Antibiotic Use and Misuse

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What we hope you will walk away with...

1) A new respect for the problem, as in: “Wow, a lot of patients get antibiotics they don’t really need…

2) Better understanding of when antibiotics are needed for upper respiratory tract infections

3) Things to think about when you do need to prescribe antibiotics:
   - Wait and See approach
   - Targeted therapies instead of broad spectrum drugs
   - High dose, short course courses of antibiotics

Antibiotic Resistance: should we be concerned?

Estimated annual number of illnesses and deaths caused by antibiotic resistance:

At least \(2,049,442\) illnesses, \(23,000\) deaths

*Estimates and figures included in this report

Estimated annual number of illnesses and deaths due to MRSA (Methicillin-Resistant Staphylococcus aureus), a unique bacterial infection that, although not originally resistant to the drugs used to treat it, is directly related to antibiotic use and misuse:

At least \(250,000\) illnesses, \(14,000\) deaths
Why antibiotic resistant infections cost us all more

- Require prolonged and costlier treatments
- Extend hospital stays
- Necessitate additional provider visits and healthcare use
- Result in greater disability and death compared to infections that are easily treatable with antibiotics


Antibiotic prescription costs in billions

For 2009, total costs $10.7 billion

Unintended consequences of antibiotic use: adverse events

- Adverse events range from minor (rash) to severe (systemic allergic reaction, including anaphylaxis)
- Antibiotics are responsible for almost 1 out of every 5 visits to emergency departments for drug-related adverse events
- Antibiotics are the most common cause of drug-related emergency department visits for children


Antibiotic Prescribing Trends in the US and Oregon

Outpatient antimicrobial therapy
1992, US

- 24% All other diagnoses
- 21% Otitis media
- 16% URI (non-specific)
- 13% Bronchitis
- 12% Pharyngitis
- 12% Sinusitis

McCag JAMA 1995;273:214
Antibiotic prescribing among adults

Antibiotic prescribing among children

Antibiotic prescribing by condition,
adults, US, 2007-9

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treated with Abx</th>
<th>% Receiving Broad-spectrum Abx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>38%</td>
<td>74%</td>
</tr>
<tr>
<td>Abx indicated</td>
<td>65%</td>
<td>65%</td>
</tr>
<tr>
<td>Abx not indicated</td>
<td>51%</td>
<td>80%</td>
</tr>
<tr>
<td>Other respiratory</td>
<td>23%</td>
<td>76%</td>
</tr>
<tr>
<td>Other</td>
<td>7%</td>
<td>52%</td>
</tr>
<tr>
<td>Skin</td>
<td>13%</td>
<td>38%</td>
</tr>
<tr>
<td>UTI</td>
<td>60%</td>
<td>69%</td>
</tr>
<tr>
<td>GI</td>
<td>10%</td>
<td>77%</td>
</tr>
</tbody>
</table>

Antibiotic prescribing by condition, children < 18, US, 2006-8

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treated with Abx</th>
<th>% Receiving Broad-spectrum Abx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>48%</td>
<td>53%</td>
</tr>
<tr>
<td>Abx indicated</td>
<td>72%</td>
<td>48%</td>
</tr>
<tr>
<td>Abx not indicated</td>
<td>30%</td>
<td>63%</td>
</tr>
<tr>
<td>Other respiratory</td>
<td>28%</td>
<td>65%</td>
</tr>
<tr>
<td>Other</td>
<td>8%</td>
<td>42%</td>
</tr>
<tr>
<td>Skin</td>
<td>19%</td>
<td>38%</td>
</tr>
<tr>
<td>UTI</td>
<td>59%</td>
<td>39%</td>
</tr>
<tr>
<td>GI</td>
<td>6%</td>
<td>54%</td>
</tr>
</tbody>
</table>


Proportion of patients filling antibiotic prescriptions vs proportion needing antibiotics, Oregon, 2013

Gonzales CID 2001;33:757-62; Oregon APAC data, 2013

Proportion of patients filling antibiotic prescriptions, by age group and syndrome, Oregon, 2013
Proportion of patients receiving broad and narrow spectrum antibiotics, by syndrome, Oregon, 2011-12

Class of antibiotics used for respiratory infections, Oregon, 2013

Review of Upper Respiratory Tract Pathogens and Trends in Resistance
**Streptococcus pneumoniae (SP)**

- Leading cause of bacterial meningitis, CAP, and AOM
- 2nd leading cause of bacteremia

**Incidence of Invasive Pneumococcal Disease by Age, Portland, Oregon EIP**

**Risk factors for acquisition of DRSP**

- Recent antibiotic use, especially macrolides
- Age < 2 years or > 65 years
- Daycare attendance
- Exposure to young children
- Immunodeficiencies and underlying diseases
- Recent hospitalization

Campbell Clin Infect Dis 1998;26:1188-95

**Proportion of pneumococcal isolates resistant to commonly used antibiotics Portland, 2001–2015**

Oregon Emerging Infections Program ABCs data
Mechanism of resistance: 
*S. pneumoniae*

- Alterations in alterations in penicillin-binding proteins
- Can overcome by increasing dose
- Rationale for use of high dose amoxicillin

*Haemophilus influenzae* (HI)

- Prior to vaccine introduction, type B leading cause of bacterial meningitis in children, as well as epiglottitis, pneumonia, septic arthritis, cellulitis, osteomyelitis, and bacteremia (especially in kids)
- Type B now very rare, only 1-2 cases per year in Oregon
- Mechanism of resistance: 25%-45% produce β-lactamase, can’t be treated with higher dose

*Moraxella catarrhalis*

- After SI and HI 3rd leading cause of AOM in children (15%-20% of cases), also causes pneumonia in adults, especially in elderly, and sinusitis
- 90% produce β-lactamase
Group A beta-hemolytic streptococcus (GAS)

- Most frequent clinical manifestations are pharyngitis and pyoderma, less commonly erysipelas, cellulitis, necrotizing fasciitis (known as "flesh-eating virus" in the tabloids), myositis, myonecrosis, and streptococcal shock syndrome

- GAS accounts for 20%-30% of pediatric cases of pharyngitis, 10% in adults

Proportion of invasive GAS isolates resistant to commonly used antibiotics
Portland, 2014

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Intermediate</th>
<th>Fully Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Penicillin</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0%</td>
<td>1%</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0%</td>
<td>10%</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>0%</td>
<td>30%</td>
</tr>
</tbody>
</table>

Oregon Emerging Infections Program ABCs data

Management of Upper Respiratory Tract Infections
Basic Strategy

• Don’t give antibiotics unless indicated
  – Wait and see option

• When giving antibiotics:
  – Narrowest spectrum possible
  – Optimal dosage, timing (high dose, short course)
  – Macrolides not good choice for pneumococcal or H. influenzae
  – Mostly useful for pertussis, some cases of community-acquired pneumonia

Diagnostic criteria for AOM

Patients with MEE (lack of mobility of TM with insufflation or presence of air-fluid interface), plus one of the following:

• Moderate to severe bulging of the TM; or
• New onset of otorrhea not due to otitis externa; or
• Mild bulging of the TM and recent (< 48 hours) onset of ear pain or intense erythema of the TM

Treatment of AOM: observation option (wait and see)

<table>
<thead>
<tr>
<th></th>
<th>6 mo – 2 yr</th>
<th>≥ 2 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otorrhea + AOM</td>
<td>Antibiotics</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Severe* Sx (bi- or unilateral)</td>
<td>Antibiotics</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Bilateral, no otorrhea</td>
<td>Antibiotics</td>
<td>Antibiotics or observation</td>
</tr>
<tr>
<td>Unilateral, no otorrhea</td>
<td>Antibiotics or observation</td>
<td>Antibiotics or observation</td>
</tr>
</tbody>
</table>

*Persistent otalgia > 48 hours, temperature ≥ 39°, or follow-up uncertain
### Treatment of Acute OM

**Wait and See:**
- Defer antibiotics for 48-72 hours
- Involve caretaker in decision
- Treat pain, acetaminophen or ibuprofen preferred, longer-lasting than topical
- Only if follow-up can be assured and pt > 6 mos

AAP Pediatrics 2013;131:e964-e999

### Treatment of Acute OM

**Antibiotic choice:**
- **Amoxicillin benefits:**
  - Narrow spectrum, good safety profile, tastes great
  - Little resistance to penicillin/amoxicillin in OR
  - 45 mg/kg/day X 10 days if < 2 yrs, 5-7 days if older
- **Risks for DRSP:** < 2 years, recent use of Abx or hospitalization, daycare, immunocompromise
  - high dose amoxicillin for DRSP
  - AOM with conjunctivitis or amoxicillin in past 30 days
  - use amoxicillin-clavulanate for H. influenza

### Alternative regimens for treatment of acute OM

- **For treatment failure:**
  - amoxicillin/clavulanate 80-90mg/kg/day bid or tid
  - cefdinir, cefpodoxime, or cefixime (consider ceftriaxone 50 mg/kg IM qd X 3 if vomiting)

- **For penicillin-allergic patients:**
  - Mild: cefdinir, cefpodoxime, or cefixime
  - Severe (hives or anaphylaxis): levofloxacin, clindamycin, consider ENT consultation and tympanocentesis
### Cough illness/bronchitis

- Bronchitis is a self-limited inflammation of the bronchial respiratory mucosa, viruses account for 90%.
- Although bacteria can be found in sputum, bronchial biopsies have not shown bacterial invasion.
- Consider pertussis, particularly if disease present in community.
- Purulent sputum usually indicates presence of sloughed tracheobronchial epithelium and WBCs.

Wenzel NEJM 2006;355:2125-30; Albert Am Family Physician 2010;82:1345-50

### Antibiotics for the common cold benefit on day 5?

**Diagram:**
![Diagram showing patients recording yellow sputum over days since enrollment]

Stott BMJ 1976;2:556

### Diagnosis and management: adults

<table>
<thead>
<tr>
<th>Duration &lt; 3 weeks</th>
<th>Duration &gt; 3 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>If no fever, chest exam is clear and VS are normal, pneumonia is highly unlikely.</td>
<td>Obtain CXR.</td>
</tr>
<tr>
<td>Recommend: avoid cigarette smoke, bronchodilators, hydration, steam to loosen secretions.</td>
<td>Most likely: postnasal drip, asthma/RAD, secondhand smoke, GER, ACE-inhibitor cough, environmental exposures, chronic bronchitis, bronchectasis, malignancy.</td>
</tr>
<tr>
<td></td>
<td>Infectious: consider B. pertussis, M. pneumoniae, C. pneumoniae.</td>
</tr>
<tr>
<td></td>
<td>Treat COPD exacerbation amoxicillin, TMP/SMX or doxycycline and 7-10d course of oral corticosteroids.</td>
</tr>
</tbody>
</table>
### Diagnosis and management: children

<table>
<thead>
<tr>
<th>Duration &lt; 4 weeks</th>
<th>Duration &gt; 4 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>• If no fever, chest exam is clear and VS are normal, pneumonia is highly unlikely</td>
<td>• Obtain CXR and spirometry (&gt;3-6 yrs)</td>
</tr>
<tr>
<td>• Recommend: avoid cigarette smoke, drink plenty of liquids, nasal saline washes, topical vapor rubs</td>
<td>• Most likely: postnasal drip, allergies, habit cough, sinusitis, CF, foreign body aspiration, asthma/RAD, secondhand smoke, GER, congenital malformations</td>
</tr>
<tr>
<td>• acetaminophen or ibuprofen for fever/pain, rest</td>
<td>• Infectious: consider B. pertussis, M. pneumoniae, C. pneumoniae</td>
</tr>
<tr>
<td></td>
<td>• Treat with macrolide or if &gt; 8 yrs, doxycycline</td>
</tr>
</tbody>
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### Sinusitis

- Antimicrobial treatment should be limited to:
  - prolonged nonspecific upper respiratory signs and symptoms (i.e. rhinorrhea and cough without improvement) for > 10 days, or
  - onset with severe symptoms or signs of fever > 39.0 C, and nasal discharge or facial pain, lasting at least 3-4 days, or
  - worsening signs/symptoms (new onset of fever, HA, or increased nasal discharge) following a URI of 5-6 days

### Duration of symptoms in 139 rhinovirus colds

- Fever/sore throat/cough/nasal discharge

Gwaltney JAMA 1967;202:158

IDSNA (Chow) Clin Inf Dis 2012;54:e72-e112
Treatment of acute sinusitis: adults

**Initial choice:**
- amoxicillin 1 gm po bid X 5-7 days

**High dose amoxicillin?**
- severe infection, daycare exposure, age>65, recent hospitalization, abx use in past 3 months, immunocompromised

**Treatment Failure:**
- High dose amoxicillin-clavulanate

**Beta-lactam allergy:**
- FQ or doxycycline

**Adjunctive measures:**
- Nasal corticosteroid spray
- Sinus irrigation

IDSA (Chow) Clin Inf Dis 2012;54:e72-e112

Treatment of acute sinusitis: children

**Initial choice:**
- amoxicillin 45-50 mg/kg/day X 7-10 days

**High dose Amoxicillin?**
- Severe infection, daycare, age <2, recent hospitalization, abx use in past 3 months, immunocompromised

**Treatment failure:**
- High dose amoxicillin-clavulanate

**Beta-lactam allergy**
- Mild (no hives or anaphylaxis): cefixime, cefdinir, or cefpodoxime
- If hives or anaphylaxis: FQ or if > 8 yrs, doxycycline

IDSA (Chow) Clin Inf Dis 2012;54:e72-e112

Treatment of acute sinusitis: other considerations

- **Duration:**
  - Adults, 5-7 days
  - Children, 10-14 days
- **Age:** doxycycline > 8 years
- **Macrolides and TMP/SMX not recommended**
- **For pts who worsen despite 72 hours of Rx or don’t improve in 3-5 days:** evaluate for resistant pathogens, inadequate dosing, a non-infectious cause (allergy, structural abnormality)
Pharyngitis

- Sore throat accounts for 1%-2% of all pt visits to primary care offices and EDs
- Most caused by viruses
- GAS only common bacterial etiology requiring treatment

<table>
<thead>
<tr>
<th>% of sore throats caused by GAS</th>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td></td>
<td>15%-30% in cooler months, rare under age 3</td>
</tr>
</tbody>
</table>


Rationale for treating GAS pharyngitis

- Relative benefit of antibiotics low:
  - Rheumatic fever now rare in US, number needed to treat=3,000-4,000
  - Doesn’t prevent acute glomerulonephritis
  - Strep due to groups C and G don’t lead to rheumatic fever and don’t need Rx
- Main benefit: antibiotics started within 2-3 days of onset shortens duration of symptoms by 1-2 days

Del Mar Cochrane Database Syst Review 2006; Cooper Ann Intern Med 2001;134:509-17

Signs and symptoms of GAS pharyngitis

1) tonsillar exudate; 2) tender anterior cervical lymph nodes; 3) no cough; 4) fever

- If 2-4 present, obtain rapid antigen test and treat if positive
- If < 2 are present, supportive care only

# Treatment of acute GAS pharyngitis

- **Adults:**
  - single dose benzathine penicillin 1.2 m.u. IM or penicillin V 500 mg po bid X 10 days or amoxicillin 775 mg po qd (FDA-approved)

- **Children <12 years:**
  - amoxicillin or penicillin V 45 mg/kg/day X 10 days (not FDA-approved, but Sanford guide recommends amoxicillin qd in kids)

- **For penicillin-allergic patients:**
  - Cephalexin or cefadroxil or clindamycin

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## Other considerations

- Must treat for at least 24 hours before return to daycare/school
- Routine testing of asymptomatic contacts not recommended
- Post-therapy culturing not recommended
- Recurrent episodes of culture-confirmed GAS may be recurrent viral episodes in chronic carrier (20% of school children)
  - Carriers unlikely to spread and are at low risk for complications themselves

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## AWARE

- **Clinicians**
  - Consensus guidelines
  - Printed materials to give patients
  - Motivational interviewing seminars

- **General public**
  - Mass media
  - Training of students in health professions
  - Development of curriculum for school
  - children, K-6, HS

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[www.healthoregon.org/antibiotics](http://www.healthoregon.org/antibiotics)