Cough, Cold and Flu… Who Knew?

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Outline

- Acute Cough Illness
  - Acute bronchitis
    - Influenza
    - Pertussis
  - Sinusitis
  - Pharyngitis
    - *Fusobacterium necrophorum*

General Approach

- Diagnosis
  - Excluding Serious Illness
  - Testing?
- Treatment
  - Symptomatic Therapy
  - Antimicrobial Therapy
- Prognosis
  - When to Return for Work; Evaluation

Management Principles for Uncomplicated Acute Bronchitis
Bronchitis
-CDC; ACP; AAFP; IDSA... 2001

“The evaluation of adults with acute cough illness... should focus on ruling out serious illness, particularly pneumonia”

- In healthy, nonelderly adults, pneumonia is uncommon in the absence of vital sign abnormalities or asymmetrical lung sounds, and CXR is usually not indicated.
- When cough >3 weeks, CXR may be warranted in absence of other known causes.

Gonzales et al., 2001

Acute Bronchitis
-Therapeutic Objectives

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Pathophysiology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>bronchial RAD</td>
<td>bronchodilators</td>
</tr>
<tr>
<td></td>
<td>mucus production</td>
<td>decongestants</td>
</tr>
<tr>
<td></td>
<td>post-nasal drip</td>
<td>sinus therapy</td>
</tr>
<tr>
<td></td>
<td>acid reflux</td>
<td>H2B; PPI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cough suppressants</td>
</tr>
<tr>
<td>Wheezing/SOB</td>
<td>bronchial RAD</td>
<td>bronchodilators</td>
</tr>
</tbody>
</table>

Resolution of Acute Bronchitis

<table>
<thead>
<tr>
<th>%Patients</th>
<th>Days with cough</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Antibiotic</td>
<td>(+) Antibiotic</td>
</tr>
</tbody>
</table>

Stott, BMJ 1976
Uncomplicated Acute Bronchitis
- azithromycin vs. vitamin C (Lancet 2002;359:1648-54)

Microbiology of Acute Cough Illness in Adults

Table 2. Comparison of cold and viral culture and PCR in the diagnosis of viral agents of acute respiratory illness in 256 previously healthy adults.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Cold culture</th>
<th>Viral culture</th>
<th>PCR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza A</td>
<td>26 (100)</td>
<td>16 (62)</td>
<td>8 (32)</td>
<td>40 (16)</td>
</tr>
<tr>
<td>Influenza B</td>
<td>4 (16)</td>
<td>2 (8)</td>
<td>0</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Influenza C</td>
<td>6 (24)</td>
<td>3 (12)</td>
<td>0</td>
<td>9 (3)</td>
</tr>
<tr>
<td>Respiratory syncytial</td>
<td>12 (48)</td>
<td>4 (16)</td>
<td>4 (16)</td>
<td>20 (8)</td>
</tr>
<tr>
<td>Parainfluenza virus</td>
<td>3 (12)</td>
<td>2 (8)</td>
<td>0</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>2 (8)</td>
<td>2 (8)</td>
<td>0</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>28 (108)</td>
<td>28 (108)</td>
<td>0</td>
<td>56 (22)</td>
</tr>
<tr>
<td>Human metapneumovirus</td>
<td>4 (16)</td>
<td>4 (16)</td>
<td>0</td>
<td>8 (3)</td>
</tr>
<tr>
<td>Human picornavirus</td>
<td>5 (20)</td>
<td>5 (20)</td>
<td>0</td>
<td>10 (4)</td>
</tr>
<tr>
<td>Human rhinovirus</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Overall</td>
<td>109 (43)</td>
<td>109 (43)</td>
<td>0</td>
<td>218 (86)</td>
</tr>
</tbody>
</table>

Microbiology of Acute Cough Illness in Adults

- Clinical characteristics

<table>
<thead>
<tr>
<th>Clinical characteristic</th>
<th>No. (%) of patients, by etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature (°C)</td>
<td>(≤ 37.5°C)</td>
</tr>
<tr>
<td>Respiratory symptoms</td>
<td>(≤ 38°C)</td>
</tr>
<tr>
<td>Fever</td>
<td>(≤ 38.5°C)</td>
</tr>
<tr>
<td>Cough</td>
<td>(≤ 39°C)</td>
</tr>
<tr>
<td>Pharyngeal symptoms</td>
<td>(≤ 40°C)</td>
</tr>
<tr>
<td>Wheezing at examination</td>
<td>(≤ 41°C)</td>
</tr>
<tr>
<td>Loss of breath</td>
<td>(≤ 42°C)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>(≤ 43°C)</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>(≤ 44°C)</td>
</tr>
<tr>
<td>Otalgia</td>
<td>(≤ 45°C)</td>
</tr>
<tr>
<td>Underlying medical condition</td>
<td>(≤ 46°C)</td>
</tr>
<tr>
<td>Environmental factors</td>
<td>(≤ 47°C)</td>
</tr>
<tr>
<td>Asthma</td>
<td>(≤ 48°C)</td>
</tr>
<tr>
<td>Cigarette use</td>
<td>(≤ 49°C)</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>(≤ 50°C)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>(≤ 51°C)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>(≤ 52°C)</td>
</tr>
<tr>
<td>Distance of stress</td>
<td>(≤ 53°C)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>6.0 (4.2)</td>
</tr>
<tr>
<td>Median (IQR, Min-Max)</td>
<td>5.0 (5.0)</td>
</tr>
</tbody>
</table>
H1N1-International

- The 2009 H1N1 influenza virus is the predominant influenza virus in circulation worldwide.
- Majority of 2009 H1N1 influenza isolates tested worldwide remain sensitive to oseltamivir (source: WHO)
  - 199 isolates tested worldwide have been found to be resistant to oseltamivir – 52 of these isolates were detected US

H1N1 Epidemiology

- Incubation period: 1-7 days
- Infectious period: -1 day until sx resolve
  - 10% still shedding virus at 10 days
  - Immunosuppressed may shed for weeks
- Median age: 12-17 years
- Hospitalized H1N1
  - Median age 32 years (Canada)
  - 30% of deaths associated with bacterial pneumonia

Symptoms:
H1N1 = seasonal flu

NYC high school outbreak (44 cases)
- cough (98%)
- fever (96%)
- headache (82%)
- sore throat (82%)
- rhinorrhea (82%)
- muscle aches (80%)
High Risk H1N1 Complications

- Children < 5 yrs (esp. < 2 yrs)
- Adults >65 yrs
- Pregnant women
- Chronic medical conditions
- Immunosuppressed
- Adolescents (age<19 yrs) on chronic aspirin therapy → Reyes syndrome

Treatment of H1N1

**CDC Quick Facts... 11/09**

- It’s not too late after 48 hrs
- No risk factors does not mean no treatment
- Treatment shouldn’t wait for laboratory confirmation
- Capsules can ease oseltamivir shortage

Are we out of the woods?

- How long do strains usually persist?
- Antigenic shift and virulence
- Oseltamivir resistance
Acute Bronchitis:
- bronchial hyperresponsiveness

Airflow obstruction in acute bronchitis without underlying lung disease

- FEV1, % predicted

Acute cough illness treatment
- bronchodilator treatment

Randomized, placebo controlled trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Disease</th>
<th>Treatment</th>
<th>Duration</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melbye 1991</td>
<td>bronchitis</td>
<td>fenoterol aerosol</td>
<td>Decrease symptoms</td>
<td>Improved FEV1</td>
</tr>
<tr>
<td>Hueston 1991</td>
<td>bronchitis</td>
<td>oral albuterol vs. erythromycin</td>
<td>Decrease cough @ 1 week</td>
<td>(41% vs. 82%)</td>
</tr>
<tr>
<td>Hueston 1994</td>
<td>bronchitis</td>
<td>albuterol aerosol vs. (placebo + erythromycin)</td>
<td>Decrease cough @ 1 week</td>
<td>(61% vs. 91%)</td>
</tr>
<tr>
<td>Littenberg 1996</td>
<td>nonspecific cough</td>
<td>albuterol aerosol</td>
<td>No benefit</td>
<td></td>
</tr>
</tbody>
</table>

OTC Cough Therapies
- Cochrane Review, 2004

- Antitussives
  - codeine: 2 trials; no differences
  - dextromethorphan: 2 of 3 trials show benefit
- Expectorants (guaifenesin): 1 of 2 trials benefit
- Mucolytics: 1 trial inconsistent benefit
- Antihistamine-Decongestant Combinations
  - 1 of 2 trials show benefit
- Dextro-salbutamol: reduced nocturnal cough only

Acute cough illness: evaluation

- summary

Patient Characteristics
- Elderly
- Immunosuppression
- COPD or CHF

Vital Sign Abnormalities
- HR > 100 bpm
- RR > 24 br/min, or
- T > 38°C

Is Influenza Likely?
- Yes
- No

PEX Findings
- Consolidation, or Pleural Effusion

Consider CXR
- Positive
- Negative

Treatment Options*
- Yes
- No

Treat Pneumonia
When to consider zebras…

- Cough > 3 weeks and normal CXR
  - Meds, asthma, GERD, postnasal drip, pertussis
- Nocturnal Cough
  - GERD/postnasal drip, cough-variant asthma, CHF

Pertussis…not just for children anymore

- DPT-related immunity wanes as early as 3 years… and absent after 10-12 years
- Attack rates as high as 100%
- 10-15% adults seeking care for persistent cough (>3 wks) have evidence of pertussis
- No clinical features distinguish pertussis in previously immunized adults

Resolution of Acute Bronchitis

Stott, BMJ 1976

![Graph showing resolution of acute bronchitis with and without antibiotics](https://via.placeholder.com/150)
Pertussis

- **Diagnosis**
  - Nasopharyngeal swab or nasal saline wash
  - PCR is now standard...
  - No FDA-licensed tests yet...
  - Coordinate with public health dept

- **Treatment**
  - Macrolides; trimethoprim-sulfa
  - Probably won’t help cough duration if started after 10 days of illness
  - Reasonable to provide empirical Abx treatment to contacts with cough, and close contacts/household members as prophylaxis.

Prevention: Pertussis Boosters

- ACIP 2007 Recs (MMWR 2006;55:RR-17)

  - **Routine**
    - Single Tdap instead of dT at age 11-18
    - Tdap (instead of dT) in adults 18-64 if > 10 years since dT

  - **Tdap when dT within 2-10 years**
    - Adult contacts of infants < 12 months
    - Women prior to pregnancy; else post-partum
    - Healthcare workers (all staff)
    - Rare Adverse Events
      - Arthus Reaction
      - Extensive Limb Swelling

Rhinovirusitis: Diagnosis

- “The clinical diagnosis of acute bacterial rhinosinusitis should be reserved for…”

  1. Rhinosinusitis symptoms ≥ 7 days
  2. Purulent nasal secretions
  3. Maxillary pain/tenderness in face/teeth

Rhinovirusitis: Diagnosis

- “…rarely some patients with acute bacterial rhinosinusitis present with dramatic symptoms of severe unilateral maxillary pain, swelling and fever”
Bacterial Sinusitis? Tough Call

- Cx (+) sinus aspirate
- purulent sinus aspirate
- CT scan (a)
- Xray (b)
- high clinical suspicion
- sinus symptoms

(a) CT scan criteria of air-fluid level or complete opacification.
(b) Xray criteria of mucosal thickening, air-fluid level or complete opacification.

Rhinosinusitis: Rx Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Patient Selection</th>
<th>Treatment Arms</th>
<th>Antibiotic Rx*</th>
<th>Placebo Rx*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lindbaek, 1996</td>
<td>clinical suspicion</td>
<td>amoxicillin; penicillin V; placebo</td>
<td>D10 86%</td>
<td>57%</td>
</tr>
<tr>
<td>van Buchem, 1997</td>
<td>CT Scan Dx</td>
<td>amoxicillin; placebo</td>
<td>D14 83%</td>
<td>77%</td>
</tr>
<tr>
<td>Stalman, 1997</td>
<td>Xray Dx</td>
<td>placebo</td>
<td>D10 85%</td>
<td>85%</td>
</tr>
<tr>
<td>Bucher, 2003</td>
<td>clinical criteria</td>
<td>amoxicillin; placebo</td>
<td>D14 75%</td>
<td>75%</td>
</tr>
<tr>
<td>Merenstein, 2005</td>
<td>clinical criteria</td>
<td>amoxicillin; placebo</td>
<td>D14 48%</td>
<td>37%</td>
</tr>
</tbody>
</table>

*Percent improved or cured

RCT: Abx +/- nasal steroids

- Williamson, JAMA 2008

<table>
<thead>
<tr>
<th>Abx + steroid</th>
<th>Abx + placebo</th>
<th>steroid + placebo</th>
<th>placebo + placebo</th>
<th>placebo + placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Sx days</td>
<td>median (IQR)</td>
<td>(n=51)</td>
<td>(n=60)</td>
<td>(n=63)</td>
</tr>
<tr>
<td></td>
<td>7 (4-14)</td>
<td>7 (4-10)</td>
<td>7 (4-14)</td>
<td>7 (5-14)</td>
</tr>
</tbody>
</table>

Rhinosinusitis: Diagnosis

“The clinical diagnosis of acute bacterial rhinosinusitis should be reserved for…” [B]

1. rhinosinusitis symptoms ≥ 7 days
2. purulent nasal secretions
3. maxillary pain/tenderness in face/teeth
Abx for Sinusitis—Meta-analysis
--Young, Lancet 2008

- Meta-analysis of clinical criteria-based RCTs of antibiotics for acute sinusitis
  - UNIQUE: aggregated patient-level data; therefore able to examine specific signs/Sx
- Results:
  - “Duration of illness or severity of symptoms did not predict antibiotic benefit”
  - “Purulent nasal discharge marginally significant”

![Odds Ratio for Cure with Antibiotic Rx for Acute Sinusitis](Young J et al, Lancet 2008)

Rhinosinusitis: Diagnosis

“The clinical diagnosis of acute bacterial rhinosinusitis should be reserved for…” [B]
- (1) rhinosinusitis symptoms ≥ 7 days
- (2) purulent nasal secretions
- (3) maxillary pain/tenderness in face/teeth

Rhinosinusitis: Abx Rx

- “Acute rhinosinusitis resolves without antibiotic treatment in most cases” [A]
  - Antibiotic treatment should be reserved for patients with moderately severe symptoms who meet criteria for clinical diagnosis of acute bacterial rhinosinusitis and for those with severe symptoms…regardless of duration of illness.
Acute Sinusitis - Therapeutic Objectives

### Symptoms
- **Pain**
  - Increased sinus pressure due to inflammation & obstruction
  - If >7-10 days of symptoms
  - NSAIDs

### Pathophysiology
- Increased sinus drainage
- Nasal saline wash
- Nasal decongestant

### Treatment
- If >7-10 days of symptoms
- NSAIDs
- Antibiotics

### Congestion
- Increased mucus production
- Oral decongestants
- Nasal steroids

### Pharyngitis: Diagnosis
- Clinically screen all adult patients with pharyngitis for the presence of 4 criteria:
  - History of fever
  - Tonsillar exudates
  - Tender anterior cervical LTN
  - Absence of cough
- Do not test or treat patients with none or only 1 of these criteria...

### Accuracy of Rapid Strep Test

<table>
<thead>
<tr>
<th>Centor Score</th>
<th>Sensitivity of RAT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pediatrics</td>
</tr>
<tr>
<td>0</td>
<td>47</td>
</tr>
<tr>
<td>1</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>90*</td>
</tr>
<tr>
<td>4</td>
<td>90*</td>
</tr>
</tbody>
</table>

*S* groups combined in study


### Pharyngitis: Abx Rx
- Test patients with 2-4 criteria using a rapid antigen test, and limit Abx to patients with positive test results*
- OR
- Test patients with 2 or 3 criteria, and limit Abx to patients with positive test results or patients with 4 criteria*
- OR
- Do not use any diagnostic tests, and limit Abx to patients with 3 or 4 criteria*
GAS Rapid negative, but patient Sx worsen… possibilities?
- False-negative rapid GAS test
- Infectious mononucleosis
- Non-group A streptococcal infection
  - Group C, Group D
- Gonorrhea
- Acute HIV
- Peritonsillar abscess
- Lemierre’s syndrome (septic thrombophlebitis)

Fusobacterium necrophorum
- Gram negative anaerobe.
- Causative agent in Lemierre syndrome
- In 15-30 yo, causes 10% of cases (about same % as group A strep)
- Not responsive to macrolides
- Suspect in adolescent/young adult with worsening Sx and neck swelling

More relevant than Strep??

<table>
<thead>
<tr>
<th>Pharyngitis</th>
<th>Events per 1 000 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A streptococcal</td>
<td>100 000</td>
</tr>
<tr>
<td>Acute rheumatic fever</td>
<td>50*</td>
</tr>
<tr>
<td>Carrel tte acute rheumatic fever</td>
<td>3</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
</tr>
<tr>
<td>Fusobacterium necrophorum</td>
<td>100 000</td>
</tr>
<tr>
<td>The Lemierre syndrome</td>
<td>250§</td>
</tr>
<tr>
<td>Long-term disability (111)</td>
<td>204</td>
</tr>
<tr>
<td>Death</td>
<td>115</td>
</tr>
</tbody>
</table>

* All rheumatic fever estimates are from reference 5.
† This estimate comes from a series of assumptions about F. necrophorum pharyngitis and the incidence of the Lemierre syndrome in adolescents.
‡ This number comes from 2 recent studies in 55 patients with the Lemierre syndrome. Given the 95% CI, the value could vary from 5 to 55.
§ This number comes from combining mortality data found in 4 published case series (8-11). The number could vary from 4 to 14, given the 95% CI.
Therapeutic Windows for Antimicrobial ARI Treatments

- Influenza Sx 2 days
- GAS pharyngitis Sx 2 days
  - To prevent ARF 10 days
- Pertussis cough 7-10 days

How to help patients say “no” to antibiotics for viral ARIs

- Illness labeling: use “chest cold”, not “bronchitis”
- Validate illness severity; focus on symptom relief
- Provide a contingency plan
- Discuss downside of unnecessary antibiotic use
  - risk of carriage/spread of antibiotic-resistant bacteria
- Patient-physician communication
  - Explain the illness
  - Spend “enough” time
  - Treat with respect

Gracias

CDC/ACP/AAFP/IDSA -Antibiotic Principles for ARIs

Bronchitis References


Acute Pharyngitis Refs


Acute Rhinosinusitis Refs