Diagnosis and management of acute respiratory tract infections

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Acute Respiratory Tract Infections

- Influenza and other respiratory viruses
  - Acute bronchitis and viral pneumonia
- Acute exacerbation of chronic bronchitis
- Community-onset pneumonia
  - HCAP is mostly dead!
Acute Bronchitis

- Despite considerable clinician and public education, about 70% of adults with acute bronchitis get antibiotics – usually a Z-Pak

- Multiple randomized trials show no benefit from antibiotics

- Patient education yields equal satisfaction
  - Antibiotics have side effects, increase risk of resistance for 90 days
  - Symptomatic Rx – analgesics, nasal decongestants, OTC cough syrup.
A 65 yo woman with acute cough illness and an important engagement...

- Over 75,000 adult prescriptions for azithromycin last 12 months Select Health
- 90% Z-paks
- Clinician and patient algorithms and educational materials available through Intermountain.net – primary care – clinical programs, bronchitis CPM
- Call it a “chest cold”
Pneumococcal resistance

- Ceftriaxone, ampicillin/amoxicillin, and levofloxacin or moxifloxacin remain highly active.

- Pneumococcal macrolide resistance
  - Blood isolates from adults
    - 19% Salt Lake Valley
  - All isolates
    - 49% Salt Lake Valley
Influenza-like illness

- Fever, myalgias, cough (usually dry/minimally productive), fatigue, headache during the winter when influenza present locally – see GermWatch, also CDC website
  - Specificity 80 – 85 % for laboratory confirmed influenza
    - but lower in older patients
  - Polymerase chain reaction (PCR)-based testing is more sensitive and specific than rapid tests

- Influenza A (seasonal), influenza B, influenza A H1N1, also other respiratory viruses

- >age 60 for complications from seasonal influenza, pregnancy, but ages 20-60 and obese for H1N1
  - Primary influenza pneumonia/ARDS, also bacterial superinfection
Influenza incidence by month in North America
Influenza

- Spread from person to person primarily through respiratory droplet transmission
- Incubation period is 1 — 4 days
- Contagious -1 to 7 days from symptom onset

http://www.cdc.gov/flu/professionals/acip/clinical.htm
Influenza Vaccination

- Everyone over 6 months of age
- Vaccine efficacy varies between years, but “herd” immunity effect at least as important as individual efficacy
- Higher dose formulation for patients over age 65 – more immunogenic, small increase in local side effects
- Recombinant influenza vaccine available for patients with severe egg allergy
- Adjuvant flu vaccine, and a cell culture-based inactivated influenza vaccine are available, but not preferred by Advisory Committee on Immunization Practices/CDC

http://www.cdc.gov/flu/professionals/acip/clinical.htm
Not “just” the flu!

- Influenza-associated deaths are 3,300 to 49,000 annually
- Case fatality rate from H1N1 with respiratory failure 30%
- Oseltamivir 75 mg bid for 5 days shortens duration of symptoms and decreases secondary complications
- Rx first 1-2 days of symptoms, and if still febrile or hospitalized
Take home message

• Our patients need more oseltamavir, and many fewer Z-Paks!
Acute exacerbation of chronic bronchitis

- In a patient previously diagnosed with COPD:
  - Cough increases in frequency and severity
  - Sputum production increases in volume and/or changes character
  - Dyspnea increases
Acute exacerbation of chronic bronchitis

- 70% are infectious in cause, either viral or bacterial
- 30% air pollution, change in medications, pulmonary embolism, cardiac disease, other
- Single best predictor is prior history of exacerbations
Acute exacerbation of chronic bronchitis

Treatment

• Exclude specific, treatable causes such as pneumothorax, heart failure

• Begin or increase albuterol/ipratropium

• Corticosteroids
  – 40 mg PO for 5 days

• Antibiotics for inpatients, but for outpatients only with moderate to severe exacerbations and sputum purulence
  – Doxycycline, Amox-Clav, Fluoroquinolone
Intermountain Pneumonia Care Process Model

- Dates back to 1995, updated for 2016
- Intended for immunocompetent patients ≥ 18 years, excluding:
  - solid organ, bone marrow or stem cell transplant recipients
  - patients receiving cancer chemotherapy or chronic (> 30 days) “high dose” corticosteroids
  - patients with congenital or acquired immunodeficiency or HIV infected with CD4 count < 350/mm³
Why Pneumonia Care Process Model?

• 7th leading cause of death in the Unites States
• $10 billion per year in treatment costs
• Evidence that well designed and implemented local treatment guidelines decrease mortality and improve other clinical outcomes

https://www.cdc.gov/pneumonia/
2007 ATS/IDSA Clin Infect Dis 44:Suppl 2, S27
Diagnosis/Definition

• “In addition to a constellation of suggestive clinical features, the diagnosis of pneumonia requires a demonstrable infiltrate by chest radiograph or CT, with or without supporting microbiological data”

• 2014 Utah Instacare data: 40% of patients diagnosed and treated for pneumonia did not have chest radiography.
Constellation of suggestive clinical features

Under-diagnosis of Pneumonia

- Atypical presentations - chest pain, abdominal pain, confusion, without prominent cough or sputum production
- In patients with suggestive symptoms, abnormal vital signs and/or abnormal chest exam predict pneumonia and indicate need for CXR

Heckerling Ann Intern Med 1990 113:664
Bushyhead Med Care 1983; 21:661-673
Benefits of a Chest X-ray

• May obtain information on etiology, prognosis, or alternative diagnosis$^1$
• May indicate the presence of complications, such as pleural effusion, multilobal disease$^2$
• Absence of infiltrates rules out CAP in most cases. Acute bronchitis is not an indication for antibiotics$^3$

Community-acquired Pneumonia
Accuracy of Clinical Diagnosis

• 236 cases of pneumonia diagnosed and treated by general practitioners without chest radiographs

• All patients had chest radiographs after discharge home or hospital admission

• 93/236 (38%) had initial radiographic infiltrate

Woodhead Lancet 1987 1: 671-674
Does chest radiograph negative pneumonia exist?

- Subsequent radiograph occasionally shows an infiltrate not seen initially
- Only 2 additional patients (1%) in Woodhead study had radiographic infiltrate at 7-10 days not seen initially
- ? Role of dehydration
  - 1 case report
  - Increased BUN and 1 liter greater fluid intake 24 hours retrospectively associated with radiographic worsening

Hash J Fam Pract 2000; 49:833
Over-diagnosis of Pneumonia

- Pneumonia a clinical syndrome....
- Pulmonary emboli, interstitial lung disease, heart failure, atelectasis, lung cancer, TB have overlapping signs and symptoms
- Patients who fail to respond to antibiotics within 3 to 5 days should be re-evaluated
- Patients with recurrent “pneumonia” should be evaluated for alternative diagnoses, e.g. chronic aspiration, hypersensitivity pneumonitis
To Admit or Not to Admit?
An important question...

- Costs are 20 times higher in hospitalized patients\(^1\)
- Less ill patients return to work and usual activities faster if treated at home\(^2\)
- Patients hospitalized after initial outpatient treatment have higher mortality\(^3\)
- Severely ill patients not initially admitted to ICU have higher mortality\(^4\)

1) Niederman Clinical Therapeutics 20:820-837, 1998
2) Labarere Chest 131:480 2007
4) Neill Thorax 51:1010 1996
CURB-65

• Score 1 point each for:
  – Confusion
  – BUN > 20
  – Respiratory rate ≥ 30/min
  – BP (systolic BP ≤ 90 mmHg or diastolic BP ≤ 60 mmHg)
  – Age ≥ 65 years

• Scoring

  0-1  Home treatment OK
  2    Ward admission or observation
  3+   Hospital admission

?Assess for ICU

Mortality, %

Additional Severity Assessment

- Sp02 < 90%
- Pleural effusion → >1 cm on decubitus CXR, > 5 cm on lateral CXR, visible on AP upright
Algorithm for Outpatient Pneumonia: Diagnosis and Triage

History, physical, chest x-ray

- No infiltrate: Look for alternative diagnosis
- Infiltrate and clinical signs & symptoms: Evaluate for admission using prediction rule

Evaluate for admission using prediction rule

- Outpatient: Diagnostic tests optional
- Hospitalize: Diagnostic tests for patients with specific conditions
Outpatient Antibiotic Therapy
No antibiotic last 3 months, no comorbidities

• Doxycycline 100 mg bid for 7 days
  – Sun sensitivity, Epigastric pain/Nausea, Category D pregnancy

• Ceftriaxone 1 gm IV/IM and/or amoxicillin 1000 mg tid plus oral azithromycin 500 mg daily for 3 days
Outpatient Antibiotic Therapy

COPD, CHF, diabetes, malignancy, or renal failure
OR antimicrobial use within last 3 months

- Ceftriaxone 1 gm IV qd or Amoxicillin 1000 mg tid
  - plus oral azithromycin or doxycycline

- Fluoroquinolone (oral unless nauseated/NPO)
  moxifloxacin 400 mg qd for 7 days or levofloxacin 750 mg for 5 days
Timing of First Antibiotic Dose

• “For patients admitted through the emergency room, the first antibiotic dose should be administered while still in the emergency department”

  – OR for mortality 0.83 (p = 0.01) when antibiotics administered within 4 hours of hospitalization

Houck  *Arch Intern Med* 2004; 164:637
Empiric non-ICU Inpatient Therapy

- Ceftriaxone 1 gm IV qd plus azithromycin or oral doxycycline
  - Change to amoxicillin 1000 mg when clinically stable to complete 7 days
  - Levofloxacin 750 mg for 5 days
Empiric ICU Therapy

- Ceftriaxone 1 gm IV q 12 plus intravenous azithromycin (levofloxacin 750 mg if macrolide allergic)
- For patients with history of hives/anaphylaxis to penicillins or cephalosporins:
  - intravenous clindamycin or carbapenem plus levofloxacin 750 mg
5-year Trends in Initial Antibiotic Use for Hospitalized Pneumonia Patients, 2006-2010 (N=95,511)

Jones BE Clin Infect Dis 2015 61(9):1403
Concept of HealthCare Associated Pneumonia (HCAP) is (mostly) dead

- Intended to identify patients with community-acquired pneumonia at increased risk for pathogens resistant to ceftriaxone or Ampicillin - sulbactam plus macrolide empiric antibiotics

- 2005 IDSA/ATS pneumonia guideline definition:
  - Hospitalization for more than 2 days within 3 months
  - Nursing home residents
  - Chronic dialysis, wound care, IV center
HCAP is (mostly) dead

- Outcomes in patients with HCAP worse when treated with HCAP guideline–concordant regimes compared to CAP therapy
  - OR for mortality 2.18, 95% CI 1.86-2.55\(^1\)
  - Survival to 28 days 65% in the compliance group and 79% in the non-compliance group (p=0.004)\(^2\)

1) Attridge Eur Respir J 2011, 38:878
Odds ratios for mortality associated with implementation of ePneumonia

Mixed effect logistic regression model adjusted for eCURB, presence of pleural effusion, gender, and PaO2/FiO2 ratio

O.R. = 1.12
P = .81

O.R. = 0.53
P = .045
Why did following HCAP guidelines not improve outcomes?

- HCAP patients are a sorry lot at high risk for mortality from multiple causes
- The HCAP criteria have poor positive and negative predictive value for the presence of resistant pathogens
- Overly broad antibiotic therapy without macrolides may worsen outcome in patients without resistant pathogens
  - ?More C-diff colitis, more renal toxicity, no immune-modulating benefit from macrolide combination therapy?
HCAP ignores important epidemiologic risk factors for resistant pathogens

- Prior antibiotic exposure
- Co-morbid illness – chronic respiratory disease, heart failure, diabetes
- Prior culture results
- Use of proton pump inhibitors
- Functional status (ambulatory or not)
- Need for enteral feeding
### Drug Resistance in Pneumonia Score

<table>
<thead>
<tr>
<th>Factor</th>
<th>Points</th>
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<tbody>
<tr>
<td>Antibiotic use &lt; 60 days</td>
<td>2</td>
</tr>
<tr>
<td>Long term care</td>
<td>2</td>
</tr>
<tr>
<td>Tube feeding</td>
<td>2</td>
</tr>
<tr>
<td>Prior drug resistant community-acquired pneumonia</td>
<td>2</td>
</tr>
<tr>
<td>Hospitalization &lt; 60 days</td>
<td>1</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>1</td>
</tr>
<tr>
<td>Poor functional status</td>
<td>1</td>
</tr>
<tr>
<td>Gastric acid suppression</td>
<td>1</td>
</tr>
<tr>
<td>Wound care</td>
<td>1</td>
</tr>
<tr>
<td>MRSA colonization (1 year)</td>
<td>1</td>
</tr>
</tbody>
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Webb BJ, Antimicrobial Agents and Chemotherapy 2016 22;60(5):2652
Recommended empiric antibiotics for patients with DRIP score 4 or greater

- Vancomycin 25 mg/kg IV
- Cefepime or Piperacillin-Tazo
- Azithromycin 500 mg IV
DRIP score 4 or greater and all ICU admitted community-acquired pneumonia patients

- Blood, sputum, tracheal aspirate, pleural fluid cultures
- Urinary antigens for pneumococcus and legionella
- Nasal swab for MRSA
- Change from Vancomycin and Cefepime to Ceftriaxone within 48 hours for patients without a resistant organism identified
### DRIP implementation study
Salt Lake Valley Hospitals 11/2014 to 10/2015

#### DRIP versus Usual Care

<table>
<thead>
<tr>
<th></th>
<th>DRIP, %</th>
<th>Usual Care, %</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Inadequate Spectrum</td>
<td>0.67</td>
<td>0.93</td>
<td>NS</td>
</tr>
<tr>
<td>Overtreatment</td>
<td>20.6</td>
<td>27.8</td>
<td>0.008</td>
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<tr>
<td>Appropriate Spectrum</td>
<td>78.6</td>
<td>71.0</td>
<td>0.005</td>
</tr>
</tbody>
</table>

B Webb, European Respiratory Society London 2016
DRIP implementation study
Salt Lake Valley Emergency Departments – 11 months

• Odds of in-hospital mortality
  – ePneumonia with DRIP (odds ratio 0.64; upper 95% confidence interval 1.04; \( p = 0.06 \))

• Decreased length of hospital stay
  – ePneumonia with DRIP (coeff – 0.147; upper 95% CI – 0.137; \( p < 0.001 \)).
Prevention

- Smoking cessation – current smoking doubles the risk of pneumococcal and legionella pneumonia

- Consider dysphagia, esophageal dysmotility, structural parenchymal/airway disease in patients with recurrent pneumonia

- PCV 13 (Prevnar) for persons ≥ 65 years and for those with selected high-risk concurrent diseases - current ACIP guidelines

- Pneumococcal polysaccharide vaccine (Pneumovax) recommended 1-2 years after PCV 13
Patient with cough <2 weeks

? Fever >37.8 C
Heart rate >100
Vr > 24
SpO₂ <88%
Focal rales

NO

? Severe myalgia, fever >37.8 C
Absence of rhinorrhea
Influenza present in community

YES → CxR

+ → Pneumonia

- → YES → Influenza

NO

↑ dyspnea, cough, sputum purulence

? Chronic bronchitis

NO

Acute bronchitis

(Asthma, CHF, Sinusitis, TB)

NO
Summary

• Accurate diagnosis of respiratory tract infections
• Fewer Zpaks, more oseltamavir, amoxicillin, doxycycline
• Objective severity measures to determine site of care
• Antibiotics given at the site of diagnosis, directed at common pathogens
• Decision support to reliably deliver care elements is linked with better clinical outcomes