Treating Common Upper Respiratory Tract Infections in an Era of Increasing Antibiotic Resistance

Urgent message: Thorough evaluation and thoughtful prescribing can help ensure responsible, effective care and patient satisfaction.

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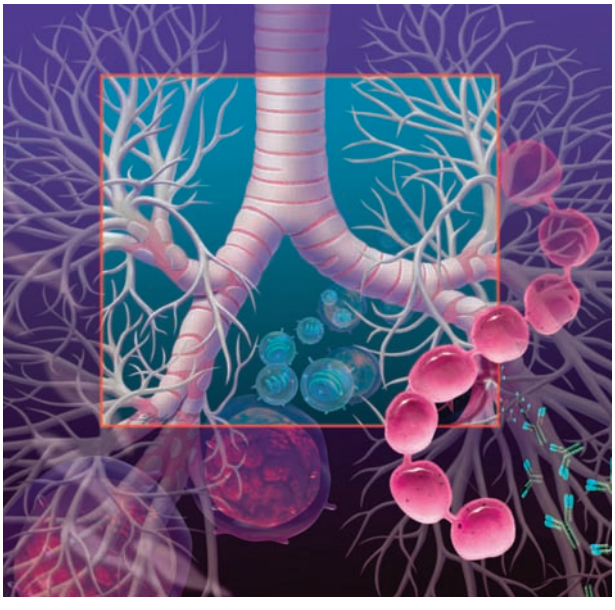
Introduction

Upper respiratory tract infections (URTIs) are among the most common reasons patients seek assistance in urgent care practice. The common cold, otitis media, acute sinusitis, and acute pharyngitis are well known to patient and provider alike. Acute bronchitis is a lower respiratory tract infection, with features similar to URTIs.These infections are most often self-limited and uncomplicated, but the approach to evaluating each patient should include examining for complications as well as rarer, more severe diseases that can mimic these simpler, common conditions. Treatment should include patient education, symptom management, and the use of antibiotics *only* if likely to improve the clinical outcome.



Data show a positive correlation between increasing levels of antibiotic use and increasing antibiotic resistance among bacteria.[1] Though in the United States there seems to be a gradually decreasing rate of antibiotic prescription for URTIs in general, overprescription is still common and there is an increasing trend toward the use of broad-spectrum antibiotics for these relatively simple infections.[2,3]

It is intuitive that a strategy of prescribing antibiotics only when necessary and only of the appropriate antimicrobial spectra will minimize the development of antibiotic resistance. Guidelines describing such use have been published by several organizations (see **Table 1** for links) and will be the primary subject of this review.

Clinical Diagnosis, Testing, and Important Complications and Disease Mimics

URTIs are often grouped together because they share a closely related anatomy and pathophysiology. The mu-

Table 1. Clinical Guidelines for the Treatment of Upper Respiratory Tract Infections

URTI	Organization	URL for clinical guideline resource (as of July 1, 2009)
Common cold	ACP	*www.annals.org/cgi/reprint/134/6/487.pdf**
	ICSI	*www.icsi.org/respiratory_illness_in_children_and_adults__guideline_/respiratory_illness_in_children_and_adults__guideline__13116.html*
Acute sinusitis	ACP	*www.annals.org/cgi/reprint/134/6/495.pdf**
	AAP	*http://aappolicy.aappublications.org/cgi/reprint/pediatrics;108/3/798.pdf**
	ICSI	*www.icsi.org/respiratory_illness_in_children_and_adults__guideline_/respiratory_illness_in_children_and_adults__guideline__13116.html*
	AAO-HNS	*www.entnet.org/qualityimprovement/upload/Adult%20Sinusitis%20Guideline.pdf*
	IDSA	Under development—due out in Fall 2010.
Acute pharyngitis	IDSA	www.journals.uchicago.edu/doi/pdf/10.1086/340949?
	ACP	*www.annals.org/cgi/reprint/134/6/506.pdf**
	ICSI	*www.icsi.org/respiratory_illness_in_children_and_adults__guideline_/respiratory_illness_in_children_and_adults__guideline__13116.html*
Acute bronchitis	ACP	*www.annals.org/cgi/reprint/134/6/518.pdf**
Acute otitis media	AAP	*http://aappolicy.aappublications.org/cgi/reprint/pediatrics;113/5/1451.pdf*
	ICSI	*www.icsi.org/otitis_media/diagnosis_and_treatment_of_otitis_media_in_children_2304.html*

ACP, American College of Physicians; ICSI, Institute for Clinical Systems Improvement; AAP, American Academy of Pediatrics; AAO–HNS, American Academy of Otolaryngology–Head and Neck Surgery; IDSA, Infectious Diseases Society of America

Compendia of all relevant clinical practice guidelines for URTIs in adults and children, updated annually, is available for download at: *www.aware.md/HealthCareProfessionals/ClinicalResources.aspx*

*Certain ACP and AAP Guidelines are over 5 years old and therefore not considered "current" by those organizations; however, pending updates, these are the most recent recommendations.

cosa of the nose, throat, bronchi, middle ear, and paranasal sinuses are essentially contiguous and are exposed to similar organisms.

Typically, the area of the respiratory tract that is *most* involved—indicated either by symptoms or on exam—and the severity of illness yield a clinical diagnosis. The majority of URTIs are viral in nature, with the remainder caused by a narrow-enough range of pathogens that focused-spectrum antibiotics can be used.

- Symptoms of the common cold can include nasal congestion and drainage, sneezing, mild sore throat and cough, and fever. Nasal symptoms usually predominate; otherwise, the widespread nature (sinuses, nose, throat, chest) of generally mild, though often aggravating, symptoms establishes this diagnosis.
- The acute onset of cough and higher fever—typically with associated headache and myalgias—generally distinguishes human, swine, and avian influenza. These particularly viral URTIs have higher rates of associated morbidity and mortality and require a different approach than will be discussed in this article. (An excellent review of the testing, evaluation, and care of patients with swine-origin H1N1 virus appeared in the October 2009 issue of *JUCM*.)
- When cough predominates, bronchitis is usually the diagnosis. Wheezing, even in patients without a history of bronchospastic disease, may be noted on exam. When cough is associated with an inspiratory whoop (usually seen only in children) or post-tussive vomiting or is severe and paroxysmal, clinicians should suspect pertussis, especially when symptoms last longer than 14 days. A higher index of suspicion (e.g. *any* cough illness lasting more than 14 days or severe cough illness of a shorter duration) will apply during an identified pertussis outbreak.[4]
- Prominent ear pain and abnormal otoscopic findings indicate otitis media.
- Sinus pain can suggest sinusitis.
- A chief complaint of sore throat typically indicates pharyngitis.

Sorting through the differential diagnosis of URTIs is largely a clinical exercise. Analyzing a patient's symptomatology and performing a systematic exam are crucial to the process of diagnosis and the exclusion of significant complications or other diseases that can present in ways similar to milder forms of infection (see **Table 2**).

On the other hand, there are no clinical criteria (e.g., the presence of fever, level of discomfort, exam findings, the color or characteristics of any produced sputum or mucous) that can be used to reliably distinguish between bacterial and viral etiologies.

Only a few diagnostic tests are needed when evalu-

Table 2. Upper Respiratory Tract Infection Complications and Differential Diagnosis

URTI	Complications	Differential diagnoses and "can't miss" mimics
Common cold	Other URTIs	Other URTIs Allergic or vasomotor rhinitis
Acute bronchitis	CHF, RAD, COPD exacerbation	Pneumonia Exacerbation of RAD, COPD, or CHF Pertussis
Acute otitis media	Mastoiditis, tympanic membrane perforation	Eustachian tube dysfunction Barotrauma Otitis externa Mastoiditis
Acute sinusitis	Intracranial infection, periorbital cellulitis	Common cold Chronic sinusitis Meningitis Wegener's granulomatosis
Acute pharyngitis	Peritonsillar or parapharyngeal space infections (though may be separate disease process); rheumatic fever and acute glomerulonephritis (for *Strep*)	Peritonsillar or parapharyngeal space infections Epiglottitis HIV primary infection Infectious mononucleosis Gonococcal pharyngitis Kawasaki disease

CHF, congestive heart failure; RAD, reactive airways disease; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus

ating patients with URTIs. Each disease mimic, however, may have its own diagnostic test(s), a discussion of which exceeds the scope of this review.

Of course, patients who are toxic-appearing or who are immunosuppressed or have other significant comorbidities should be evaluated very aggressively; the recommendations that follow do not apply to these subsets of patients.

Appropriate testing

No diagnostic testing is required for patients with the common cold. However, confirming respiratory syncytial virus (RSV) or influenza infection in febrile pediatric patients with rapid "point-of-care" testing has been shown to reassure clinicians and safely decrease antibiotic prescription and unnecessary further work-ups for other infections.

Complications and mimics of the common cold include any of the other URTIs and allergic and vasomotor rhinitis. Typically, the presence of fever suggests URTI, while ongoing nasal congestion and rhinorrhea in a patient without fever suggest noninfectious rhinitis.

No diagnostic testing is needed to confirm acute bronchitis, though a chest radiograph should be performed if pneumonia is suspected. Pneumonia may be more likely in an older or ill-appearing patient; if there is fever, hypoxemia, tachycardia, or tachypnea; or if abnormalities are present on lung exam.

Those with acute bronchitis symptoms and a history of asthma, chronic obstructive pulmonary disease, or congestive heart failure may be having an exacerbation of chronic disease, either as their primary problem, or triggered by a concomitant chest infection. An assessment of past history and risk factors, as well as physical exam and, when needed, chest radiograph findings can usually establish the diagnosis.

In most situations, for suspected cases of pertussis, the recommended strategy involves both polymerase-chain reaction (PCR) testing and culture, health department reporting, empiric treatment, and close follow-up. A lower threshold for empiric treatment will apply during an indentified pertussis outbreak.[4] Local infectious disease specialists, health departments, and the CDC are important resources to consult to balance the need to identify and treat this disease while avoiding treating everyone who has a prolonged cough with antibiotics.

No testing is necessary to make the diagnosis of acute otitis media or sinusitis. There is no proven beneficial role for sinus radiographs in the diagnosis or treatment of sinusitis, and CT scanning of the sinuses should be reserved for refractory or severe cases being treated in conjunction with specialty care.

The diagnosis of otitis media should include acute onset of ear pain and physical exam evidence of tympanic membrane (TM) inflammation and middle-ear effusion (i.e., bulging TM, air-fluid level, otorrhea, or decreased TM mobility on pneumatic otoscopy). Mimics of otitis media are usually distinguishable on exam, and specific palpation of the mastoid process is important in any patient with ear pain.

Features traditionally associated with the clinical diagnosis of sinusitis—nasal obstruction, purulent nasal discharge, pain on bending forward, maxillary toothache, presence of a two-stage illness with sinus symptoms following a URTI—have variable sensitivity and specificity.[5]

One of the more common mimics of acute sinusitis is the exacerbation of chronic sinusitis. There is no specific number, but any patient presenting with his or her "usual sinus infection" three or more times per year probably requires a different approach than just an antibiotic prescription and a pat on the back. For these patients, strongly consider a work-up for chronic sinusitis and its causes (anatomic osteomeatal disease, chronic rhinitis, etc.), typically in conjunction with a specialist. And, though it occurs rarely, patients with sinusitis combined with signs of pulmonary and/or renal disease should be promptly referred for work-up for Wegener's granulomatosis.

Diagnostic testing does play a role in the management of acute pharyngitis. Older guidelines presented options for purely clinical diagnosis, emphasizing the cost effectiveness of such an approach, but the most recent recommendations emphasize obtaining positive rapid antigen testing or culture for group A beta-hemolytic *Streptococcus* (GABHS) *before* beginning antibiotic treatment. Some guidelines recommend that, in the face of an initial negative rapid antigen test, patients with a high chance of GABHS (based on age and other risk factors) should have a throat culture obtained before discharge from the clinic. Patients with a prior history of rheumatic fever are at high risk of recurrence and should be followed very closely when they develop pharyngitis or any possible Streptococcal infection.

Any patient with sore throat should be thoroughly examined for swelling or other abnormalities of the uvula and peritonsillar and other parapharyngeal spaces. Drooling, stridor, and trismus are nonspecific but typically indicate severe disease and the need for urgent specialty consultation or ED transfer.

In the absence of such severe symptoms, finding any of these disease mimics at the earliest possible stage requires consideration of the full range of possible diagnoses—maintaining a high index of suspicion—for every patient with a sore throat.

Of the many viral etiologies for pharyngitis, some can result in higher rates of morbidity, including Epstein Barr virus and cytomegalovirus, both of which can cause an acute-mononucleosis-type syndrome of fever, malaise, lymphadenopathy, and frequently splenomegaly and usually mild hepatitis.

Primary infection with human immunodeficiency virus (HIV) can result in a similar clinical picture and should be considered in patients with appropriate risk factors.

Suspicion of gonococcal pharyngitis is also engendered by risk factor assessment.

Kawasaki disease presents more often as stomatitis than as pharyngitis, but it is important to keep this diagnosis in mind due to the potential complication of affected children developing coronary artery aneurysms. Suspect the diagnosis and obtain urgent consultation for children under 10-years-old (particularly under 3 years of age) with fever for five days or more, and a syndrome including conjunctivitis, polymorphous rash or desquamation, cervical lymphadenopathy, and any combination of fissured lips, stomatitis, pharyngitis, and/or strawberry tongue.[6]

Treatment and Disposition

Toxic-appearing and otherwise unstable patients—those with airway, breathing, and circulatory compromise—require an aggressive approach, with initial rapid evaluation and stabilization (supplemental oxygen and intravenous fluid boluses and airway interventions, if within the scope of the clinic and clinician) and prompt ambulance transport to the emergency department.

Patients who have compromised immunity, significant comorbidities (e.g., chronic obstructive pulmonary disease, pulmonary fibrosis, cystic fibrosis, congestive heart failure, hepatic and renal disease, etc.), or refractory, persistent, or frequently recurrent URTIs require more complex decision-making than that described here.

In general, however, stable, otherwise healthy patients with uncomplicated URTIs who are maintaining their hydration—who will be the overwhelming majority of patients in most practices—can be treated very simply at home.

In every situation, explain to patients what they should expect and discuss precautions for immediate re-evaluation, as well as specific timing for return if not improving. Schedule next-day follow-up for patients for whom the level of illness is unclear. Because every disease has a time course and even uncommon things will occur the longer one practices, use good communication and close clinical follow-up as your safety net for every patient.

Common cold, bronchitis, and viral pharyngitis

Existing clinical practice guidelines emphasize the importance of not prescribing antibiotics for patients with a common cold, acute bronchitis, and viral pharyngitis. Symptomatic care can include acetaminophen or a nonsteroidal anti-inflammatory medication (if there are no contraindications) for fever, aches, and pain. Stronger analgesics may be reasonable in patients who fail to get relief with these, e.g., to facilitate oral fluid intake in those with pharyngitis.

Often, patients desire relief from cough; unfortunately, no preparation has consistently shown clinical benefit. A potential limitation in this research, however, is that comparison is often made with a placebo, yet no placebo exists for clinicians to prescribe or recommend! It is probable that, as long as the possible side effects are considered by the patient and provider, prescription of some sort of cough suppressant is reasonable.

In patient with bronchitis, some studies have shown variable benefit for the use of beta-agonist inhalers, like albuterol, to help with cough and chest congestion; the presence of wheezing on exam may indicate a greater chance of benefit in a particular patient.

Otitis media and acute sinusitis

For both acute otitis media and sinusitis, the decision to treat with antibiotics may be based on available guidelines, plus the knowledge that placebo-controlled studies have shown rates of up to 80% resolution without antibiotics for these conditions.[7]

A study published in 2007 in the *British Medical Journal*[8] estimated that over 4,000 patients with otitis media would need to be treated with an-

Table 3. Recommended Antibiotic Regimens for Uncomplicated Respiratory Tract Infections

Respiratory tract infection	First-line antimicrobial therapy	Alternate therapy
Common cold	None	None
Acute sinusitis	None or amoxicillin	Doxycycline Trimethoprim/sulphamethoxazole Cefdinir, cefprozil, cefuroxime, cefpodoxime Amoxicillin/clavulanate Respiratory fluoroquinolones Clarithromycin Azithromycin
Acute pharyngitis	Penicillin, if *Strep* testing is positive	For *penicillin-allergic** patients: Second-generation cephalosporins Erythromycin Clindamycin
Acute bronchitis	None	None
Acute otitis media	Amoxicillin (high-dose) 80-90 mg/kg daily divided BID	Amoxicillin/clavulanate For penicillin-allergic* patients: Cefuroxime Cefdinir Cefpodoxime Azithromycin Clarithromycin Ceftriaxone

* Some patients who report prior allergy to penicillin also have allergic reactions to cephalosporins; if a person has had anaphylaxis or other severe allergy to penicillin, it is safest to avoid cephalosporins.

tibiotics to prevent a serious complication (e.g., mastoiditis) in one patient; a similar "number needed to treat" of over 4,000 applied to preventing serious complications of URTI and sore throat.

Specifically, antibiotic treatment *is* recommended for all of those under 6 months of age who have a diagnosis of otitis media. There is an option to observe and withhold antibiotics in children between 6 months and 2-years-old if the diagnosis is uncertain or the condition is not severe, and for those 2 years and older unless the diagnosis is certain *and* the disease is severe.

When antibiotics are used, focused-spectrum therapy is recommended (see **Table 3**). Amoxicillin is still first line, although because of the prevalence of drug resistance among pneumococcus, a high-dose regimen (80 mg/kg/day to 90 mg/kg/day, divided BID) is recommended.

For all patients with otitis media, attention to analgesia (oral and topical) is strongly emphasized. Decongestants and antihistamines have not been shown to be helpful.[9] There are no specific guidelines for adults with otitis media.

For acute sinusitis, existing guidelines recommend using antibiotics in patients with severe symptoms or moderate symptoms that are worsening after five to 10 days or not improved after 10 days. Again, focused-spectrum antibiotics (**Table 3**) are first line for uncomplicated infections if antibiotics are felt to be necessary.

Studies have yielded a range of results regarding the use of nasal steroid sprays, and a *Cochrane Review*[10] of the literature found them to be possibly effective. Antihistamines may cause drying of nasal secretions and impede drainage, and are generally avoided in patients with sinusitis.

Interestingly, some new evidence[11] suggests that, though a specific patient may indeed have sinusitis, there may be no reliable clinical indicators to tell a clinician whether antibiotics might be helpful or harmful to that patient.

GABHS pharyngitis

Penicillin-resistance among GABHS has been reported to be nonexistent or extremely rare. (In contrast, macrolide resistance is rising.) Concerns have been raised regarding penicillinase activity among other organisms inhabiting the throat at the same time as a GABHS infection, but these seem to impact mostly disease-related outcomes such as culture-proven eradication of the pathogen, rather than patient-oriented outcomes such as duration of illness or the development of complications.

For all of these reasons, guidelines continue to recommend penicillin as first-line antimicrobial therapy for GABHS pharyngitis in patients who are not allergic to it. For penicillin-allergic patients, a narrow-spectrum alternative antibiotic should be used (**Table 3**).

Adjunctive systemic corticosteroids for one to three days (at most) may help decrease pain associated with GABHS pharyngitis.

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the 48-hour visit and determined the need for further intervention and measured wound erythema, induration, and fluctuance. Measurements were repeated by a second, similarly blinded physician. All patients were contacted by phone 10-15 days after the initial visit to determine if their abscesses had required additional interventions.

Patients were randomized to the packing group (n=23) or the non-packed group (n=25). Only 34 subjects (66%) returned for the 48-hour follow-up visit. Thirteen were from the non-packed group and 21 from the packed group. Four of the patients in the packed group and five of the patients in the non-packed group required intervention at follow-up.

Ten of the 11 patients in the non-packed group who did not return for follow-up and were contacted by phone reported that they did not think the abscess required re-evaluation and that they were pain free. Only one of the three patients in the packed group who did not follow up was reached and reported moderate pain but did not return to the ED.

There was no difference between the groups in pre-procedural pain scores. Subjects in the packed group reported higher pain scores in both the immediate post-procedural period and at the 48-hour follow up visit. There was no significant difference in the amount of ibuprofen taken, but patients in the packing group took a mean of 3.1 narcotic pain pills, compared with a mean of 0.91 pills in the non-packed group.

Given the prevalence of community acquired methicillin-resistant *Staph aureus*, it is unlikely that we will see a reduction in the prevalence of cutaneous abscesses. However, if the evidence bears out, elimination of packing of simple abscesses will save time and money and reduce patient discomfort. ■

URTI, continued from page 18

A note on dehydration

A complication of any of the URTIs in children, and sometimes adults, is dehydration. Fever and other mechanisms can increase insensible fluid loss, and malaise and sore throat can decrease fluid intake. Discuss fever control, analgesia, and appropriate oral hydration with each patient; occasionally providing intravenous fluid rehydration may be necessary.

Patient Satisfaction

There is no evidence that patient satisfaction is related to getting an antibiotic prescription for a URTI. In addition, data show that clinicians are not able to determine whether any particular patient expects such a prescription or not.

Studies do link patients' satisfaction to their receiving discussions of their diagnoses, as well as attention to alleviation of their symptoms.

Several years ago, the concept of a delayed or "safety net" prescription was introduced. This strategy involved giving a patient an antibiotic prescription, along with instructions to wait for several days of no improvement before filling and beginning to take it. This approach was shown in several studies to be safe, to reduce antibiotic use, and to be satisfactory to patients. However, a recent review[12] combining many studies showed that prescribing no antibiotic, rather than giving a safety net prescription, resulted in similar clinical and patient satisfaction outcomes, assuming clinicians felt that is was safe not to prescribe antibiotics for a URTI.

Conclusion

Antibiotic prescribing has a direct impact on the development of antimicrobial resistance. URTIs are a common chief complaint in urgent care practice, and the tendency to overprescribe antibiotics exists. A variety of guidelines and data from the medical literature can assure the clinician that antibiotics are not necessary for the majority of uncomplicated URTIs in most patients. ■

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