An Evidence-Based Treatment of Upper Respiratory Tract Infections

Ralph Gonzales, MD, MSPH
Professor of Medicine; Epidemiology & Biostatistics
University of California, San Francisco
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Outline

- Acute cough illness
  - Bronchitis; pertussis; influenza
- Sinusitis
- Pharyngitis
- Special Topics
  - How to say “no” to antibiotics
  - Therapeutic windows
General Approach

- Making the Diagnosis
  - Excluding Serious Illness
  - Do I need a Diagnostic Test?
- Determining Treatment
  - Symptomatic Therapy
  - Antimicrobial Therapy
- Communicating Prognosis
  - When to Return for Evaluation
Management Principles for Uncomplicated Acute Bronchitis
“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

Stott, BMJ 1976

Days with cough

% Patients

No Antibiotic

(+) Antibiotic
Uncomplicated Acute Bronchitis
- azithromycin vs. vitamin C (Lancet 2002;359;1648-54)

Return to Usual Activities

Figure 3: Cumulative proportion of patients who had returned to their usual daily activities.
These results are a summary of four sources of data: day 1 face-to-face interview (baseline), day 3 and day 7 telephone interviews (“Have you returned to your usual activities at work, home, or school? If yes: ‘What was that?’”), and a patient’s symptom diary (returned by mail at the end of the follow-up period).
Acute Bronchitis: bronchial hyperresponsiveness

Airflow obstruction in acute bronchitis without underlying lung disease

FEV1, % predicted

Eur Resp J 1994; 7:1239
**Acute cough illness treatment**
- **bronchodilator treatment**

Randomized, placebo controlled trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Condition</th>
<th>N</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melbye</td>
<td>bronchitis</td>
<td>73</td>
<td>fenoterol aerosol</td>
<td>Decrease symptoms</td>
</tr>
<tr>
<td>1991</td>
<td></td>
<td></td>
<td></td>
<td>Improved FEV1</td>
</tr>
<tr>
<td>Hueston</td>
<td>bronchitis</td>
<td>34</td>
<td>oral albuterol vs.</td>
<td>Decrease cough @ 1 week</td>
</tr>
<tr>
<td>1991</td>
<td></td>
<td></td>
<td>erythromycin</td>
<td>(41% vs. 82%)</td>
</tr>
<tr>
<td>Hueston</td>
<td>bronchitis</td>
<td>46</td>
<td>albuterol aerosol vs.</td>
<td>Decrease cough @ 1 week</td>
</tr>
<tr>
<td>1994</td>
<td></td>
<td></td>
<td>(placebo + erythro)</td>
<td>(61% vs. 91%)</td>
</tr>
<tr>
<td>Littenberg</td>
<td>nonspecific cough</td>
<td>104</td>
<td>albuterol aerosol</td>
<td>No benefit</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

Acute Cough Illness with or w/o phlegm

Patient Characteristics
Elderly
Immunosuppression
COPD or CHF

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

Yes
Is Influenza Likely?

No

Consider CXR
Positive
Treat Pneumonia

No

PEx Findings
Consolidation, or Pleural Effusion

Yes

Treatment Options*

No

Negative

Yes
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

FIGURE. Number of reported pertussis cases, by year — United States, 1922–2005
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
Pertussis

- **Diagnosis**
  - **Dacron** nasopharyngeal swab or nasal saline wash
  - PCR is now standard... much better sensitivity than culture or DFA; but still false-negatives and periodic false-positives c/w serology.
    - No FDA-licensed tests yet...
  - Coordinate with public health dept

- **Treatment**
  - Macrolides; trimethoprim-sulfa if macrolide-allergy
  - Probably won’t help cough duration if started after 10 days of illness, which can last 3-6 months
  - Reasonable to provide empirical Abx treatment to contacts with cough, and close contacts/household members as prophylaxis.
The CDC *now* recommends pertussis booster for all of the following groups, except...

1. Adolescents
2. Elderly (>65 years)
3. Post-partum women
4. Physicians and nurses
5. Physician office staff
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
In a 35 yo woman with purulent nasal discharge for 10 days, which additional symptom would warrant antibiotic therapy?

1. Ear pain
2. Sore throat
3. Cough
4. Tooth ache
5. Hoarse voice
Rhinosinusitis: Diagnosis (1)

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

(1) rhinosinusitis symptoms $\geq$ 7 days +

(2) purulent nasal secretions +

(3) maxillary pain/tenderness in face/teeth
Rhinosinusitis: Diagnosis (2)

“…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 + CT Scan Dx</td>
<td>amoxicillin; penicillin V; placebo</td>
<td>D10</td>
<td>86%</td>
</tr>
<tr>
<td>van Buchem 1997</td>
<td>clinical suspicion + Xray Dx</td>
<td>amoxicillin; placebo</td>
<td>D14</td>
<td>83%</td>
</tr>
<tr>
<td>Stalman, 1997</td>
<td>clinical criteria</td>
<td>doxycycline; placebo</td>
<td>D10</td>
<td>85%</td>
</tr>
<tr>
<td>Bucher, 2003</td>
<td>clinical criteria (only 32% Sx ≥ 7 days)</td>
<td>amox-clavulanate; placebo</td>
<td>D14</td>
<td>75%</td>
</tr>
<tr>
<td>Merenstein, 2005</td>
<td>clinical criteria (100% Sx &gt; 7 days)</td>
<td>amoxicillin; placebo</td>
<td>D14</td>
<td>48%</td>
</tr>
</tbody>
</table>

*Percent improved or cured
Williamson, JAMA 2008
-Abx +/- nasal steroids RCT

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Sx days</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abx + steroid</td>
<td>7 (4-14)</td>
<td>51</td>
</tr>
<tr>
<td>Abx + placebo</td>
<td>7 (4-10)</td>
<td>60</td>
</tr>
<tr>
<td>Steroid + placebo</td>
<td>7 (4-14)</td>
<td>63</td>
</tr>
<tr>
<td>Placebo + placebo</td>
<td>7 (5-14)</td>
<td>61</td>
</tr>
</tbody>
</table>

**Note:** Defined as when a patient reports 0 or 1 for all of the 11 diary items.

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Rhinosinusitis: Diagnosis (1)

“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
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 (1)

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

(1) rhinosinusitis symptoms $\geq$ 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

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<tr>
<th>Symptoms</th>
<th>Pathophysiology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>- increased sinus pressure due to inflammation &amp; obstruction</td>
<td>- ↑ sinus drainage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- nasal saline wash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- nasal decongestant</td>
</tr>
<tr>
<td></td>
<td>- if &gt;7-10 days of Sx</td>
<td>- NSAIDs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Antibiotics</td>
</tr>
<tr>
<td></td>
<td>- ↑ bacterial infection risk</td>
<td></td>
</tr>
<tr>
<td>Congestion</td>
<td>- increased mucus production</td>
<td>- oral decongestants</td>
</tr>
<tr>
<td></td>
<td>- infection; recurrent; allergic</td>
<td>- nasal steroids</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In a 25 yo man with severe sore throat, which clinical feature decreases his likelihood of having strep throat?

1. History of fever
2. Tonsillar exudate
3. Cough
4. Anterior cervical lymphadenopathy
5. Hoarse voice
Pharyngitis: Diagnosis

- “Clinically screen all adult patients with pharyngitis for the presence of 4 criteria:”
  - history of fever
  - tonsillar exudates
  - tender anterior cervical LAN
  - absence of cough
- “Do not test or treat patients with none or only 1 of these criteria…”
# Spectrum Bias in GAS Test

## Sensitivity of RAT

<table>
<thead>
<tr>
<th>Centor Score</th>
<th>Pediatrics</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>47</td>
<td>61*</td>
</tr>
<tr>
<td>1</td>
<td>65</td>
<td>61*</td>
</tr>
<tr>
<td>2</td>
<td>82</td>
<td>76</td>
</tr>
<tr>
<td>3</td>
<td>90*</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>90*</td>
<td>97</td>
</tr>
</tbody>
</table>

*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 [D], OR
• “Test patients with 2 or 3 criteria, and limit Abx to patients with positive test results or patients with 4 criteria” [D], OR
• “Do not use any diagnostic tests, and limit Abx to patients with 3 or 4 criteria [B]”
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)
# Streptococcal Pharyngitis - Therapeutic Objectives

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Pathophysiology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>☢ sore throat</td>
<td>-inflammation</td>
<td>-NSAIDs</td>
</tr>
<tr>
<td></td>
<td>-infection</td>
<td>-antibiotics</td>
</tr>
</tbody>
</table>
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
Therapeutic Windows in ARI Treatments

- Influenza Sx 2 days
- GAS pharyngitis Sx 2 days
  - To prevent ARF 10 days
- Pertussis cough 7-10 days
Gracias
CDC/ACP/AAFP/IDSA
-Antibiotic Principles for ARIs


Bronchitis References

Acute Rhinosinusitis Refs

Acute Pharyngitis Refs


