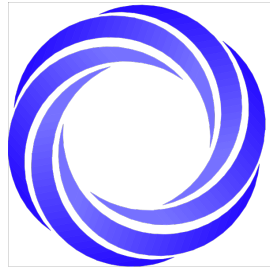


Antibiotics & Common Infections: Stewardship, Effectiveness, Safety & Clinical Pearls

Welcome
We will begin shortly.



The Canadian Pharmacists Association is pleased to be collaborating with the following organizations:



National Collaborating Centre
for Infectious Diseases

Centre de collaboration nationale
des maladies infectieuses



Public Health
Agency of Canada

Agence de la santé
publique du Canada



PHARMACY
ASSOCIATION
OF SASKATCHEWAN



CANADIAN
PHARMACISTS
ASSOCIATION

ASSOCIATION DES
PHARMACIENS
DU CANADA

Today's Speakers

Zack Dumont, BSP, ACPR

Regina Qu'Appelle Health Region & RxFiles, SK

Brenda Schuster, BSP, ACPR, PharmD, FCSHP

Regina Crossings Centre & RxFiles, SK

With content adapted, with permission, from:



Disclosure(s)

No pharmaceutical industry funding

RxFiles

- Receives grant from Saskatchewan Health through Saskatoon Health Region for academic detailing in Saskatchewan
- Receives revenue from sale of book and subscriptions from outside SK

Not for profit; not for loss!



Learning Objectives

- To understand which common infections are of predominantly viral etiology and be able to better communicate this to patients, when evidence and clinical judgment suggest antibiotics are not required
- To be able to recommend symptomatic treatment that may be effective and appropriate for common viral infections
- To be able to discern when antibiotic treatment may be appropriate for acute sinusitis, pharyngitis, and bronchitis, & to evaluate prescriptions for the appropriate dose & duration
- To be able to use relevant local susceptibility data for rational empiric antibiotic selection for community acquired pneumonia and appreciate the growing resistance concerns for bacterial agents such as macrolides.
- To highlight the role of pharmacists in appropriate antibiotic use



Antibiotic Trivia

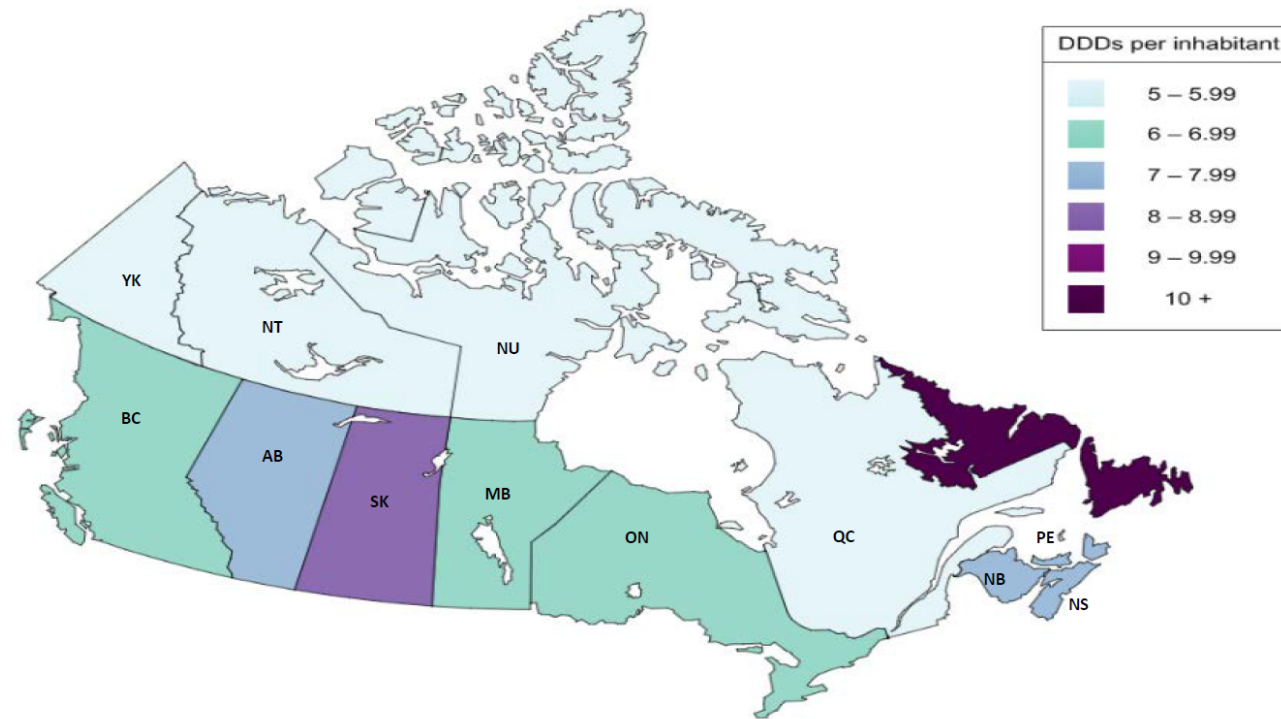
- What is the recommended dose and duration for amoxicillin for upper respiratory tract infections?
 - A) 500 mg po BID x 10 days
 - B) 500 mg po TID x 5 days
 - C) 1000 mg po TID x 7 days
 - D) all of the above

- Jot down your response and we'll revisit at the end



CANADIAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM – REPORT 2016

Total antimicrobials dispensed through community pharmacies within provinces or territories in Canada, 2014⁷





Antibiotics & Common Infections

Stewardship, Effectiveness, Safety & Clinical Pearls

October 2016

RxFiles

Fall/Winter 2016-2017

Acute Bronchitis

Community Acquired Pneumonia

Pharyngitis

Sinusitis

ANTIMICROBIAL RELATED LINKS

CANADIAN GUIDELINES

Bugs & Drugs (Alberta/BC): <http://www.bugsanddrugs.ca/>



MUMS Guidelines - "Orange Book" (Anti-infective Review Panel): <http://www.mumshealth.com>



PATIENT RESOURCES



Canadian Antibiotic Awareness: <http://www.antibioticawareness.ca> which includes:

1. **Viral Prescription Pad** for respiratory infections (download or order for free), provides information about symptomatic relief for viral infections and indicates when patients should consider a return visit.

2. **Talking with Patients about When to Use Antibiotics** provides communication tips to effectively address requests for antibiotics for viral infections.

Enhanced communication skills reduce antibiotic prescribing (27% absolute risk reduction - ARR).

3. **Posters for office** A poster displayed in the practice waiting room stating a commitment to reducing antibiotic use reduces inappropriate antibiotic use (20% ARR).

<http://www.dobugsneeddrugs.org/wp-content/uploads/info-sheet-english.pdf>

4. **Handouts for Patients** <http://healthy Canadians.gc.ca/drugs-products-medicaments-produits/buying-using-achat-utilisation/antibiotic-resistance-antibiotique/material-materiel/brochure-eng.php>

OTHER

www.rqhealth.ca/antimicrobialstewardship

For more public/patient resource links see: www.RxFiles.ca/ABX

ANTIMICROBIAL STEWARDSHIP

There are world-wide efforts that look for strategies to deal with the challenge of growing antimicrobial resistance. How can we all work together to be stewards of this important, but limited resource?

SELECT ANTIBIOTIC RESISTANT PATHOGENS OF MAJOR CONCERN

- methicillin-resistant *Staphylococcus aureus* (MRSA)
- multi-drug resistant *Streptococcus pneumoniae* (MRSP)
- vancomycin-resistant *enterococci* (VRE)
- multi-drug resistant *Escherichia coli* & other gram negative bacteria (e.g. ESBL)

KEY STRATEGIES FOR REDUCING ANTIBIOTICS

- vaccinations to prevent infections and decrease antibiotic use
- practice and educate on infection prevention (wash hands, avoid touching eyes, cough etiquette, stay home when sick)
- avoid antibiotics for infections of predominantly viral cause
- use of point-of-care tools/tests
- treat infection, not contamination
- avoid treating positive cultures in the absence of signs/symptoms

STRATEGIES WHEN ANTIBIOTICS INDICATED

- Whenever suitable:
 - use narrow-spectrum agent
 - use shorter duration therapy
- tailor empiric antibiotic choice & dosage according to local bacterial prevalence and resistance patterns
- calculate weight-based dose in kids
- if patient experiences an adverse reaction, provide patient education and document details to avoid labelling a side effect as an "allergy"
- discourage saving of "left-over" antibiotics for future use

¹ http://www.cdc.gov/media/releases/2011/i0407_antimicrobialresistance.pdf

GETTING STRATEGIES TO WORK - REAL WORLD

- Public, patient & provider education over time to change expectations
- Realistic appreciation for viral versus bacterial etiologies
- Delayed prescriptions for select conditions with instructions to fill only if symptoms do not resolve or condition worsens. (Offer to those who value convenience.)
- *"It's easy to prescribe antibiotics. It takes time, energy & trust not to do so."*¹ Success lies in changing the culture & the understanding of antibiotic limitations, benefits & harms.

ANTIBIOTIC HARMS - UNDERAPPRECIATED

→ To the Patient

- 1 in 5 emergency room visits for adverse drug events (ADEs) are from antibiotics.
- Antibiotics are the most common cause of ADEs in children, accounting for 7 of the top 15 drugs leading to ADE-related ER visits.
- Antibiotic associated diarrhea, including *Clostridium difficile* diarrhea
- Cardiac - QT interactions: with clarithromycin & fluoroquinolones
- Central nervous system (CNS) adverse effects (e.g. dizziness, headache, sleep disturbance, seizure, encephalopathy)
- Hyperkalemia (cotrimoxazole)
- Skin: minor/major (e.g. cotrimoxazole)
- Tendon rupture (fluoroquinolones)
- Risk of drug interactions (warfarin, statins/macrolides, ...)
- ↑ risk of secondary fungal infections
- ↑ risk of an untreatable infection in the patient due to ↑ bacterial resistance

→ To Society

- financial costs of treating adverse reactions (USA: \$20 billion in excess healthcare costs)¹
- antimicrobial resistance: more difficult to treat infections over time, leading eventually to no adequate options

For what's inside, see [Table of Contents, Page 2](#)



CANADIAN PHARMACISTS ASSOCIATION

ASSOCIATION DES PHARMACIENS DU CANADA

Case – 5 yo female

- Cough x 7/7, sputum production, wheezing
- Unremarkable medical history, NKDA

- *How would you respond?*



RxFiles

Fall/Winter 2016-2017

Clinic and pharmacy posters

Available at

www.RxFiles.ca/ABX



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DU CANADA

www.pharmacists.ca

Management of Bronchitis

- What is the value of using antibiotics?
- If antibiotics are out, what can be done?
 - What about DM? Bronchodilators?
- Patients should be educated to see their prescriber when?



PEARLS for the MANAGEMENT of ACUTE UNCOMPLICATED BRONCHITIS

- **Antibiotics are NOT recommended**, as bronchitis is predominantly viral.
- Advise on treatments that will provide **symptomatic relief**: maintaining hydration & ↑ humidity. Cough suppressants may be considered for managing cough, & inhaled bronchodilators if wheezing is present. **Honey may help children**.
- Patients should see their prescriber if: 1) symptoms worsen, 2) new symptoms develop (e.g. dyspnea, fever, vomiting), 3) cough >1month, or 4) >3 episodes/yr.

PRE-TREATMENT CONSIDERATIONS

- Inappropriate antibiotic use is driving resistance & leading to a crisis. Please examine your own prescribing practices. Refer to newsletter cover.
- **The majority of acute uncomplicated bronchitis cases are viral (90% in adults & 95-100% in children).**
- **Antibiotics are NOT recommended** for acute uncomplicated bronchitis. Several RCTs assessing the efficacy of antibiotics for this indication have failed to show a benefit; however, up to 80% of adults in the U.S. still receive an antibiotic.
- Acute **uncomplicated** bronchitis is self-limiting. Cough usually persists for 1 to 3 weeks, although up to 50% of viral cases will have a cough beyond 3 weeks. Airway hyperactivity may last up to 6 weeks. Recommend symptom management.
- Acute **complicated** bronchitis (e.g. history of smoking, impaired lung function, chronic heart disease, immunocompromised) may require further investigation (e.g. lung function tests, chest x-ray).
- Rule out **pneumonia** if the following signs are present: HR>100bpm, RR >24 breaths/min, oral temperature >38°C, or findings of local consolidation.
- **Coloured sputum** does not reliably differentiate between bacterial or viral origin.
- **Fever** is uncommon, & may be indicative of influenza or pneumonia.
- If the patient has confirmed **pertussis**, see RxFiles pg 78 for antibiotic regimens. Uncommon, but there is the occasional outbreak. Encourage vaccination.

MOST COMMON PATHOGENS

- Viral – e.g. *Influenza A, Influenza B, Parainfluenza, RSV, & Adenovirus*

EMPIRIC DRUG REGIMENS OF CHOICE & SUSCEPTIBILITY CONCERNS

Antibiotics are not recommended for acute uncomplicated bronchitis.

- Multiple studies & meta-analyses assessing antibiotics for the treatment of acute uncomplicated bronchitis have shown no benefit or modest improvement, along with an ↑ risk of adverse events.
- For example, a 2014 Cochrane review (17 RCTs, n=3,936) evaluating antibiotics (beta-lactams, doxycycline, macrolides, TMP-SMX) vs placebo found no difference in clinical improvement. Antibiotics ↓ cough (NNT=6), night cough (NNT=7) & mean duration of cough by 0.5 days, but ↑ risk of adverse events (NNH=5, primarily gastrointestinal related).

SYMPTOM MANAGEMENT no quality evidence, but anecdotally may help

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| NONPHARM | <ul style="list-style-type: none"> • ↑/maintain hydration • ↑ humidity (e.g. PRN humidifier to maintain 30-50% humidity) | <ul style="list-style-type: none"> - No evidence for or against. - Hydration: caution in HF & CKD patients - Humidifier: clean frequently to ↓ risk of bacteria/fungi growth |
| | Honey 2.5 to 10mL po HS Not recommended in <1yr due to concerns with infant botulism | <ul style="list-style-type: none"> - No strong evidence for or against. - Cochrane review (3 RCTs, n=568): better than placebo, but inferior to dextromethorphan in ↓ cough frequency (cough duration not assessed). |
| COUGH SUPPRESSANTS | Dextromethorphan (DM) e.g. BENYLIN DM, ROBITUSSIN DM | <ul style="list-style-type: none"> - May ↓ number of coughing episodes but does not ↓ duration of illness. - Not recommended in children under 6 years of age due to safety & efficacy concerns. <small>HEALTH CANADA</small> |
| | 10-30mg po q6-8hr PRN | |
| BRONCHODILATORS | Salbutamol <small>VENTOLIN</small> 100mcg 2 puffs inhaled QID | <ul style="list-style-type: none"> - Limited evidence (1 study with fenoterol, n=80). - May ↓ duration of cough in patients with wheezing/airflow obstruction when used x 1wk (NNT=2, NNH=2 for tremor, shakiness, nervousness). |
| | Ipratropium <small>ATROVENT</small> 20mcg 4 puffs QID | <ul style="list-style-type: none"> - Limited evidence (1 study, n = 14 for 3 weeks) in post-infectious cough. - May improve daytime & nighttime cough, & dyspnea associated with coughing. |

- **Encourage prevention** e.g. smoking cessation, ↓ exposure to second-hand smoke.

Not routinely recommended for symptom management:

- * Oral or inhaled corticosteroids are not recommended in patients with acute bronchitis without asthma.
- * Expectorants (e.g. guaifenesin): most evidence failed to show a benefit.

Clinical Q&A

Should pts ≥ 65yrs be treated with an ABX to ↓ the risk of developing pneumonia?

- No, but patients presenting with signs of pneumonia should undergo investigation (e.g. chest x-ray).
- A previous retrospective cohort study (1991 to 2001) suggested that individuals with acute bronchitis who were ≥65 years may benefit from antibiotics (NNT to prevent 1 additional case of pneumonia in the month following acute bronchitis was 39 for those ≥65 years, & 199 for those between 16-64 years of age).
- However, a 2013 RCT (n=1,038) comparing amoxicillin 1000mg po TID x 7 days to placebo showed no difference in duration or severity of symptoms up to 1 month, regardless of age. There was an ↑ risk of adverse events (nausea, rash, diarrhea) with the amoxicillin group (NNH=22).

Abbreviations: ABX=antibiotic CKD=chronic kidney disease HF=heart failure NNH=number needed to harm NNT=number needed to treat RCTs=randomized controlled trials TMP-SMX=trimethoprim/sulfamethoxazole

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Case – 5 yo female

- Cough x 7/7, sputum production, wheezing
- Unremarkable medical history, NKDA

- *How would you respond?*
 - No antibiotic
 - Honey 2.5 to 10 mL po HS
 - Humidifier in bedroom
 - Acetaminophen 10 to 15 mg/kg po q4h prn
 - Viral Rx – sample on next slide



RxFiles

Fall/Winter 2016-2017

Viral prescriptions pads

Available in over a dozen languages at

www.RxFiles.ca/ABX

Rx

Patient Name: _____ Date: _____

The symptoms you presented with today suggest a VIRAL infection.

- Upper Respiratory Tract Infection (Common Cold): Lasts 7-14 days
- Flu: Lasts 7-14 days
- Acute Pharyngitis ("Sore Throat"): Lasts 3-7 days, up to ≤ 10 days
- Acute Bronchitis/"Chest Cold" (Cough): Lasts 7-21 days
- Acute Sinusitis ("Sinus Infection"): Lasts 7-14 days

You have not been prescribed antibiotics because antibiotics are not effective in treating viral infections, can cause side effects (e.g. diarrhea, yeast infections) and may even cause serious harm.

When you have a viral infection, it is very important to get plenty of rest and give your body time to fight off the virus.

If you follow these instructions, you should feel better soon:

- ➔ Rest as much as possible
- ➔ Drink plenty of fluids
- ➔ Wash your hands frequently
- ➔ Take over-the-counter medication, as advised:

- Acetaminophen (e.g. Tylenol®) for fever and aches
- Ibuprofen (e.g. Advil®) for fever and aches
- Naproxen (e.g. Aleve®) for fever and aches
- Lozenge (cough candy) for sore throat
- Nasal spray (e.g. Salinex®, Flonase®, Nasacort® or Otrivin®) for nasal stuffiness. {NOTE: observe label directions; some products are problematic if overused!}
- Other: _____

Please return to your provider if:

- ➔ Symptoms do not improve in _____ day(s), or worsen at any time
- ➔ You develop a high fever (above 38°C, or _____ as directed)
- ➔ Other: _____

Prescriber _____

This "Viral Prescription Pad" has been adapted from the RQHR Antimicrobial Stewardship Program www.rqhealth.ca/antimicrobialstewardship, and is available in other languages. <http://www.rxfiles.ca/rxfiles/uploads/documents/ABX-Viral-Prescription-Pad-Languages.pdf>



Visit www.RxFiles.ca/ABX for more information.



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- I need help with my husband's cough...what can you recommend??
 - What questions might you ask to make an clinical assessment?



Can you tell me

How long has he had the cough ?

Productive /dry?

Chest cold?
Other symptoms?
SOB? temp?

Other medical conditions?



Case – 64 yo SOB, T 38.1, feels awful



- Today: CXR revealed pneumonia
- Clarithromycin 500 mg bid x 10 day for pneumonia
- PMH: hyperlipidemia
- Meds: atorvastatin 10 mg daily

| CRB-65 | | |
|--|-------------------|-------------------------------|
| Criteria | | Points |
| <u>C</u> onfusion: new onset based on a specific mental test, or disorientation to person, place or time | | 1 |
| <u>R</u> espiratory rate ≥ 30 breaths/minute | | 1 |
| Low <u>B</u> lood pressure: SBP < 90 mmHg or DBP ≤ 60 mmHg | | 1 |
| Age ≥ 65 years | | 1 |
| Score | Risk of Mortality | Suggested Management |
| 0 | $< 2\%$ | • Outpatient |
| 1-2 | $\sim 9\%$ | • Consider hospital admission |
| ≥ 3 | $> 19\%$ | • Hospital admission |



EMPIRIC DRUG REGIMENS OF CHOICE

PREVIOUSLY HEALTHY ADULT OUTPATIENT WITH NO RECENT ANTIBIOTIC USE

Most Common Bacterial Pathogen: Gram +ve: *Streptococcus pneumoniae*

Potential Pathogens: Atypical pathogens (*M. pneumoniae*, *C. pneumoniae*)

| | | |
|---|---|---|
| <p>Doxycycline</p> | <p>200mg po Day 1, then 100mg po BID x 5-7 days</p> | <p>✓ Based on SK antibiogram data^{RQHR, SDCL, SHR}, doxycycline has good activity against common/potential CAP pathogens (i.e. <i>S. pneumoniae</i> & atypical pathogens).</p> |
| <p>Amoxicillin</p> <p>may consider adding a macrolide if concerned about atypical pathogens (see Clinical Q&A)</p> | <p>1000mg po TID x 5-7 days</p> <p>Clarithromycin preferred if no major DIs e.g. warfarin, digoxin, statin, as may result in less resistance than azithro (t½).</p> <p>Clarithromycin: 500mg po BID x 5-7 days, or XL 1000mg po daily x 5-7 days</p> <p>Azithromycin: 500mg po daily x 3 days, or 500mg po Day 1, then 250mg daily x 4 days</p> | <p>Amoxicillin:</p> <p>✓ <i>S. pneumoniae</i> (even intermediate susceptibility isolates) remain sensitive to high-dose amoxicillin.</p> <p>✗ Does not cover atypical pathogens. See Clinical Q&A on whether atypical pathogen coverage is needed.</p> <p>Macrolides:</p> <p>✓ May be added to amoxicillin to cover atypical pathogens.</p> <p>✗ There are concerns with using macrolides as monotherapy due to ↑ <i>S. pneumoniae</i> resistance. 2015 SK susceptibilities: RQHR 70%, SDCL 62%, SHR 80% (but 70% in 2014).</p> |



ADULT OUTPATIENT with COMORBIDITIES / ABX RESISTANT RISK FACTORS*

Most Common Bacterial Pathogen: Gram +ve: *S. pneumoniae*

Potential Pathogens: Gram –ve: *H. influenza, M. catarrhalis, K. pneumoniae*

Atypical pathogens: *M. pneumoniae, C. pneumoniae, Legionella*

| | | |
|--|--|---|
| Doxycycline | 200mg po Day 1, then 100mg po BID x 5-7 days | ✓ As above, & will also cover <i>S.aureus</i> & potential gram –ve pathogens. |
| Amox - Clav CLAVULIN | 875mg po BID x 5-7 days | Amoxicillin - Clavulanate: ✓ This category of patients may be at ↑ risk of beta-lactam resistance, which is addressed with the addition of clavulanate to amoxicillin. ✗ Does not cover atypical pathogens . See Clinical Q&A on whether atypical pathogen coverage is needed. Macrolides: as above |
| may consider adding a macrolide re: atypical pathogens (see Clinical Q&A) | see above macrolide options/dosing | |

Fluoroquinolones should be reserved for treatment failures, comorbidities with recent antibiotic use, allergies or documented infections with highly drug-resistant bacteria. Examples: levofloxacin ^{LEVAQUIN} 500-750 mg po once daily x 5 days
moxifloxacin ^{AVELOX} 400 mg po once daily x 5 days



Comorbidity or Risk factors for Abx resistant *S. Pneumoniae*

- age greater than 65
- cardiac
- pulmonary disease
- renal disease
- hepatic failure
- malnutrition or acute weight loss (more than 5%)
- malignancy
- diabetes
- immunosuppression
- smoking
- alcoholism
- hospitalizations or broad spectrum abx in last 3 months



Case – 64 yo SOB, T 38.1, feels awful



- Clarithromycin 500 mg bid x 10 day for pneumonia
- PMH: hyperlipidemia
- Meds: atorvastatin 10 mg daily
- Plan:
 - Provide symptomatic support (Analgesics for fever, aches, cough suppressant? Honey?)
 - Follow-up phone call 48-72hr: If not improving or feeling worsening refer to physician for possible treatment failure, fax recommendations for switch in therapy
 - Ensure annual influenza vaccine, pneumococcal vaccine appointment in future

COMMUNITY ACQUIRED PNEUMONIA: Management Considerations

PEARLS for the MANAGEMENT of COMMUNITY ACQUIRED PNEUMONIA (CAP)

- A **chest x-ray** is recommended to confirm suspected pneumonia. IDSA'07 LOE: moderate
- The **CRB-65 score** can be used to help identify adults who may require hospital admission due to a higher risk of mortality.
- ***S. pneumoniae*** is the most common bacteria, even in those with comorbidities.
- **Doxycycline** covers the majority of bacterial CAP pathogens (e.g. *S. pneumoniae*, *S. aureus*, *H. influenzae* & atypicals). Standard duration of therapy is **5 to 7 days**.
- There is limited data on the role of **corticosteroids** in outpatients.
- Recommend the **influenza vaccine** every fall.
- Recommend the **pneumococcal vaccine** x1 for those **≥65 years of age**, or at high risk regardless of age (e.g. chronic cardiac or pulmonary disease, DM, CKD).
- Patients should see their prescriber if symptoms worsen or do not improve within **48-72 hours**. Cough, fatigue or dyspnea may persist for up to **1 month**, or longer.



COMMUNITY ACQUIRED PNEUMONIA

Role of the Pharmacist

- Review for correct drug, dose, duration, drug interactions, contraindications/allergies
- Educate patients on what to expect and how to manage side effects, when to return to physician
- Set up appropriate expectations on when then may feel better, what to do if they feel worse
- Access patients for potential treatment failures
- Provide recommendations for alternate therapy for treatment failures
- Provide recommendations for how to manage significant drug interactions



Case – 15 year-old boy with strep throat

- Mother is very upset:
 - The locum who is filling in for her regular physician wouldn't prescribe an antibiotic, and instead took a throat swab
 - It's Friday; swab won't be processed until next week
 - She shows you her son's throat, and says, "Look at all that pus! It's clearly a bacterial infection."
 - Great-uncle had acute rheumatic fever due to strep throat
 - She asks you to recommend another physician... one that will prescribe an antibiotic!



SHOULD ANTIBIOTICS BE USED TO TREAT PHARYNGITIS?

- 80-90% of adults (>70% of children) do NOT require antibiotics as infection likely viral.

| Modified Centor (or McIssac) Score | | |
|---|---------------------------------|---|
| Criteria | | Points |
| Temperature > 38°C (>100.5 °F) oral temperature used in Centor score (adults) | | 1 |
| Absence of cough | | 1 |
| Swollen, tender anterior cervical nodes | | 1 |
| Tonsillar swelling or exudate | | 1 |
| Age 3 to 14 years | | 1 |
| Age 15 to 44 years | | 0 |
| Age ≥ 45 years | | -1 |
| Score | Risk of Streptococcal Infection | Suggested Management |
| -1 to 0 | 1 to 2.5% | - Symptomatic treatment - No RADT, culture or antibiotic needed |
| 1 | 5 to 10% | |
| 2 | 11 to 17% | - RADT or throat swab for culture. - If positive for GAS ⇒ antibiotic. |
| 3 | 28 to 35% | |
| ≥4 | 51 to 53% | |

Modified Centor score: sensitivity 94% (95% CI 92-97%), specificity 54% (95% CI 49-59%). Lower specificity leans towards false positives & over-treatment.

- **Exceptions:** the modified Centor score may not accurately predict risk of GAS during epidemics or in high risk populations, e.g. individuals with a history of rheumatic fever, valvular heart disease, or immunosuppression. Use clinical judgment & consider testing (RADT/throat swab) more broadly.



SHOULD ANTIBIOTICS BE USED TO TREAT PHARYNGITIS?

- 80-90% of adults (>70% of children) do NOT require antibiotics as infection likely viral.
- Patients with a positive throat swab should receive an antibiotic to ↓ the risk of complications. See modified Centor score on left column, & antibiotic table below.
- The turn-around-time for throat swab results can take a few days. However, antibiotics started within 9 days of symptom onset in confirmed GAS will prevent rheumatic fever.
- If antibiotics are started empirically, ensure agent is discontinued if throat swab negative.

Duration of Antibiotic Therapy:

- Confirmed bacterial pharyngitis should be treated with 10 days of antibiotics (exception: if azithromycin is used in penicillin allergic patients; other options available).
- Patients will likely have clinical improvement within the first few days of therapy, but 10 days of therapy is recommended for preventing acute rheumatic fever, & short courses are not as effective for treating the infection.
 - E.g. a meta-analysis comparing 5 vs 10 days of penicillin (2 RCTs, n=309) concluded short courses were inferior in achieving bacterial cure, OR 0.29 (CI 95% 0.13-0.63).



SYMPTOM MANAGEMENT

| | | |
|---------------------|--|--|
| SYSTEMIC ANALGESICS | e.g. Ibuprofen ^{ADVIL, g} Peds: 5-10 mg/kg po q6-8hr PRN (maximum 40mg/kg/day) Adults: 400mg po q6-8hr PRN | - Ibuprofen ↓ associated pain more than acetaminophen & placebo. - Reduces fever. |
| | Acetaminophen ^{TYLENOL, g} Peds: 10-15mg/kg po q4-6hr PRN (maximum 75 mg/kg/day) Adults: 1000mg po q4-6hr PRN | - Less effective than NSAIDs for ↓ associated pain but more effective than placebo. - Reduces fever. |
| MEDICATED LOZENGES | Benzocaine ^{CEPACOL ES, CHLORASEPTIC} 10mg lozenge q2hr PRN | - Alleviates throat pain if used frequently. - Avoid in children due to: <ul style="list-style-type: none"> ▪ risk of choking ▪ concerns with methemoglobinemia |
| MEDICATED SPRAYS | Phenol ^{CHLORASEPTIC} 5 sprays q2hr PRN | - No evidence, but anecdotally may provide relief from associated pain. |
| RINSES | <ul style="list-style-type: none"> • Gargling or drinking warm liquids e.g. warm salt water rinse, tea • Benzydamine ^{TANTUM, PHARIXIA} 15mL gargle or rinse q1.5-3hr PRN | - Little evidence, but anecdotally provide relief from associated pain. |

Not recommended for symptom management:

- ✗ Routine use of corticosteroids. ↓ in duration of pain is not considered clinically significant, and NSAIDs/acetaminophen have less adverse events.
- ✗ Chinese herbals: insufficient evidence to support use. If patient insists, encourage a product with a Natural Product Number (NPN).



MOST COMMON BACTERIAL PATHOGEN

- Group A Streptococcus (GAS) (outpatient Group C and G strep do not require antibiotics)

EMPIRIC DRUG REGIMENS OF CHOICE & SUSCEPTIBILITY CONCERNS

| FIRST LINE | | |
|---|--|--|
| No antibiotic | - Majority of cases are viral. - Only use antibiotics in confirmed bacterial pharyngitis. | - See Symptom Management following page. |
| Penicillin V | Peds: ≤ 27 kg: 40mg/kg/day \div BID or TID x10 days (maximum 750mg/day) >27 kg & Adults: 300mg TID x 10 days, or 600mg BID x 10 days | - 1 st line due to narrow spectrum of activity, efficacy, safety & low cost. - No documented resistance to GAS. |
| Amoxicillin | Peds: 40mg/kg/day \div BID or TID x10 days (maximum 1000mg/day) Adults: 500mg BID x 10 days | Compared to penicillin: - broader spectrum than required; as effective - liquid more palatable for children 😊 |
| PENICILLIN ALLERGY: TYPE IV HYPERSENSITIVITY (e.g. rash) | | |
| Cephalexin | Peds: 25-50mg/kg/day \div BID or QID x10 days (maximum 1000mg/day) Adults: 250mg QID x 10 days, or 500mg BID x 10 days | - No documented resistance to GAS. |
| PENICILLIN ALLERGY: TYPE I HYPERSENSITIVITY (i.e. anaphylaxis) | | |
| Do not use the following antibiotics unless confirmed GAS & confirmed type I reaction to penicillin, due to concerns with \uparrow resistance to macrolides & adverse events e.g. <i>C. diff.</i> | | |
| Clindamycin | Peds: 20mg/kg/day \div TID x10 days (maximum 900mg/day) Adults: 300mg TID x 10 days | Macrolide considerations: - Clarithromycin x 10 days was superior to azithromycin x 5 days for bacterial eradication (NNT=9) in adults, but equivalent for clinical cure. - \uparrow GI side effects with erythromycin. - Azithromycin 3 vs 5 days: no head-to-head trials. Both regimens provide same total dose over the course of therapy (i.e. 60mg/kg/d; 1.5g). |
| Clarithromycin | Peds: 15mg/kg/day divided BID x10 days (maximum 500mg/day) Adults: 250mg BID x 10 days | |
| Erythromycin | Peds: 40mg/kg/day \div BID or TID x10 days (maximum 2000mg/day) Adults: 250mg QID x 10 days | |
| Azithromycin | Peds: 12mg/kg/day daily x 5 days, or 20mg/kg/day daily x3 days (max 500mg/d) Adults: 500mg Day 1, 250mg x Days 2-5, or 500mg daily x 3 days | |



Case – 15 year-old boy with strep throat

- Mother is very upset:
 - The locum who is filling in for her regular physician wouldn't prescribe an antibiotic, and instead took a throat swab
 - It's Friday; swab won't be processed until next week
 - She shows you her son's throat, and says, "Look at all that pus! It's clearly a bacterial infection."
 - Great-uncle had acute rheumatic fever due to strep throat
 - She asks you to recommend another physician... one that will prescribe an antibiotic



PEARLS for the MANAGEMENT of PHARYNGITIS

- The majority of pharyngitis cases do **NOT** require antibiotics as they are viral infections (80-90% in adults, >70% in children).
- Pharyngitis is typically self-limiting (often 3-7 days; up to ≤ 10 days).
- A validated clinical decision rule e.g. modified Centor score can help identify low risk patients who do not require diagnostic testing (see below) or antibiotics.
- For confirmed Group A Streptococcus (GAS) pharyngitis, penicillin for 10 days is the drug of choice. There is no documented GAS resistance to penicillin.
- Advise on treatments that will provide symptomatic relief: NSAIDs, acetaminophen, medicated throat lozenges, topical anesthetics, warm liquids.
- Patients should see their prescriber if: 1) symptoms worsen, 2) symptoms take longer than 3 to 5 days to resolve, &/or 3) unilateral neck swelling develops.



Case – 32 year old female

- Complaining of “a cold in her sinuses”:
 - +++ nasal secretions
 - Unable to breath out of nostrils when lying down
 - +++ sinus pain
- 2 hour wait at walk-in clinic
 - asking for an OTC to manage her symptoms while she is waiting



ACUTE SINUSITIS VIRAL OR BACTERIAL

Purulent nasal discharge
AND
Nasal obstruction
OR
Facial
pain-pressure-fullness



ACUTE SINUSITIS BACTERIAL

Signs & symptoms
that persist without
improvement for ≥ 10 days
OR
Worsens within 10
days after an initial
improvement

98% Viral Sinusitis: antibiotics NOT required

1.7% Bacterial Sinusitis: antibiotics NOT required

0.3% Bacterial Sinusitis: may require antibiotics

- The colour of mucus should not be used to diagnosis a bacterial sinusitis infection (indicative of inflammation, but not of bacteria).



Acute Sinusitis

- Sinusitis is self-limiting. ~85% of bacterial cases will improve within 2 weeks without antibiotics. In other words, out of 1000 patients presenting with sinusitis, 5 to 20 patients would have bacterial sinusitis, and 4 to 17 of these bacterial cases would resolve **without** antibiotics.
- Compared to placebo, antibiotics (beta-lactams, macrolides, FQ) have not been shown to ↓ duration of pain or illness. The NNT for clinical improvement is high (NNT=7 to 18), & a systematic review including patients with symptoms for ≥7 days failed to show a benefit with antibiotics. Antibiotic AE primarily GI related were common (NNH=8 to 12).
- Watchful waiting is an option for some patients



Antibiotic Watchful Waiting should be considered in patients who:

- present with symptoms that have not worsened, or
- have had symptoms for less than 10 days and
- you feel confident in their ability for follow up (ie. antibiotic will be started in the acute sinusitis symptoms fail to improve after 7 days or worsen at any time)



SYMPTOM MANAGEMENT

| | | |
|-----------------|--|--|
| ANALGESICS | <ul style="list-style-type: none"> Acetaminophen ^{TYLENOL, g} <ul style="list-style-type: none"> 10-15mg/kg q4-6hr PRN (max 75mg/kg/day) 1000mg po q6hr PRN (max 3.2-4g/day) Ibuprofen ^{ADVIL, g} <ul style="list-style-type: none"> 5-10mg/kg q6-8hr (max 40mg/kg/day) 400mg po q6-8hr PRN | <ul style="list-style-type: none"> No quality evidence but should reduce fever & treat localized pain. |
| DECONGESTANTS | <ul style="list-style-type: none"> Xylometazoline ^{OTRIVIN} (≥12 yrs & adults): 2-3 sprays/nostril q8-10hr PRN Pseudoephedrine: ^{SUDAFED} <ul style="list-style-type: none"> 6-11yrs: 30mg po q4-6hr PRN (max 120mg/d) ≥12 yrs & adults: 60mg po q4-6hr PRN, or 120mg ER po q12h PRN | <ul style="list-style-type: none"> Limited evidence with xylometazoline. May relieve congestion & promote sinus drainage. Topical preparations: less systemic absorption (oral AE: CV, insomnia); limit to 3-5 days to prevent rebound symptoms |
| CORTICOSTEROIDS | <p>INTRANASAL (not recommended in <3yrs)</p> <ul style="list-style-type: none"> Fluticasone ^{FLONASE, g} 50 mcg 2 sprays in each nostril once daily Mometasone ^{NASONEX, g} 50 mcg 2 to 4 sprays each nostril twice daily <p>ORAL (only for severe sinusitis)</p> <ul style="list-style-type: none"> Prednisone 40 to 60mg po daily x 7 days | <ul style="list-style-type: none"> INTRANASAL: modestly effective for ↓ pain & nasal congestion (NNT=15/2-3wks), vs placebo. May lessen symptoms by 3.5 days. Mild AE (e.g. epistaxis, nasal itching). ORAL: may provide benefit for severe sinusitis, in combination with an antibiotic (NNT=7 for symptom improvement or resolution). No benefit with monotherapy. |
| NONPHARM | <ul style="list-style-type: none"> warm facial packs saline nasal drops/rinses/irrigation <ul style="list-style-type: none"> 150mL hypertonic saline nasal irrigation ^{NETI POT} daily Saline spray ^{SALINEX} 1 spray TID-QID PRN | <ul style="list-style-type: none"> No quality evidence but anecdotally may promote mucus drainage. Anecdotally, nasal drops/sprays may help. Limited conflicting evidence with nasal irrigation; may ↓ symptoms, ↑ quality of life, ↑ mucociliary clearance & ↓ use of other sinusitis medications. |



MOST COMMON BACTERIAL PATHOGENS

- *S. pneumoniae*, *H. influenzae*, *M. catarrhalis* (in children), *S. aureus*

EMPIRIC DRUG REGIMENS OF CHOICE

| MILD to MODERATE (symptoms <10 days or no worsening in symptoms) | | |
|--|--|--|
| No antibiotic | 98-99.5% of cases are viral | - See symptom management |
| MILD to MODERATE (symptoms ≥10 days or worsens within 10 days) | | |
| Amoxicillin | Peds: 40-90mg/kg/day ÷ BID or TID x 10 days (maximum 3g/day) Adults: 500mg to 1000mg po TID x 5 - 10 days* | - <i>S. pneumoniae</i> susceptible to high-dose amoxicillin, even isolates with intermediate susceptibility. |
| SEVERE (fever ≥39°C AND purulent nasal discharge or facial pain x 3-4 days) or TREATMENT FAILURE WITH AMOXICILLIN (symptoms not resolved after 3-5 days) | | |
| Amoxicillin / Clavulanate <small>CLAVULIN 4:1 or 7:1 ratio</small> <small>Dose listed as per amoxil component</small> | 45mg/kg/day ^{CLAVULIN} ÷ BID x 10 days (±45mg/kg/day amoxicillin ÷ BID) (max total daily dose of amox is 3g) Adults: 500mg po TID (or 875mg po BID of 7:1 ratio form) x 5 - 10 days* | - Covers all of the common bacterial pathogens. - Addition of clavulanate ↑ risk of GI AE (use 7:1 ratio formulation & BID dosing to lessen). |
| PENICILLIN ALLERGY: TYPE IV HYPERSENSITIVITY (e.g. rash) | | |
| Cefuroxime | Peds: 30-40mg/kg/day ÷ BID (max 1000mg/day) x 10 days Adults: 250mg to 500mg po BID x 5 - 10 days* | |
| PENICILLIN ALLERGY: TYPE I HYPERSENSITIVITY (i.e. anaphylaxis) | | |
| Doxycycline | Peds: ≥ 9 years: 4mg/kg/day ÷ BID (max 200mg/day) x 10 days Adults: 200mg po Day 1, then 100mg po BID x 5 - 10 days* | |
| Clarithromycin [¶] | Peds: 15mg/kg/day ÷ BID (max 500mg/dose) x 5-10 days Adults: 500mg po BID or 1000mg XL po daily x 5 - 10 days* | |
| Azithromycin [¶] | Peds: 10mg/kg Day 1, then 5mg/kg daily Days 2-5 (maximum 500mg Day 1, 250mg Days 2-5) Adults: 500mg po Day 1, then 250mg po daily Days 2-5 | |

*5 days of therapy should be sufficient in uncomplicated adults. See below.

[¶] Clarithromycin is the preferred macrolide, unless major drug interactions (e.g. warfarin, digoxin, statin), as azithromycin may lead to more resistance (re: t½).



Treatment Evidence Summary

Duration of therapy, if needing to treat with an antibiotic:

- In healthy adults suffering from sinusitis, short courses (e.g. 5 days) have the same benefit as longer courses of therapy (e.g. 10 days), with less harm.
- A meta-analysis (12 RCTs, n=4430) found no difference in clinical success (cure or improvement of symptoms) with short courses (3 to 7 days) versus longer courses (6 to 10 days) of the same antibiotic. A sensitivity analysis (7 RCTs, n=2715) comparing 5 versus 10 days did not find a difference in clinical success either. Overall, there was no difference in adverse events. However, in the sensitivity analysis (5 vs 10 days), short courses had fewer adverse events (OR 0.79, 95% CI 0.63-0.98).
- Older patients with comorbidities were excluded from the trials, and therefore we do not have evidence to support a shorter course of therapy in this population.
- A longer course of therapy (i.e. 10 days) is still recommended for children, based on the available evidence.



Case – 32 year old female

- Complaining of “a cold in her sinuses”:
 - +++ nasal secretions
 - Unable to breath out of nostrils when lying down
 - +++ sinus pain
- 2 hour wait at walk-in clinic
 - asking for an OTC to manage her symptoms while she is waiting



PEARLS for the MANAGEMENT of ACUTE SINUSITIS

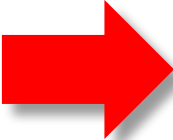
- Most cases **do NOT** require antibiotics as 98-99.5% of infections are viral.
- Viral & bacterial sinusitis have similar symptoms, but symptoms that worsen or are prolonged (≥ 10 days) suggest bacterial involvement.
- Advise on treatments that provide **symptomatic relief**: analgesics, saline nasal drops/rinses, decongestants, warm facial packs, & corticosteroids.
- **Amoxicillin** is the antibiotic of choice for **bacterial** sinusitis.
Reserve macrolides for patients with true penicillin allergies.
- Patients should see their healthcare provider if symptoms worsen or take longer than 10 days to resolve.




Antibiotic Trivia

- What is the recommended dose and duration for amoxicillin for upper respiratory tract infections?

- A) 500 mg po BID x 10 days
- B) 500 mg po TID x 5 days
- C) 1000 mg po TID x 7 days

 D) all of the above

 Pharyngitis

 Sinusitis (500-1000 mg TID)

 Community-acquired pneumonia



Pharmacist Role in URTI (and in all infectious diseases)

- To be ***Antibiotic Stewards***
 - That means...
 - Patient education antibiotic resistance and stewardship
 - Educate patients on symptomatic management of URTIs
 - Assess for appropriate antibiotic, dose, and duration for indication
 - Assess for drug interactions, provide recommendations
 - Provide recommendations if current therapies are not ineffective



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SINUSITIS PHARYNGITIS BRONCHITIS



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Antibiotics: Potential Harms

Antibiotics are a valuable resource and judicious use is very important. For many serious infections (e.g. pneumonia, bacterial meningitis, sexually transmitted infections) the benefits of antibiotics clearly outweigh potential harms. However, for conditions that are primarily viral (e.g. pharyngitis, acute sinusitis, acute bronchitis), the benefits are minimal and likely outweighed by harms. Of note: antibiotic-related adverse drug events account for 1 out of every 5 visits to the Emergency Department.¹

| | | |
|---|--|---------------------------------|
| Common Adverse Events | Overall NNH = 8-12 | Yeast infection NNH = 23 |
| <ul style="list-style-type: none"> In a meta-analysis (10 trials, 2450 patients) comparing antibiotics to placebo for acute rhinosinusitis, common adverse events (such as nausea, vomiting, diarrhea, or abdominal pain) occurred in 27% of patients on antibiotics versus 15% on placebo (NNH = 8-12).^{2,5} The antibiotics used in this meta-analysis included penicillins, macrolides, and tetracyclines. Trials examining other populations have found similar numbers of adverse events.^{3,4,5} A recent meta-analysis comparing amoxicillin or amox/clav to placebo found risk of yeast infection (candidiasis) ~ 8x higher in those on antibiotics (NNH = 23).⁶ | | |
| Allergic Reactions | NNH from 20 (rash, hives) to 10,000 (anaphylaxis) | |
| <p>Allergic reactions can occur with any antibiotic; penicillin in particular is well studied. About 5-10% of patients will self-report a penicillin allergy;^{7,8} however the vast majority of these reactions are delayed reactions, occurring days to weeks after initiating therapy, and do not typically indicate a true allergy.⁹ Anaphylaxis occurs in about 0.01% of patients taking penicillin; about 10% of these reactions are fatal (i.e. 0.001% of all patients prescribed penicillin).^{10,11,12}</p> | | |
| Serious Adverse Events | NNH from 300 to 30,000 | |
| <p>Rare but serious adverse events are associated with all antibiotics. Large, long-term randomized controlled trials are uncommon, and so it is difficult to put a precise estimate on how prevalent these events are. However, some adverse events include:</p> <ul style="list-style-type: none"> Clostridium difficile infection: associated most often with clindamycin (RR=4), cephalosporins, and fluoroquinolones; risk varies depending on patient factors.^{13,14,15} Stevens Johnson Syndrome, Toxic Epidermal Necrolysis, & other severe skin reactions: these events occur a few times per 100,000 antibiotic prescriptions.¹⁶ Cotrimoxazole in particular has a higher association than most other antibiotics.¹⁷ QT prolongation: associated most often with macrolides (esp. clarithromycin and erythromycin) and fluoroquinolones (esp. levofloxacin and moxifloxacin). Risk of QT prolongation is also dependent on other factors (e.g. cardiac, metabolic, other drugs, etc.). See RxFiles QT Prolongation page 32 (11th Ed). Tendon rupture with fluoroquinolones: one large cohort study found a risk of 3.5% for tendon rupture in adults over the age of 65.¹⁸ Hyperkalemia with cotrimoxazole: in older adults taking medications which can raise potassium (such as ACEIs, ARBs, spironolactone, or NSAIDs), cotrimoxazole was associated with sudden death (NNH ≈ 300).^{19,20} Contraceptive failure/drug interaction? Although this is thought to be unlikely, there is a small but real risk & a backup birth control method is always recommended. | | |
| Other | There are many other less common harms than can be covered here! e.g. serum sickness like reactions, pulmonary fibrosis with nitrofurantoin, tooth discoloration with tetracyclines | |
| Antibiotic Resistance | NNH as low as 1??? Every course of antibiotic is likely to result in some emerging resistance which could affect the next choice of antibiotic regimen for that individual, especially if within 3 months of the previous antibiotic. Of course the NNH for catastrophic resistance would be much higher. | |
| <p>Resistance to an antibacterial can develop quickly. For example, strains of <i>Streptococcus pneumoniae</i> resistant to levofloxacin were documented in the same year levofloxacin was introduced to the market.²¹ Rare, but worrisome, reports of bacteria resistant to every available antimicrobial can be found in the literature.²²</p> <p>The good news is that when prescribing patterns change, resistance rates decline.^{23,24}</p> | | |

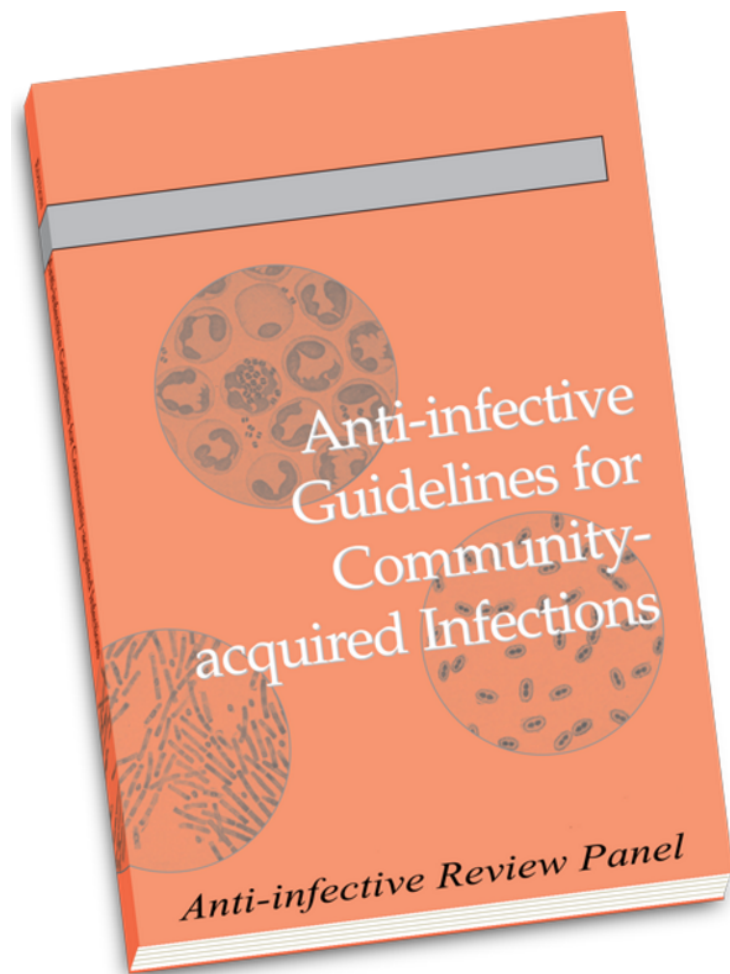
Quotes from the team ☺: *Harms speak louder when there is little or no benefit to offset them!*

www.RxFiles.ca/ABX



Additional Antibiotic References

Many available in print AND mobile apps



Questions



Thank you!

This presentation and any resources will be available online to CPhA members at <http://www.pharmacists.ca/index.cfm/education-practice-resources/professional-development/pharmacy-practice-webinars/>



Bonus Antibiotic Trivia

- Does the risk of antibiotic resistance differ among the macrolides (erythromycin, clarithromycin, azithromycin)?



Bonus Antibiotic Trivia

- Local antibiogram data:
 - Erythromycin is the macrolide used to represent the 3 macrolides
 - Sensitivity to erythromycin can be assumed as sensitivity to clarithromycin and azithromycin
 - Exception: erythromycin does not cover *H. influenzae*
- Observational and serum concentrations
 - Suggest that azithromycin leads to more resistance and resistances that lasts longer

