Pneumonia Mimics

Jim Allen, MD,
Professor of Internal Medicine
Division of Pulmonary & Critical Care Medicine
Ohio State University Medical Center

Causes of Community-Acquired Pneumonia in Outpatients

<table>
<thead>
<tr>
<th>Cause</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. pneumonia</td>
<td>50%</td>
</tr>
<tr>
<td>V. parahaemolyticus</td>
<td>10%</td>
</tr>
<tr>
<td>S. pneumonia</td>
<td>10%</td>
</tr>
<tr>
<td>C. pneumonia</td>
<td>15%</td>
</tr>
<tr>
<td>Legionella</td>
<td>5%</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>5%</td>
</tr>
<tr>
<td>Unknown</td>
<td>5%</td>
</tr>
</tbody>
</table>
**July**  
Case #1  
- 87 year old woman with community-acquired pneumonia  
- Improves partially with empiric antibiotics

**October**  
Case #1  
- Re-admitted with recurrent pneumonia  
- No improvement with empiric antibiotics  
- Undergoes BAL; cultures all negative

**August**  
Case #1  
- Re-admitted with recurrent pneumonia  
- Improves partially with empiric antibiotics

**October**  
Case #1  
- After 4 admissions to the hospital, transferred for long-term antibiotics
November

- After 3 weeks, BAL now growing acid fast bacteria
- After 4 weeks, identified as M. tuberculosis
- Infection control nightmare begins

Case #1

TB Case Rates,* United States, 2009

- ≤ 3.5 (year 2000 target)
- 3.6–3.8
- > 3.8 (national average)

*Cases per 100,000.

Reported TB Cases*, United States, 1982–2009

*Updated as of July 1, 2010.

Percentage of TB Cases Among Foreign-born Persons, United States*

*Updated as of July 1, 2010.
### Tuberculosis in 2011

- “Shoot first, ask questions later”
- Respiratory isolation *when TB suspected*
- 4 drug treatment
- Always check drug sensitivities

### History

**Case #2**

- 80 year old man admitted with hypoglycemia and status epilepticus
- Persistent anoxic encephalopathy and respiratory failure
- Transferred for ventilator weaning after 6 days in ICU

### The moral of the story: Don’t get bit by red snappers

- After 4 weeks:
  - Still ventilator dependent
  - Daily fevers to 102 F despite 1 week of empiric antibiotics
  - Blood eosinophil count 570
  - BAL: 11% eosinophils; no pathogens
### Case #2

**Diagnosis: phenytoin-induced lung disease**

- Antibiotics stopped
- Phenytoin stopped
- Short course corticosteroids
- Fever & pulmonary infiltrates resolved
- Respiratory failure resolved and weaned off of the ventilator

### Common Drugs:

- Phenytoin
- Macrodantin
- Amiodarone
- Minocycline
- Methotrexate
- Bleomycin
- Sulfasalazine
- Cocaine
- ACE inhibitors (cough)
- Sulfasalazine

### Drug-induced lung disease:

- Can be very easy to miss
- Clues:
  - Peripheral pulmonary infiltrates
  - Blood eosinophilia (>350/cmm)
  - BAL eosinophilia
  - Skin rash
- Diagnosis of exclusion

### Mesalamine (Asacol)

- [Image of mesalamine (Asacol) with CT scan]
Drug-induced lung disease may be very difficult to confirm.
Re-challenge is risky.
www.pneumotox.com is a great resource.
Doctors cause more disease than we realize.

Case #3
- 79 year old man
- Cough and dyspnea onset in November 2009
- Hospitalized with pneumonia in February 2010 and treated with empiric antibiotics
- Improved but not back to normal when seen in April 2010

The morals of the story:
- Former smoker
- Landscaper
- Exam: crackles in the lower left lung
- Labs: eosinophil count = 460
- Not taking any candidate drugs for drug-induced lung disease
Case #3

Anti-strongyloides antibody positive

After treatment with ivermectin
**Strongyloides**

- Lives in the intestine
- Once infected, always infected
- Corticosteroids are worm fertilizer
- Serology is the best diagnostic test

**Strongyloides is sneaky**

- 87 year old mother of OSU physician
- Recurrent “colitis”, eosinophilia, pulmonary infiltrates and cough for 20 years
- Positive anti-strongyloides antibody
- Symptoms resolved with ivermectin

**You’ll miss it if you only order the regular stool O&P exam**

- 35 YO CM with tuberous sclerosis and severe mental retardation
- Recurrent fevers & pseudomonas pneumonia
- Persistent fevers and blood eosinophilia (up to 2,700/mcL)
- Stool O&P negative (antigenic)
**The morals of the story:**

- Worms are everywhere
- Non-resolving pneumonia + peripheral eosinophilia = order a strongyloides antibody titer

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**History (cont)**

**Case #4**

- PMH – no illnesses
- Sx – architectural designer; 100 PY smoker; son is a radiology resident
- ROS – all negative
- Moist crackles RLL posterior; no egophony

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**History**

**Case #4**

- 64 yr old man exposed to black dust in ceiling tiles during remodeling Feb, 2004
- Diagnosed with RLL pneumonia by CXR and symptoms improved with ATB
- Subsequent CXRs and CTs showed progression of infiltrates

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**Labs (Dec, 2004)**

**Case #4**

- Fungal serologies, urine histo antigen all neg
- BAL – 52% MP, 27% N, 15% L, 6% E; negative AFB, fungal cultures; cytology negative
- Transbronchial biopsy – calcified granuloma with histo organisms seen
- Brushings – negative cytology
<table>
<thead>
<tr>
<th>May, 2005</th>
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<tbody>
<tr>
<td><strong>Case #4</strong></td>
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<tr>
<td>- Repeat BAL: negative cultures, negative cytology</td>
<td>- Severe hypoxemia</td>
</tr>
<tr>
<td>- Surgical lung biopsy: possible cryptogenic organizing pneumonia</td>
<td>- Admitted to ICU and subsequently has 6 week hospitalization for antibiotics &amp; steroids</td>
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<tr>
<td></td>
<td>- Declined 2nd surgical lung biopsy</td>
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<tr>
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<td>- Eventually discharged home with hospice</td>
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<td>- Died January, 2007</td>
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<table>
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<th>February, 2006</th>
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<table>
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<th>Clinical Course (con’t)</th>
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<tr>
<td>- Trial of prednisone 40 mg/day – no subjective improvement</td>
</tr>
<tr>
<td>- Repeat BAL Dec, 2005: 71% MP, 18% N, 10% L, 1% E; negative cultures and cytology</td>
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<tr>
<td>- Transbronchial biopsy = no cancer</td>
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<table>
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<tr>
<th>Autopsy slides</th>
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### Bronchoalveolar carcinoma

- The great impersonator
- Often hard to diagnose in life even with surgical biopsy

- Radiographic presentations:
  - Lobar consolidation
  - Solitary pulmonary nodule
  - Diffuse patchy infiltrates
  - Multiple pulmonary nodules

### Non-small cell lung cancers

- Adenocarcinoma
- Squamous cell carcinoma
- Large cell undifferentiated carcinoma
- Bronchoalveolar carcinoma

### The moral of the story: Non-resolving pneumonia is usually not pneumonia
Case #5

- 69 year old woman admitted with cough in November 2009
- Improved transiently with cefpodoxime but relapsed after 2 weeks
- Re-admitted in February 2010 and improved again with levofloxacin; BAL bacterial, fungal, AFB cultures negative

Case #5

- Normal IgG
- Negative anti-CCP
- Negative ANA
- Normal Quantiferon
- Normal alpha-1-antitrypsin
- Normal fungal titers
- Normal hypersensitivity panel
- Normal serum protein electrophoresis
- Normal CBC

Case #5

- Sent home and told to not take antibiotics
- Returned for bronchoscopy when antibiotic-free
- BAL:
  - 34% macrophages
  - 54% neutrophils
  - 11% lymphocytes
  - 1% eosinophils
Case #5

- Bronchial washings and BAL = Mycobacterium avium complex

M. avium complex

- Occurs in:
  - Naturally occurring water sources
  - Animals
  - Heated water systems
  - Incidence probably underestimated
  - Just growing it doesn't mean you've got it!

Frequency of non-tuberculous mycobacterial infections

- M. avium complex: 61%
- M. kansasii: 10%
- M. fortuitum: 19%
- Others: 10%
**M. avium complex: four main clinical syndromes**

1. HIV-associated
   - Male
   - Pre-existing lung disease
   - Age
   - Alcoholism
   - Upper lobe infiltrates or cavities

2. Cavitary lung disease

3. Cystic fibrosis-associated

4. Mid-lung disease
   - Otherwise healthy women
   - Over age 50 yrs
   - Lingular or RML nodular disease
   - Present with cough and no systemic symptoms
   - “Lady Windermere Syndrome”

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**M. avium complex: other pulmonary syndromes**

- Infection associated with pectus excavatum
- Solitary pulmonary nodule
- Hypersensitivity pneumonitis (“hot tub lung”)

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**Lady Windermere’s Fan (1892)**

- Reich JM & Johnson RE. *Mycobacterium avium complex pulmonary disease presenting as isolated lingular or middle lobe pattern: The Lady Windermere Syndrome*. Chest 1992; 101:1605

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**44 year old woman with:**

- Lichen planus treated with a TNF inhibitor
- Lymphoma treated with rituxamab
- Recurrent pneumonia
- Respiratory failure requiring transfer to LTACH for ventilator wean

**BAL = Mycobacterium abscessus**

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**Oscar Wilde**
45 year old man with ‘refractory pneumonia’

- Recurrent bronchitis & pneumonia
- Transiently improves with antibiotics
- BAL = M. avium complex

Mycobacterium Avium Complex: Treatment

- Clarithromycin (1,000mg) or azithromycin (500mg) three times a week
- Rifampin (600 mg) or rifabutin (300 mg) three times a week
- Ethambutol (25mg/kg) three times a week
- Streptomycin two to three times per week should be considered for the first eight weeks as tolerated
- Treat for a long, long, long time

51 year old woman with chronic lymphocytic leukemia

- Bronchiectasis + Nodules = MAC

58 year old woman with recurrent pneumonia and cough

Bronchiectasis

Nodules

The moral of the story: A high-resolution chest CT sometimes paints a picture worth a thousand chest x-rays

Case #6

- 19 yr old OSU undergraduate student
- 3 days of increasing:
  - Dyspnea
  - Pleuritic chest pain
  - Fever
  - Myalgias

- 3 days of increasing:
  - Dyspnea
  - Pleuritic chest pain
  - Fever
  - Myalgias

- Physical exam:
  - Tachypneic with labored respirations
  - Temperature = 101 F
  - Lungs = scant bibasilar crackles

- Laboratory studies:
  - WBC = 15,000
  - pO2 = 46 (room air)
Case #6

- Intubated on presentation
- BAL:
  - 60% eosinophils
  - 20% macrophages
  - 15% lymphocytes
  - 5% neutrophils
- All cultures negative

Acute Eosinophilic pneumonia

- Chest X-ray:
  - Kerley B lines
  - Interstitial infiltrates
  - Alveolar infiltrates
  - Pleural effusions
- Lab:
  - Average WBC 17,000
  - Blood eosinophils not usually elevated
  - Average pO2 57 mm
  - IgE sometimes elevated
  - PFTs:
    - Restriction
    - Low diffusing capacity

Acute Eosinophilic pneumonia

- Presentation:
  - Average symptoms 4 days
  - Average age 29 yrs
  - Symptoms:
    - Cough 100%
    - Dyspnea 95%
    - Chest pain 73%
    - Myalgias 50%
    - >40% “beginner” smokers

- Exam:
  - Average temperature 101 degrees F
  - Average respiratory rate 32/min
  - Crackles in 80%

Acute Eosinophilic Pneumonia Day #1
### Acute Eosinophilic Pneumonia

- **Typical BAL:**
  - 37% eosinophils
  - 20% lymphocytes
  - 15% neutrophils
  - 28% macrophages
- **Lung biopsy:**
  - Intra-alveolar eosinophils

### Acute Eosinophilic Pneumonia Treatment:

- Methylprednisolone 125 mg/6 hours until respiratory failure resolves
- Prednisone 60 mg/d - taper over a month
- Relapses do not occur

### Acute Eosinophilic Pneumonia: Causes/Mimics

- Idiopathic
- Cigarette smoking
- Prescription drugs
- Street drugs
- Organic dust inhalation
- Parasites

### Acute eosinophilic pneumonia among US Military personnel deployed in or near Iraq


- 18 cases out of 183,000 deployed military
- 78% recently beginning to smoke
- BAL = 40% eosinophils
- 2/3 required mechanical ventilation
- 2 died
- Survivors recovered completely

Why eosinophils and football don’t mix

Case #7

- 51 year old man with cough and dyspnea for 3 weeks. No improvement after a course of azithromycin and albuterol
- Non-smoker who works in sales. He has a hot tub
- Exam: dry crackles on the right
- PFTs: restriction with low diffusing capacity
- Lab: autoimmune serologies, fungal serologies, hypersensitivity serologies all negative

The moral of the story: A bronchoscopy can be a powerful thing
Cryptogenic Organizing Pneumonia

- Clinical presentation:
  - 40-60 years old
  - Symptoms less than 2 months
- Causes: autoimmune conditions, drugs, idiopathic
- Lung biopsy required for confident diagnosis
- Treatment:
  - Prednisone (2/3 patients respond)
  - Duration = >6 months

Cryptogenic organizing pneumonia (aka “BOOP”: Bronchiolitis Obliterans Organizing Pneumonia) (aka cryptogenic organizing pneumonia)
Sub-pleural clearing in BOOP

History

- 66 yr old with severe emphysema
- Home O2 for 4 years
- Meds: inhaled steroid, tiotropium, PRN albuterol
- Former banker; quit smoking 8 years ago

The moral of the story:
A non-resolving pulmonary infiltrate and a non-diagnostic bronchoscopy is an invitation to a surgical biopsy

History leading to admission

- October - COPD exacerbation treated with steroids & doxycycline
- November - admitted with RUL pneumonia treated with moxifloxacin
- March - RUL pneumonia treated with moxifloxacin
- April – still had RUL infiltrate
Case #8

Bronchoscopy
- Right upper lobe occluded by an endobronchial mass
- Cultures negative
- Cytology and endobronchial biopsy negative

Repeat Bronchoscopy
- Washings/brushings negative
- Biopsy - respiratory epithelium with moderate mixed acute and chronic inflammation; fragment of foreign material consistent with vegetable material
- Following the bronchoscopy, he expectorated a mummified kernel of corn

Bronchoalveolar lavage
- Cell differential = 84% neutrophils
- Gram positive cocci, Gram positive rods, Gram positive beaded bacilli
- Re-review of BAL and both biopsies by GMS stain indicate branching filamentous bacteria consistent with actinomyces
## Pulmonary Actinomyces
- All ages - peak age = 4th & 5th decades
- Male:female = 2:1 to 4:1
- Risk factors: poor dental hygiene, emphysema, chronic bronchitis, alcoholism, bronchiectasis
- Usual presentation = abnormal x-ray
- Not usually associated with immunosuppression

## Radiology
- Pneumonia - like pattern
  - Tends to cross fissures
  - Can invade adjacent tissues
- CT:
  - Airspace consolidation
  - Mass
  - Pleural effusions (small)
  - Mediastinal adenopathy

## Actinomycosis
- Anaerobic (often won’t grow)
- Tends to cross thoracic boundaries
- Often has “companion bacteria”
- Three presentations:
  - Cervicofacial
  - Abdominopelvic
  - Thoracic

## Upper lobe consolidation
![Upper lobe consolidation image]
<table>
<thead>
<tr>
<th>Right middle lobe consolidation</th>
<th>Mass-like with erosion into chest wall and ribs</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulmonary nodule</th>
<th>Actinomycosis: Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3.png" alt="Image" /></td>
<td>- Penicillin</td>
</tr>
<tr>
<td></td>
<td>- Drainage when possible</td>
</tr>
<tr>
<td></td>
<td>- Alternative antibiotics:</td>
</tr>
<tr>
<td></td>
<td>- Doxycycline</td>
</tr>
<tr>
<td></td>
<td>- Erythromycin</td>
</tr>
<tr>
<td></td>
<td>- Clindamycin</td>
</tr>
</tbody>
</table>
The morals of the story:
1. The gram stain report may have more information than the culture report
2. Corn does not belong in the airway

Case #9
- Fails to improve despite 3 weeks of antibiotics
- Sed rate 120 seconds
- Referred for surgical lung biopsy

History
- 48 year old man with pneumonia and anemia
- Progressive dyspnea for 2 months
- Blood and bronchoalveolar lavage cultures all negative
- Referred for antibiotics & pulmonary rehabilitation

Image of lung in at the time of VATS
Case #9

Wegener’s granulomatosis

Consider in:
- Alveolar hemorrhage
- Lung cavities
- Pulmonary infiltrate + hematuria
- Elevated cANCA highly suggestive (but not diagnostic)
- Diagnosis requires biopsy
- Treatment = steroids plus cyclophosphamide
The moral of the story: Maintain a healthy sense of skepticism about referral diagnoses that don’t make sense

Case #10

41 year old woman with dyspnea and cough for 2 months. No improvement after a course of azithromycin
- PMH: hypertension and hypothyroidism
- SH: non-smoker; teacher’s aid for MRDD pre-school children
- Exam: basilar right-sided crackles
- Sent for evaluation for possible surgical lung biopsy

And then she said...

- “And oh by the way, did I tell you that we raise goats and donkeys in the barn in our back yard?”
- “And oh by the way, did I tell you we have a Quaker Parrot? And Cockatiels? And Parakeets?”
- “And oh by the way, did I tell you we have birds living in our attic and there’s a hole in my closet ceiling so that my clothes are covered with bird feathers and bird poop?”
Case #10

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Normal Value</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canary Feathers</td>
<td>&lt;17</td>
<td>34 (H)</td>
</tr>
<tr>
<td>Finch Feathers</td>
<td>&lt;12</td>
<td>59 (H)</td>
</tr>
<tr>
<td>Parrot Droppings</td>
<td>&lt;14</td>
<td>91 (H)</td>
</tr>
<tr>
<td>Parrot Proteins</td>
<td>&lt;12</td>
<td>50 (H)</td>
</tr>
<tr>
<td>Pigeon Droppings</td>
<td>&lt;70</td>
<td>78 (H)</td>
</tr>
<tr>
<td>Pigeon Feathers</td>
<td>&lt;22</td>
<td>60 (H)</td>
</tr>
</tbody>
</table>

**Hypersensitivity Pneumonitis**

- Etiology often hard to identify
  - Birds
  - Hot tubs
  - Occupation
  - Drug
  - T-suppressor cell alveolitis
- Treatment:
  - Remove offending antigen
  - Prednisone
- Outcome:
  - Complete resolution
  - Chronic fibrosis

**Hot Tub Hypersensitivity**
Drug-induced Hypersensitivity

Feather pillow Hypersensitivity

The moral of the story:  
- Birds are bad  
- Feather pillows are just as bad  
- Hot tubs are worse

Clinical approach to non-resolving infiltrates:  
- Take a history!  
- Never, ever, ever, ever miss tuberculosis  
- Chest CT scan  
- Bronchoscopy  
- Surgical lung biopsy if all else fails
The moral of the story:
Sometimes non-resolving pneumonia is just pneumonia