



Antibiotics: Why and Why Not

Academic
Detailing
Service





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To receive a 20% special discount (before taxes and S & H) on the guideline book use the order form at www.mumshealth.com and include the following PROMO Code: **NSAD 2012**. The offer is valid until December 2012.

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“Seek simplicity, and mistrust it.”

Alfred North Whitehead



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Dalhousie Academic Detailing 2012: Selected Antibiotics For Community Acquired Respiratory and Urinary Tract Infections

Class	Generic Name	Brand Name Product (Brand name may no longer be manufactured) * no generic available	Treatment choice for infections due to:					Need to adjust dose for renal function?	Comment
			S.pneumoniae	H. influenzae	C. pneumoniae	E.coli in urine	P.aeruginosa		
Beta-lactams	Penicillin	n/a	+					no	Drug of choice for Group A streptococci. All beta-lactams cover non-pneumococcal streptococci.
	Ext.-spectrum penicillin	Amoxil	+	+/-		+/-		yes	Drug of choice for S.pneumoniae. Giving high dose amoxicillin may overcome intermediate level penicillin resistance.
	Penicillin / B-lactamase inhibitor	Clavulin	+	+				yes	Enhanced activity against gram negative organism, including β-lactamase producing organisms.
	1 st gen Cephalosporin	Keflex	+			+/-		yes	Broad spectrum of activity.
	2 nd gen Cephalosporin	Ceftin	+	+				yes	Enhanced gram negative coverage in 3 rd generation.
	3 rd gen Cephalosporin	Cefzil	+	+				yes	Cephalosporins should not be used as empiric therapy for UTI due to resistance and lower efficacy rates. Cephalixin may be a treatment option for a pregnant woman.
	Ceftriaxone	Rocephin (IM/IV)	+	+			no	2 nd and 3 rd generation cephalosporins can be given to an individual with a history of a non-immunological reaction to penicillin or amoxicillin	
	TMP / SMX	Septra and Bactrim	+/-	+			+	yes	Increasing S.pneumoniae, H.influenzae and E.coli resistance.
	Trimethoprim	Proloprim					+	yes	
	Nitrofurantoin	MacroBID					+	Avoid if CrCl<60ml /min	First line alternative for uncomplicated UTI. Remains highly active against E.coli (urine).
	Doxycycline	Vibramycin	+	+	+			no	First line alternative for lower respiratory infections due to atypical pathogens. Good coverage against S.pneumoniae and atypicals. Not recommended for children under 8 yrs.
	Erythromycin	Eryc, EES						no	Increasing S.pneumonia resistance.
	Clarithromycin	Biaxin BID / Biaxin XL*	+/-	+/-	+			yes	Azithromycin may promote resistance to a greater extent than clarithromycin.
	Azithromycin	Zithromax						No	Macrolides generally have poor/no activity against H.influenzae.
	Norfloxacin	Noroxin						yes	Broad spectrum of activity - Reserve for severe infections or those with no other treatment options (due to the importance for other indication and concern of resistance with overuse)
	Ciprofloxacin	Cipro / Cipro XL*	+	+	+		+	yes	
	Levofloxacin	Levaquin	+	+	+		+	yes	
	Moxifloxacin	Avelox*	+	+	+		no	no	

+ reasonable treatment choice; +/- may be reasonable for some patients

Reference for renal function adjustment: Drug Prescribing in Renal Failure by Aronoff GR et al. Free access at www.kdp-baptist.louisville.edu/renalbook/



Background Information

Microorganisms

- In the **respiratory** tract, the most common **bacterial** pathogens are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, and *Chlamydomphila pneumoniae*.
 - Most respiratory infections are caused by **viruses** and do not require antibiotics.
 - When antibiotics are necessary, treatment is empiric to cover the above microorganisms.
 - The exception is pharyngitis where the bacterial pathogen is usually *Group A Streptococcus* which responds to penicillin.
- In the **urinary** tract, the most common bacterial pathogen is *Escherichia coli*.

Resistance and Antibiotic Stewardship

- Resistance to antibiotics is an increasing problem because new antibiotics are not being developed.
- A major cause of resistance is previous exposure to antibiotics. Pneumococcal resistance to
 - Macrolides has been associated with use of azithromycin to a greater extent than with clarithromycin (odds ratio 9.9 vs 3.9).
 - Fluoroquinolones has been associated with previous use of fluoroquinolones (odds ratio 12.1).
- **Strategies to minimize antibiotic resistance**
 - Prescribe antibiotics only when **necessary**. Viral infections and some bacterial infections will resolve **without** antibiotics.
 - Use the proper **dosage** of antimicrobial needed to achieve a minimal effective concentration at the site of infection. This may require high doses of some antibiotics.
 - Treat for the shortest effective **duration** to minimize exposure of both pathogens and normal microbiota to antimicrobials and minimize the selection for resistance.
 - Limit the spectrum of activity of antibiotics to that specifically required to treat usual pathogens.
 - In general, do not replace **older** antibiotics (generally more narrow spectrum and less expensive) with newer drugs unless they are substantially more effective or less toxic.
 - Reserve **fluoroquinolones** for severe infections because of their importance for other indications and concern of developing resistance with overuse.

Using Antibiotic Recommendation Tables in This Document

- Green indicates first line treatment choices, yellow second line, and red third line. Fluoroquinolones are always listed as red choices.
- Within each colour, antibiotics are randomly listed. Not all antibiotics in each class are listed and others may be appropriate e.g., cephalosporins.
- Because azithromycin has been shown to promote resistance to a greater extent than clarithromycin, with the consensus of our content experts, we have listed clarithromycin when a macrolide is recommended.



Before Starting Antibiotics

Take an antibiotic history. If the patient has used an antibiotic within the last 3 months, consider selecting an antibiotic from a different class.

Understand your patient's risk factors for having a resistant organism. The following factors are associated with increased risk of having a resistant organism:

- Antibiotic use in past 3 months
- Chronic symptoms
- Exposure to daycare
- Chronic systemic disease
- Long term corticosteroid use

Consider a second line alternative therapy if:

- The risk of bacterial resistance is high.
- There is a higher risk of complication associated with treatment failure (the consequences of treatment failure are greatest).
- A patient has not responded to first line therapy.
- A patient is unable to take first line therapy due to allergy or intolerance.

- **Local and national resistance patterns**

- Local and national surveillance data indicate the following resistance patterns:
 - Macrolides: Increasing *S. pneumoniae* resistance, currently ~ 20%.
 - TMP/SMX: Increasing *S. pneumoniae*, *H. influenzae*, and *E. coli* resistance, all currently ~20%.
 - Fluoroquinolones
 - Levofloxacin, Moxifloxacin: *S. pneumoniae*, *H. influenzae* resistance is low (<2%).
 - Reserve these drugs for serious or recalcitrant infections to keep resistance low.
 - Ciprofloxacin:
 - Local urinary *E. coli* resistance ~7%.
 - Generally, reserve ciprofloxacin for suspected respiratory infections with *Pseudomonas* and UTI if other agents can not be used.
 - Doxycycline: *H. influenzae* resistance is low (\leq ~5%); *S. pneumoniae* resistant is 17%.
 - Nitrofurantoin: Local urinary *E. coli* resistance is low (~4%).
 - Amoxicillin: *S. pneumoniae* resistance is low (~3%); *H. influenzae* resistance is higher (~20%). *H. influenzae* resistance to Amox/Clav is low (~1%).
- Resistance found in vitro does not necessarily translate into clinical failure. One theory is that antibiotics may achieve higher concentrations at the site of infections than are reflected in laboratory testing.



Allergy to penicillins

- When considering allergy to penicillins, it is important to clarify whether a reaction is an immunologic reaction or a non-immunologic side effect such as vomiting, diarrhea, or non-specific rash.
 - Immunologic reactions can be categorized as
 - **Immediate:** onset within 1 hour (Type I): e.g., hives, swelling, anaphylaxis
 - **Delayed:** onset after 72 hours (Type II, III, IV): e.g., serum sickness, Stevens-Johnson syndrome, toxic epidermal necrolysis
 - Non-immunologic reactions are typically maculopapular rashes.
- The most common type of immunologic reaction is type I which when severe can lead to life-threatening anaphylaxis. Estimates of the incidence of anaphylactic reaction to penicillin range from 0.004% to 0.015% (4 to 15 per 100,000 treatment courses).
 - Less than 10% of patients with a reported history of penicillin allergy have a true allergy.
- Non-immunologic rashes appear in 1% to 4% of people taking penicillins or cephalosporins and are usually not a contraindication for the future use of the drug.
- **Generally**, it is possible to differentiate the rash of a type I reaction from a non-immunologic rash by the time of onset (<1 hour vs >72 hours). In addition, if the rash is **nonurticarial** and **nonpruritic** it is unlikely to be type 1.
 - However these differentiations are **not** absolute.
- Patients who are labelled as being allergic to penicillins or cephalosporins may be denied treatment with an inexpensive, effective antibiotic. Therefore our content expert suggests that **all** patients with a suspected antibiotic allergy be referred to an allergist to rule in or rule out true allergy.
- Until assessed by an allergist:
 - A patient with a history suggestive of a non-immunologic reaction to penicillins (i.e., vague history of only a rash) can be prescribed a second or third generation cephalosporin such as cefuroxime, cefprozil, or ceftriaxone.
 - A patient with a history suggestive of **type I** allergic reaction to penicillins should **not** receive a penicillin or a cephalosporin.
- Patients with a history suggestive of a delayed, severe, non-type I immunologic reaction, i.e. serum sickness, Stevens-Johnson, or toxic epidermal necrosis, should **never** receive the drug again. These individuals will usually have systemic symptoms.

For adult and pediatric referrals
Halifax Allergy and Asthma Associates
 5657 Spring Garden Road, Suite 503
 Halifax, NS, B3J 3R4
 t: 902-425-3927 f: 902-425-3928

For pediatric referrals
IWK Allergy Clinic
 t: 902-470-6392
 f: 902-470-7308



Pharyngitis

- 80% to 90% of cases are not group A Streptococcal infection and do **not** require treatment.
- Most decisions to prescribe antibiotics can be guided by the total score on the following scale.

Criteria	Points	Scoring
• Temperature >38°C	1	≤ 1 No culture or antibiotic
• Absence of cough	1	
• Swollen tender anterior cervical nodes	1	2-3 Perform culture or rapid antigen test. If either is positive, treat.
• Tonsillar swelling or exudate	1	In children, if rapid antigen is negative, a culture is required to confirm result.
• Age 3-14 years	1	
• Age 15-44 years	0	≥4 Start antibiotic therapy. If culture or rapid antigen test is performed, discontinue antibiotic if result is negative.
• Age ≥ 45 years	-1	

This score should not be used in epidemic situations; in populations in which rheumatic fever remains a problem, such as First Nations communities; and those people with a history of rheumatic fever, valvular heart disease, and/or immunosuppression.

RED FLAGS

- Individuals who experience significant difficulties swallowing, especially if associated with drooling, altered voice (“hot potato voice”) or airway obstruction (stridor) should be considered to have epiglottitis, peritonsillar abscess, or retropharyngeal abscess, until proven otherwise.
- Patients between the ages of 15 to 24 who develop bacteremic symptoms or unilateral neck swelling should be treated empirically with penicillins or cephalosporins rather than macrolides.

Antibiotic	Pediatric Regimen	Cost per kg per day
Penicillin V	≤ 27 kg: 40 mg/kg/day divided BID or TID Maximum 750 mg/day >27 kg: adult dose	\$0.03 – 0.09
Amoxicillin	40 mg/kg/day divided BID or TID	\$0.06
Clarithromycin	15 mg/kg/day divided BID	\$0.19
Cefprozil	15 mg/kg/day divided BID	\$0.05
Cefuroxime	20 mg/kg/day divided BID	\$0.15
Duration of therapy is 10 days for all regimens		

Antibiotic	Adult Regimen	Cost /day
Penicillin V	600 mg BID	\$0.29
Clarithromycin	250 mg BID	\$2.20
Cefprozil	250 mg BID	\$1.39
Cefuroxime	250 mg BID	\$1.45
Duration of therapy is 10 days for all regimens		



Otitis Media

- **Otitis media with effusion** is the presence of fluid in the middle ear **without** signs and symptoms of acute infection and may occur after an episode of acute otitis media. Antibiotics are **not** recommended.
- **Acute otitis media** is characterized by
 - Acute onset: **rapid** onset of ear pain or unexplained irritability in a preverbal child **AND**
 - Middle ear **effusion AND** middle ear **inflammation** indicating this fluid is pus.
 - Signs of middle ear effusion
 - Immobile tympanic membrane (as demonstrated by pneumatic insufflation, tympanogram or acoustic reflectometry) or fluid in ear canal from tympanic membrane rupture
 - +/- Opacification of the tympanic membrane (not secondary to scarring)
 - +/- Loss of the bony landmarks behind the tympanic membrane
 - +/- Visible air fluid level behind the tympanic membrane
 - Signs of middle ear inflammation
 - **Bulging** tympanic membrane with discolouration (hemorrhagic, red, gray, or yellow)
- Visit www.hawkelibrary.com for images of otitis media.
- **RED FLAG:** Suspect acute **mastoiditis** in the presence of fever, marked retroauricular edema or erythema and tenderness, and outward protrusion of the auricle.
- For most children with acute otitis media antibiotics are not warranted. Spontaneous resolution is to be expected in 80%-90% of cases. Watchful waiting with an analgesic can be used in many cases.

The Canadian Pediatric Society states **watchful waiting** with an **analgesic** for 48 to 72 hours may be appropriate if

- | | |
|---|---|
| <ul style="list-style-type: none"> • Child is older than 6 months • Illness is not severe: otalgia is mild, temp <39°C without antipyretics • Parents can recognize signs of worsening and easily access follow-up care | <ul style="list-style-type: none"> • Child does not have <ul style="list-style-type: none"> • Chronic disease: Immunodeficiency, cardiac, pulmonary • Down syndrome • Cleft palate • History of complication of otitis media (i.e. suppurative complications or chronic perforation) |
|---|---|
- Parents should seek immediate medical re-assessment if
 - Symptoms worsen or new symptoms appear (e.g., rash, drowsiness, difficulty breathing, vomiting).
 - If treating with an antibiotic, symptoms should improve within **one to two** days and resolve within two to three days of starting antibiotics. If they do not, switch to a different antibiotic.



Antibiotic	Regimen for Acute Otitis Media		Cost/kg/day
Amoxicillin	80 mg/kg/day	Divided BID or TID (maximum 3 grams/day)	\$0.10
Clarithromycin	15 mg/kg/day	Divided BID	\$0.19
Amox/Clav	Amoxicillin 90 mg/kg/day Clavulanate 6.4 mg/kg/day	Divided BID. Additional amoxicillin must be added to amox/clav products	Cost varies
Cefprozil	30 mg/kg/day	Divided BID	\$0.10
Cefuroxime	30 to 40 mg/kg/day	Divided BID	\$0.23 – \$0.30
Ceftriaxone	50 mg/kg/day IM or IV once daily x 3 days (reserve for emergency department)		
Duration of therapy	≤ 2 years old = 10 days > 2 years old = 5 days Complicated or frequently recurrent = 10 days		

- **Uncomplicated** acute otitis media in presence of **chronic perforation or ventilation** tubes
 - Presents as painless discharge
 - **Ciprodex** otic drops 4 drops BID for 5 days. (**7.5 ml/\$28**) (Ventilation tubes require tragal pump.)
 - May need oral therapy if evidence of systemic illness, spread beyond middle and external ear, treatment failures, or special populations (e.g., immunocompromised).
- In **acute** otitis media with **acute** perforation, use combined oral antibiotics and Ciprodex.



Acute Bacterial Rhino-Sinusitis

- Most cases (>98%) of acute sinusitis are **viral**, resolve within 5 to 7 days and **do not require antibiotics**.
- Viral sinusitis is the most common predisposing factor for acute bacterial rhino-sinusitis.
- Two main bacteria involved are *Streptococcus pneumoniae* and *Haemophilus influenzae*. Infections due to *Moraxella catarrhalis* are infrequent in adults but account for about 25% of cases in children.
- A **diagnosis** of acute bacterial rhino-sinusitis can be made if a patient has at least 2 major symptoms, (one of which must be **O** or **D**) AND
 - Symptoms worsen after 5-7 days OR
 - Persist for at least 7-10 days OR
 - There is purulence with high fever for 3-4 days

Major Symptoms*	RED FLAGS for urgent referral include
<p>P Facial Pain/pressure/fullness</p> <p>O Nasal Obstruction*</p> <p>D Nasal purulence/discolored postnasal Discharge*</p> <p>S Hyposmia/anosmia (Smill)</p> <p>* At least 1 symptom must be nasal Obstruction or nasal purulence/discolored postnasal Discharge.</p>	<ul style="list-style-type: none"> • Systemic toxicity • Altered mental status • Severe headache • Swelling of the orbit or change in visual acuity • Suspected orbital or intracranial complications

- Consider **treatment with antibiotics** if symptoms are **severe** (i.e. hard to tolerate and interfering with productivity, activity or sleep) OR a patient has co-morbidities.
- Antibiotics **may** speed up recovery time. However, overall response rates at 14 days are similar for both antibiotic-treated and untreated patients.
- A patient-level meta-analysis of 2547 patients from nine trials showed a number need to treat of 14 (95% CI: 9 to 30) for resolution of symptoms. 64% of patients were cured at 14 days **without** antibiotics.

Antibiotic	Regimen	Cost per day
Amoxicillin	500mg TID	\$1.03
Amox/Clav	500 mg TID or 875 mg BID	\$2.00 - \$2.52
Doxycycline	200 mg for 1 st dose then 100 mg BID	\$1.17
Clarithromycin	500 mg BID	\$3.26
Cefuroxime	250 - 500 mg BID	\$1.45-\$2.90
Levofloxacin	500 mg OD	\$2.42
Moxifloxacin	400 mg OD	\$6.45

Duration of therapy is generally 10 days.

Expect symptoms to improve but not completely disappear at the end of therapy. Some persistence of symptoms is not an indication for immediate prescription for a second antibiotic.



- Symptomatic treatment (i.e. analgesics, oral decongestants, topical decongestants, saline irrigation) is recommended if symptoms are **mild to moderate**, do not worsen, OR have not persisted > 7 days.
- Guidelines suggest topical intranasal steroids **may** offer some benefit.
 - A Cochrane review of objectively **confirmed** cases found benefit: NNT 14 (95% CI 9 to 34) for 2 to 3 weeks.
 - A large RCT of **primary care** patients found no benefit from intranasal steroids.



Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD)

- AECOPD is defined as a sustained worsening of dyspnea, cough, or sputum production. Sustained implies a change from baseline lasting 48 hours or more.
 - It **may** lead to an increase in the use of maintenance medications, and/or supplementation with additional medication such as bronchodilators, systemic steroids, and oxygen. We are focusing mostly on the need for and choice of antibiotics in treating AECOPD.
- In acute bronchitis in the **absence** of COPD, ≥ 90% of cases are viral and do not need antibiotics. Cough can last > 3 weeks in 25% of cases.
 - If a patient has risk factors for COPD (e.g., smoking history) and symptoms of a lower respiratory tract infection, consider **pre-** and **post-**bronchodilator spirometry after the acute episode has resolved to rule in or rule out a diagnosis of underlying COPD.
- In AECOPD the number of **cardinal symptoms** helps determine the need for antibiotic therapy. Increasing **purulence** (darker yellow or darker green) is a key symptom.

Cardinal Symptoms of AECOPD	
Increase in dyspnea Increased sputum volume Increased sputum purulence	} Sustained for 48 hours compared to baseline
<u>One cardinal symptom:</u>	Treatment with antibiotics may not be necessary
<u>Two cardinal symptoms:</u>	Treat with antibiotics if one symptom is increased purulence
<u>Three cardinal symptoms:</u>	Always treat with antibiotics

- For a **complicated** patient or a patient with significant **dyspnea**, consider oral prednisone 25 to 50 mg/day for 7 to 10 days.
 - With increased dyspnea but **no** increased sputum purulence, oral prednisone may be sufficient (no antibiotics).
 - However with increased dyspnea **and** increased sputum purulence, antibiotics are also indicated.

Complicated patients have any one of the following risk factors:	
• FEV ₁ < 50% predicted	• Use of home oxygen
• ≥ 4 exacerbations per year	• Use of chronic oral steroids
• Significant cardiac disease (ischemic heart disease, heart failure)	• Use of antibiotics in past 3 months



Antibiotic	Regimen for AECOPD	Cost per day
Simple (low risk patient)		
Doxycycline	200 mg for 1 st dose then 100 mg BID	\$1.17
Amoxicillin	500 mg TID	\$1.03
Cefuroxime	500 mg BID	\$2.90
Clarithromycin ^a	500 mg BID	\$3.26
Complicated (high risk) patients or treatment failure^b		
Amox/Clav	500 mg TID or 875 mg BID	\$2.00 - \$2.52
Levofloxacin	500 mg OD x 7 days or 750 mg OD x 5 days	\$2.42 - \$6.55
Moxifloxacin	400 mg OD	\$6.45
Risk for <i>P. aeruginosa</i> (FEV₁ < 35% predicted OR have multiple risk factors OR have constant purulent sputum)		
Ciprofloxacin	500-750 mg BID	\$2.24 - \$4.09
<p>Duration of therapy is usually 7 to 10 days.</p> <p>Expect symptoms to improve but not completely disappear at the end of therapy. Symptoms may not completely resolve for several weeks.</p>		

a. Clarithromycin may be less effective against *H. influenzae* and is usually reserved for B-lactam allergy.

b. Treatment failure: clinical deterioration after 72 hour or no improvement with first line treatment.

- Review strategies to decrease the risk of recurrence such as optimal use of maintenance medications, smoking cessation, vaccinations, and pulmonary rehabilitation.
- At some point, complicated patients should be referred for evaluation by a specialist.



Community Acquired Pneumonia

- The usual causative micro-organisms include *Streptococcus pneumoniae*, *Haemophilus influenzae*, and the atypical organisms *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*.
- It is difficult to distinguish the causative organism from clinical presentation or X-ray, and initial antibiotic therapy is empiric.
- Guidelines acknowledge that the need to cover for *C. pneumoniae* and *M. pneumoniae* is uncertain but our local experts consider it important to do so.
- A chest X-ray is encouraged whenever possible to support the clinical diagnosis.
- Patients should be advised to seek re-evaluation if their condition becomes worse or does not improve within 48 to 72 hours at which time the chest X-ray should be repeated.

Adults

- Need for hospitalization can be guided by the **CRB-65** score giving 1 point for each criterion.

Criteria	Scoring
Confusion (<u>new onset</u> based on a specific mental test or disorientation to person, place, or time) Respiratory rate ≥ 30 breaths/minute Low blood pressure (systolic, <90 mm Hg; or diastolic, ≤ 60 mmHg) Age ≥ 65 years	≤ 1 Can be treated as outpatients 2 Can be admitted to hospital ward ≥ 3 Often require ICU care
Ratings may change over a short period of time and repeat assessments over several hours may be necessary. Low risk patients may still be considered for admission because of <ul style="list-style-type: none"> • Inability to reliably take oral medications or receive outpatient care, and/or • Multiple risk factors falling just above or below thresholds for the score 	



Antibiotic	Regimen for CAP in Outpatient Adults	Cost per day
MONOTHERAPY previously healthy, low risk patient and no risk factors for drug-resistant <i>S pneumoniae</i>		
Doxycycline	200 mg for 1 st dose then 100 mg BID	\$1.17
Clarithromycin	500 mg BID	\$3.26
DUAL THERAPY presence of comorbidities ^a , antimicrobial use within the previous 3 months, or other risk factors for drug-resistant <i>S. pneumoniae</i> i.e. exposure to children in day care		
Choose one of the above drugs ^b and add a 2 nd drug from below. If an antibiotic has been used in previous 3 months ensure a different class of drug is used.		
Amoxicillin	1.0 g TID	\$2.06
Cefuroxime	500 mg BID	\$2.90
TREATMENT FAILURE (worsening after 72 hours or no response after completion of therapy) and if there is no fluoroquinolone use in previous 3 months		
Levofloxacin	750 mg OD	\$6.55
Moxifloxacin	400 mg OD	\$6.45
Duration of therapy is usually 7 to 10 days for all regimens except levofloxacin (5 days).		

a. Comorbidities include chronic heart, lung, liver, or renal disease, diabetes, alcoholism, malignancies, asplenia, immunosuppression.

b. In theory doxycycline inhibits the action of amoxicillin; however our clinical experts do not consider this to be clinically important.

Some antibiotics not recommended in community acquired pneumonia are

- Azithromycin: Promotes *S. pneumoniae* resistance.
- Cephalexin: No activity against penicillin-intermediate/resistant *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, *C. pneumoniae* and *M. pneumoniae*.
- Cefixime: Poor activity against *S. pneumoniae* and *S. aureus*. Inactive against *C. pneumoniae* and *M. pneumoniae*.
- Ciprofloxacin: Poor activity against *S. pneumoniae*.
- Trimethoprim-sulfamethoxazole: Poor activity against *S. pneumoniae*.



Pediatric Community Acquired Pneumonia (3 months to 17 years)

- Viruses are the most frequent cause of pneumonia in the first five years of a child's life.
- Canadian pediatric guidelines state
 - Pneumonia is overdiagnosed in the absence of radiological confirmation.
 - Radiological confirmation is encouraged whenever possible to support the clinical diagnosis and may be useful if the child subsequently deteriorates.

Indications for referral or hospitalization	
<ul style="list-style-type: none"> • Oxygen saturation <92% • Hypotension • Dehydration • Sepsis • Chest retractions 	<ul style="list-style-type: none"> • Inability to eat or drink or comply with oral meds • Concerning social situation • Vomiting • Tachypnea • Evidence of lung abscess or empyema
<p>There should be a low threshold for admitting children younger than six months of age because it can be difficult for caregivers to recognize deterioration.</p>	

Source: Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Pneumonia in healthy Canadian children and youth: Practice points for management. Paediatr Child Health 2011;16(7):417-20. To see the full document, please visit www.cps.ca.

Age-specific criteria for tachypnea		
Age	Approximate normal respiratory rate	Upper limit for defining tachypnea
< 2 months	34 – 50	60
2 – 12 months	25 – 40	50
1 – 5 years	20 – 30	40
>5 years	15 – 25	30

Source: Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Pneumonia in healthy Canadian children and youth: Practice points for management. Paediatr Child Health 2011;16(7):417-20. To see the full document, please visit www.cps.ca.

Antibiotic	Regimen for Outpatient Pediatric CAP	Cost per kg per day
Amoxicillin	80 mg/kg/day divided TID – maximum 1 gram TID	\$0.09
Amox/clav	100 mg/kg/day divided TID – maximum amox 500 mg TID	Cost varies
Clarithromycin	15 mg/kg/day divided BID – maximum 500 mg BID	\$0.18
Cefprozil ^a	30 mg/kg/day divided BID – maximum 500 mg BID	\$0.10
<p>Duration of therapy is 7 to 10 days for all regimens</p>		

- a. Cefprozil can be used in case of non type 1 allergy to penicillin but does not cover *S pneumoniae* as well as amoxicillin and does not cover *Chlamydomphila pneumoniae* and *Mycoplasma pneumoniae*.



Uncomplicated Urinary Tract Infections in Women

- Urinary tract infections are among the most common bacterial infections in adults. Uncomplicated infections are limited to the lower urinary tract; fever is uncommon.
- The best indicators for antibiotic use are classic symptoms (dysuria, frequency, urgency) **plus** pyuria.
- Empiric antibiotic therapy should target *E.coli* which causes 85 to 90% of UTIs.
- Urine culture is not generally recommended unless there is failure to respond to empiric therapy or recurrence.
- There is increasing resistance of UTI pathogens to commonly used antibiotics.
 - Resistance of *E. coli* to TMP/SMX is estimated at approximately 18% in Nova Scotia.
 - Broad spectrum empiric therapy should be avoided. Fluoroquinolones (norfloxacin, levofloxacin, and ciprofloxacin) should be reserved for severe infections or intolerance to other antibiotics.
- **Nitrofurantoin** is a reasonable first line treatment choice. It is effective against *E.coli* and resistance has remained low. It is a narrow spectrum antibiotic that concentrates in the urine.

Antibiotic	Regimen for EMPIRIC Therapy	Cost per day
Nitrofurantoin	50-100 mg QID or Macrobid 100 mg BID	\$0.73 – \$0.97 Macrobid \$1.53
TMP/SMX	1 DS tab BID	\$0.25
Trimethoprim	100 mg BID or 200 mg OD	\$0.56 – \$0.58
Norfloxacin	400 mg BID	\$2.75
Levofloxacin	500 mg OD	\$2.42
Ciprofloxacin	250 mg BID or 500 mg Ext. Release OD	\$1.98 – \$3.35
Duration of therapy: 3 days for TMP, TMP/SMX, and fluoroquinolones 5 days for nitrofurantoin		

Other antibiotics and regimens are appropriate if culture confirms susceptibility.
E.g., for susceptible organisms, amoxicillin, amox/clav, and cephalexin should be given for 7 days.

Do Not Use Antibiotics

- Moxifloxacin is not indicated for treatment of UTIs because it does not concentrate in the urine.
- Amoxicillin and cephalosporins are not recommended for **empiric** therapy due to relatively high rates of resistance and lower efficacy.
- Except during pregnancy and before genitourinary procedures, there are no indications for screening or therapy for asymptomatic UTI.
- In perimenopausal and postmenopausal women, atrophic urethritis can cause urgency, frequency, and dysuria despite sterile urine and may respond to **topical** vaginal estrogen.



Urinary Tract Infections in the Elderly and Long Term Care Patients

- Asymptomatic bacteriuria is common in long term care: men 15%-30%; women 25%-50%.
 - Screening for asymptomatic bacteriuria is not recommended, even in the elderly.
 - Asymptomatic bacteriuria **should not** be treated with antibiotics. Pyuria accompanying asymptomatic bacteriuria is **not** an indication for antimicrobial treatment.
 - Pyuria indicates inflammation in the genitourinary tract, but does not differentiate symptomatic from asymptomatic UTI.
 - Positive urine cultures are virtually always associated with pyuria (>90%) and neither is sufficient for a diagnosis or treatment of UTI.
- A patient with a chronic **indwelling catheter** will always have bacteriuria, but antibiotic treatment is only warranted if they are symptomatic.
- Changes in the character of the urine such as odor, color, or turbidity are associated with bacteriuria, but are not a reliable predictor of UTI and are usually attributed to other diagnoses such as incontinence or dehydration.
- Acute symptoms may be difficult to recognize because of impaired communication, dementia, or comorbid illnesses.

When should bacteriuria be treated?

Recommendations from different sources vary somewhat. However they all differentiate between patients with and without an indwelling catheter.

In a patient **with an indwelling catheter**, the presence of at least one of the following is an indication for treatment:

- New costovertebral angle tenderness
- Fever
- Unexplained delirium
- Rigors with or without identified cause

In a patient **without an indwelling catheter**, patients must have **acute** signs and symptoms:

- Dysuria alone **OR**
- Unexplained delirium **OR**
- Fever **AND** at least one of the following
 - New or worsening urgency, frequency, or urinary incontinence
 - Suprapubic pain
 - Costovertebral angle tenderness
 - Gross hematuria

A urine specimen for culture should **always** be obtained before initiating antibiotics, to rule in or rule out UTI and to help select an antibiotic.

Choice of **antibiotic therapy** is similar to that of uncomplicated UTI, but duration of therapy is usually **7 days** (10 – 14 days in presence of fever or more severe systemic symptoms).

- **Nitrofurantoin** is contraindicated in **renal impairment** ($\text{CrCl} < 60 \text{ mL/min}$) and resistance is higher in LTC population than in other settings (21% vs 6 to 8%).
 - Long term use has been associated with pulmonary fibrosis.



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Regimen Tables

Pharyngitis				
Antibiotic	Pediatric	Cost/kg day	Adult	Cost /day
Penicillin V	≤ 27 kg: 40 mg/kg/day divided BID or TID Maximum 750 mg/day >27 kg: adult dose	\$0.03 – 0.09	600 mg BID	\$0.29
Amoxicillin	40 mg/kg/day divided BID or TID	\$0.06		
Clarithromycin	15 mg/kg/day divided BID	\$0.19	250 mg BID	\$2.20
Cefprozil	15 mg/kg/day divided BID	\$0.05	250 mg BID	\$1.39
Cefuroxime	20 mg/kg/day divided BID	\$0.15	250 mg BID	\$1.45

Duration of therapy is 10 days for all regimens

Antibiotic	Acute Otitis Media		Cost/kg/day
Amoxicillin	80 mg/kg/day	Divided BID or TID (maximum 3 grams/day)	\$0.10
Clarithromycin	15 mg/kg/day	Divided BID	\$0.19
Amox/Clav	Amoxicillin 90 mg/kg/day Clavulanate 6.4 mg/kg/day	Divided BID. Additional amoxicillin must be added to amox/clav products	Cost varies
Cefprozil	30 mg/kg/day	Divided BID	\$0.10
Cefuroxime	30 to 40 mg/kg/day	Divided BID	\$0.23 – \$0.30
Ceftriaxone	50 mg/kg/day IM or IV once daily x 3 days (reserve for emergency department)		
Duration of therapy	≤ 2 years old = 10 days > 2 years old = 5 days Complicated or frequently recurrent = 10 days		

Antibiotic	Acute Sinusitis	Cost per day
Amoxicillin	500mg TID	\$1.03
Amox/Clav	500 mg TID or 875 mg BID	\$2.00 - \$2.52
Doxycycline	200 mg for 1 st dose then 100 mg BID	\$1.17
Clarithromycin	500 mg BID	\$3.26
Cefuroxime	250 - 500 mg BID	\$1.45-\$2.90
Levofloxacin	500 mg OD	\$2.42
Moxifloxacin	400 mg OD	\$6.45

Duration of therapy is generally 10 days.

Antibiotic	AECOPD	Cost per day
Simple (low risk patient)		
Doxycycline	200 mg for 1 st dose then 100 mg BID	\$1.17
Amoxicillin	500 mg TID	\$1.03
Cefuroxime	500 mg BID	\$2.90
Clarithromycin ^a	500 mg BID	\$3.26
Complicated (high risk) patients or treatment failure^b		
Amox/Clav	500 mg TID or 875 mg BID	\$2.00 - \$2.52
Levofloxacin	500 mg OD x 7 days or 750 mg OD x 5 days	\$2.42 - \$6.55
Moxifloxacin	400 mg OD	\$6.45
Risk for <i>P. aeruginosa</i> (FEV₁ < 35% predicted OR have multiple risk factors OR have constant purulent sputum)		
Ciprofloxacin	500-750 mg BID	\$2.24 - \$4.09

Duration of therapy is usually 7 to 10 days. Expect symptoms to improve but not completely disappear at the end of therapy. Symptoms may not completely resolve for several weeks.

a. Clarithromycin may be less effective against *H. influenzae* and is usually reserved for B-lactam allergy.

b. Treatment failure: clinical deterioration after 72 hour or no improvement with first line treatment.

Regimen Tables

Antibiotic	CAP in Outpatient Adults	Cost per day
MONOTHERAPY previously healthy, low risk patient and no risk factors for drug-resistant <i>S pneumoniae</i>		
Doxycycline	200 mg for 1 st dose then 100 mg BID	\$1.17
Clarithromycin	500 mg BID	\$3.26
DUAL THERAPY presence of comorbidities ^a , antimicrobial use within the previous 3 months, or other risk factors for drug-resistant <i>S. pneumoniae</i> i.e. exposure to children in day care		
Choose one of the above drugs ^b and add a 2 nd drug from below. If an antibiotic has been used in previous 3 months ensure a different class of drug is used.		
Amoxicillin	1.0 g TID	\$2.06
Cefuroxime	500 mg BID	\$2.90
TREATMENT FAILURE (worsening after 72 hours or no response after completion of therapy) and if there is no fluoroquinolone use in previous 3 months		
Levofloxacin	750 mg OD	\$6.55
Moxifloxacin	400 mg OD	\$6.45
Duration of therapy is usually 7 to 10 days for all regimens except levofloxacin (5 days).		

- a. Comorbidities include chronic heart, lung, liver, or renal disease, diabetes, alcoholism, malignancies, asplenia, immunosuppression.
 b. In theory doxycycline inhibits the action of amoxicillin; however our clinical experts do not consider this to be clinically important.

Antibiotic	Outpatient Pediatric CAP	Cost per kg per day
Amoxicillin	80 mg/kg/day divided TID – maximum 1 gram TID	\$0.09
Amox/clav	100 mg/kg/day divided TID – maximum amox 500 mg TID	Cost varies
Clarithromycin	15 mg/kg/day divided BID – maximum 500 mg BID	\$0.18
Cefprozil ^a	30 mg/kg/day divided BID – maximum 500 mg BID	\$0.10
Duration of therapy is 7 to 10 days for all regimens		

- a. Cefprozil can be used in case of non type 1 allergy to penicillin but does not cover *S pneumoniae* as well as amoxicillin and does not cover *Chlamydomphila pneumoniae* and *Mycoplasma pneumoniae*.

Antibiotic	Empiric UTI Therapy	Cost per day
Nitrofurantoin	50-100 mg QID or Macrobid 100 mg BID	\$0.73 – \$0.97 Macrobid \$1.53
TMP/SMX	1 DS tab BID	\$0.25
Trimethoprim	100 mg BID or 200 mg OD	\$0.56 – \$0.58
Norfloxacin	400 mg BID	\$2.75
Levofloxacin	500 mg OD	\$2.42
Ciprofloxacin	250 mg BID or 500 mg Ext. Release OD	\$1.98 – \$3.35
Duration of therapy:		3 days for TMP, TMP/SMX, and fluoroquinolones 5 days for nitrofurantoin

Other antibiotics and regimens are appropriate if culture confirms susceptibility. E.g., for susceptible organisms, amoxicillin, amox/clav, and cephalexin should be given for 7 days.