: children <2, adults ≥65 years
- Comorbid conditions:
  - Chronic pulmonary
  - Cardiovascular (except HTN alone)
  - Renal, hepatic, hematologic, metabolic (DM)
  - Neurologic, neuromuscular (cerebral palsy, epilepsy, CVA, SCI)
- Immunosuppression (caused by meds, HIV infection)
- Pregnant or post-partum (<2 wks) women
- Persons <19 years on long-term aspirin
- American Indians & Alaskan Natives
- Morbidly obese (BMI ≥40)
- Residents in NH or chronic-care facilities

### Follow-up Response, Expected improvement?

- Clinical improvement w/ effective abx: 48-72 hrs
- Fever can last 2-5 days with Pneumococcus, longer with other etiologies, esp Staph aureus
- CXR clearing
  - If healthy & <50 yo, 60% have clear CXR x 4 wks
  - If older, COPD, bacteremic, alcoholic, etc. only 25% with clear CXR x 4 wks
- Switch from IV to PO
  - Hemodynamically stable, improving clinically
  - Able to ingest meds with working GI tract

### HAP Treatment Guideline

* Guideline was published in 1996 by American thoracic society and separated patients into three groups, each with a set of probable pathogens.
* Group 1: mild to moderate HAP with no risk factor
* Group 2: mild to moderate HAP with risk factor
* Group 3a: severe HAP, early-onset with no risk factor
* Group 3b: severe HAP, late-onset or with risk factor

#### Group 1 & 3A

<table>
<thead>
<tr>
<th>Core Pathogens</th>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Aminoglycoside or ciprofloxacin plus 1 of the following:  Antipseudomonal penicillin or antipseudomonal β-lactam/β-lactamase inhibitor combination</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>Cefepime, ceftazidime or cefepime plus metronidazole</td>
</tr>
<tr>
<td>MRSA</td>
<td>Vancomycin if MRSA suspected</td>
</tr>
</tbody>
</table>

#### Group 2

<table>
<thead>
<tr>
<th>Core Pathogens</th>
<th>Core Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive cocci</td>
<td>Cephalexin</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>Second-generation or nonpsuedonomal third-generation β-lactam/β-lactamase combination</td>
</tr>
<tr>
<td>Methicillin-susceptible S. aureus</td>
<td>If allergic to penicillin: Fluoroquinolone or clindamycin + aztreonam</td>
</tr>
<tr>
<td>Gram-negative bacilli (non-Pseudomonas)</td>
<td>Enteobacter</td>
</tr>
<tr>
<td>E. coli</td>
<td>Klebsiella</td>
</tr>
<tr>
<td>Proteus</td>
<td>Serratia marcescens</td>
</tr>
<tr>
<td>H. influenzae</td>
<td></td>
</tr>
</tbody>
</table>


#### Group 3B

<table>
<thead>
<tr>
<th>Core Pathogens</th>
<th>Core Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaerobes (recent abdominal surgery, witnessed aspiration)</td>
<td>Clindamycin or β-lactam/β-lactamase inhibitor combination (alone)</td>
</tr>
<tr>
<td>Staphylococcus aureus (coma, head trauma, diabetes mellitus, renal failure)</td>
<td>Vancomycin (until MRSA ruled out)</td>
</tr>
<tr>
<td>Legionella (high-dose steroids)</td>
<td>Erythromycin ± rifampin</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa (prolonged ICU stay, steroids, antibiotics, structural lung disease)</td>
<td>See Table 3</td>
</tr>
</tbody>
</table>

Reducing ventilator-associated pneumonia in ICU

- Ventilation-associated pneumonia
- > 48 h after intubation
- HAP = hospital acquired pneumonia
  > 48 h after hospital admission

What we do know about VAP:
- A common and severe complication of mechanical ventilation
- Increases mortality, morbidity and costs

Pathogenes

<table>
<thead>
<tr>
<th>Early VAP</th>
<th>Late VAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aereus</td>
<td>Pseudomonas</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>Klebsiella</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>Acinetobacter</td>
</tr>
<tr>
<td></td>
<td>Stenotrophomonas</td>
</tr>
</tbody>
</table>

Treatment

- Broadspectrum antibiotics
- Multiresistance