URTIs: recommended diagnosis and treatment in general practice

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Although antibiotics have only a minor role to play in the management of most upper respiratory tract infections, it can be difficult to recognise when there might be serious complications. In our Drug review the authors describe the features and usual treatment of common URTIs, followed by sources of further information.

The upper respiratory tract is the site of infection for a large number of viral and bacterial pathogens – some of these infections remain localised, whereas others may spread to adjacent systems or cause generalised disease. The term upper respiratory tract infection (URTI) encompasses a number of diseases that, due to the spectrum of anatomical sites involved, causative organisms and numerous host and environmental factors, have a corresponding diverse range of presentations.

Acute infections of the upper respiratory tract contribute significantly to consultation statistics in general practice: the fourth national study of morbidity in general practice suggested a rate of 772 per 10 000 person years,1 accounting for roughly 10 per cent of all consultations.

NICE produced guidelines for the prescription of antibiotics in 2008 (reviewed in 2012),2 and this article will consider the diagnosis and treatment of URTIs within the framework of those guidelines.

In an era of raised awareness of the emergence of antibiotic resistance related to overprescription of antimicrobials, antibiotic stewardship has become an increasingly important part of assessing respiratory tract infections in general practice.3 The quick reference guide as part of the NICE guidelines includes a care pathway to assist this decision.4

Common cold5

The common cold is generally a mild, self-limiting illness of viral origin, characterised by upper respiratory tract symptoms. The virus most commonly associated with cold symptoms is rhinovirus, but the same syndrome may be caused by other viruses, such as coronavirus, respiratory syncytial virus (RSV), influenza virus, parainfluenza virus and adenovirus. Recently, human metapneumovirus and human bocavirus have been identified as causative agents in a small number of patients.
Colds occur year-round but do demonstrate a seasonal peak, being less common in warmer months. Many individuals may suffer multiple clinical infections per year, reflecting both the fact that a number of viruses are able to cause the disease and that reinfection may occur with the same virus type. Transmission of common cold-causing viruses occurs by dispersal of small-particle aerosols (droplet nuclei), large-particle aerosols (that are briefly suspended in air) and direct contact with infectious secretions on skin or environmental surfaces.

Routine laboratory tests are not helpful in the diagnosis or management of colds: the clinical picture is diagnostic. After an incubation period of 12–72 hours, the predominant symptoms are those of nasal congestion, sneezing and rhinorrhea, but cough, sore throat and fever may also occur. The presentation is similar in both children and adults; however, in young children parainfluenza virus and RSV infections may lead to viral pneumonia, croup or bronchiolitis.

Clinically significant complications may occur, including acute otitis media and sinusitis; these may be viral in nature or due to bacterial superinfection.

Although the viral pathogen can be detected from a respiratory sample by molecular methods (polymerase chain reaction – PCR), this is not generally justified in general practice as it does not alter management. Bacterial cultures may be indicated when there is concern about an alternative diagnosis.

Treatment
Several Cochrane reviews exist on the subject of the common cold, offering an evidence base for treatment. Most importantly, in keeping with the viral aetiology of the disease, the evidence supports the commonsense assertion that antibiotics have no role in treatment. Steam inhalation and increasing oral fluid intake did not demonstrate any benefit either.7,8

Additionally, there is insufficient evidence that would support the routine use of complementary or alternative therapies, such as Chinese medicinal herbs,9 vitamin C,10 garlic11 or Echinacea preparations.12 NSAIDs have been shown to alleviate some of the symptoms of colds but have no effect on disease course.13 Generally treatment is symptomatic only.
Influenza

Influenza is an acute, usually self-limiting, febrile illness caused by influenza virus (most commonly type A or type B). It is associated with outbreaks of varying severity almost every winter, with epidemics occurring every few years. Other viruses, e.g., parainfluenza virus, can cause a similar picture, leading to the commonly used term ‘flu-like illness’.

Usual manifestations are fever, malaise and cough; however, serious pneumonic infection may occur and this can become complicated by bacterial infection.

In 2009 the emergence of a pandemic strain of an influenza A (H1N1) virus of swine lineage lead to a number of control measures in the UK, including an immunisation programme for at-risk groups, the development of a swine flu clinical package and the widespread availability of antiviral therapy. Up-to-date information about both seasonal and pandemic influenza can be found on the Public Health England (PHE) website.

Diagnosis may be made on the basis of PCR tests on respiratory specimens or retrospectively by serological methods.

Treatment

The mainstay of control is the seasonal influenza vaccine for at-risk groups and healthcare workers. The recommended antivirals for treatment are the neuraminidase inhibitors oseltamivir (Tamiflu) and zanamivir (Relenza). In the primary-care setting antivirals should only be used once the Department of Health issues notice that influenza is circulating and that antiviral agents can be used. A algorithm produced by PHE is available to guide antiviral treatment.

Pharyngitis (see Figure 1)

Acute pharyngitis describes a syndrome of sore throat, fever and pharyngeal inflammation; there are numerous potential causative micro-organisms (see Table 1). Most cases are of viral origin and may occur as part of the presentation of a common cold.

Syndromes

Streptococcal pharyngitis is the most important of the bacterial infections of the pharynx; those due to group A beta-haemolytic streptococci (GAS), also known as Streptococcus pyogenes. Its importance is due to the possibility of development of postinfectious sequelae: these may be suppurative, e.g., local abscess formation, or nonsuppurative. The nonsuppurative complications, such as acute rheumatic fever or poststreptococcal glomerulonephritis, are currently uncommon in the UK.

Pharyngitis due to GAS has certain characteristic epidemiological and clinical features (see Table 2). This disorder occurs primarily in children 5–15 years of age, and usually in the winter or early spring. Symptoms develop after a short incubation period of two to four days. In severe cases of streptococcal pharyngitis, there is marked pharyngeal pain, odynophagia and fever.

The clinical features of pharyngeal infection with strains of groups C and G beta-haemolytic streptococci are similar to those of GAS, including the occurrence of purulent exudate, fever and anterior cervical lymphadenopathy.
**Pathogen** | **Associated disorders/symptoms**
--- | ---
**Bacterial** | Tonsilitis and scarlet fever
- *Strep. pyogenes*
- Strep. groups C and G
- Mixed anaerobes
- *Neisseria gonorrhoeae*
- *Corynebacterium diphtheriae*
- *Arcanobacterium haemolyticum*
- *Neisseria meningitidis*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes* (GAS)

**Viral** | Common cold
- Rhinovirus/coronavirus
- Adenovirus
- Herpes simplex virus types 1 and 2
- Parainfluenza virus
- Coxsackie virus A
- Epstein-Barr virus
- Influenza A and B virus

**Mycoplasmal** | Pneumonia and bronchitis
- *Mycoplasma pneumoniae*

**Chlamydial** | Acute respiratory disease
- *Chlamyphila psittaci*
- *Chlamyphila pneumoniae*

**Diagnosis**
In the patient presenting with acute pharyngitis it is important to identify those caused by GAS, as this is the only commonly occurring aetiology for which specific antibiotic therapy is definitely indicated. Bacterial culture of a throat swab remains the standard for the diagnosis of streptococcal pharyngitis, and an appropriately taken specimen may have a sensitivity of up to 90–95 per cent.

Rapid antigen detection tests (RADTs) are quick, near-patient tests for GAS. These may be less sensitive than cultural methods but provide an immediate result and are highly specific, so false positives are uncommon. However, RADTs are infrequently employed in UK clinical practice.

Where the clinical picture is suggestive of infectious mononucleosis, diagnosis may be aided by the presence of a positive heterophile antibody test (Paul-Bunnell or ‘spot’ test). This is more than 80 per cent sensitive in the second week of illness, although may be negative early in the disease. Serological tests are useful in cases where the Paul-Bunnell test is negative but the clinical syndrome and peripheral blood film are consistent with infectious mononucleosis.

Investigations are rarely necessary for other viral causes of pharyngitis.

**Treatment**
Resistance to penicillin has never been reported in GAS, so it remains the treatment of choice for patients with streptococcal pharyngitis. Standard therapy is oral phenoxymethylpenicillin (penicillin V) for 10 days, or erythromycin for patients with a penicillin allergy (see Table 3), with the aim of preventing the development of postinfectious sequelae. Treatment should be initiated if the presence of the organism is confirmed on culture or RADT, or if there are clinical or epidemiological grounds to suspect that GAS is the pathogen. While adjunctive analgesic treatment may be considered (avoid aspirin in children), the use of corticosteroids is not recommended.

Use of the Centor criteria has been recommended to distinguish disease caused by GAS: the presence of three or four of tonsillar exudate, tender anterior cervical lymph nodes, absence of cough, and history of fever has a positive predictive value of 35–53 per cent for streptococcal infection.

There is usually no urgency in commencing treatment while awaiting laboratory confirmation as the disease is generally self-limiting; furthermore, therapy to prevent acute rheumatic fever may be safely postponed for up to nine days.

Treatment is indicated for other bacterial infections, such as gonorrhoea or diphtheria, but specific recommendations are beyond the scope of this review.

**Acute laryngitis**
This is a common illness characterised by inflammation of the larynx. It presents as hoarseness of the voice, often in the context of a URTI. Aetiology is rarely defined in clinical practice, but
infectious laryngitis may be viral or bacterial in origin – it is most frequently viral. Common viral agents include parainfluenza virus, rhinovirus, influenza virus and adenovirus. There is only scant good-quality evidence regarding antibiotic treatment of laryngitis in adults, and those data do not demonstrate any benefit.

Epiglottitis
Acute epiglottitis (supraglottitis) is an infection of the soft tissues of the epiglottis and adjacent structures, the most feared consequence of which is rapid, total airway obstruction. Historically this was a disease of young children and usually caused by Haemophilus influenzae type b (Hib). Now, with the advent of widespread vaccination against Hib, this organism and the incidence of the disease in children are both significantly less common.

The symptoms include fever, irritability, sore throat and progressive stridor – the classic presentation is of a child struggling for breath, leaning forward and drooling oral secretions. Diagnosis depends on direct visualisation of an oedematous cherry-red epiglottis, but this should not take place unless there are immediate facilities to secure the airway in case examination precipitates obstruction. Because of this risk, a child suspected of having acute epiglottitis should be managed as a medical emergency and referred to hospital.

Otitis media (see Figure 2)
Acute otitis media (AOM) is a common disease of children and, correspondingly, a common cause of antibiotic prescription in this age group. It is characterised by inflammation of the middle ear of rapid onset, presenting with local symptoms (ear pain, discharge or decreased hearing) and systemic signs (fever, irritability).

<table>
<thead>
<tr>
<th>Features suggestive of Strep. pyogenes</th>
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<tbody>
<tr>
<td>• sudden onset</td>
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<tr>
<td>• sore throat</td>
</tr>
<tr>
<td>• fever, headache</td>
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<tr>
<td>• nausea, vomiting and abdominal pain</td>
</tr>
<tr>
<td>• inflammation of pharynx and tonsils</td>
</tr>
<tr>
<td>• patchy discrete exudate</td>
</tr>
<tr>
<td>• tender, enlarged anterior cervical nodes</td>
</tr>
<tr>
<td>• patient aged 5–15 years</td>
</tr>
<tr>
<td>• presentation in winter and early spring</td>
</tr>
<tr>
<td>• history of exposure</td>
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<table>
<thead>
<tr>
<th>Features suggestive of viral aetiology</th>
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</thead>
<tbody>
<tr>
<td>• conjunctivitis</td>
</tr>
<tr>
<td>• coryza</td>
</tr>
<tr>
<td>• cough</td>
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<tr>
<td>• diarrhoea</td>
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Note: these findings cannot definitely predict the presence of Strep. pyogenes tonsillitis; they can, however, identify persons for whom the probability of Strep. pyogenes tonsillitis is high.

Table 2. Features of pharyngitis/tonsillitis due to infection with Strep. pyogenes and viruses
Inflammation of the middle ear usually follows a viral infection: congestion in the mucosa of the eustachian tube leads to obstruction and stasis of middle ear secretions. Bacterial pathogens, if present, may then multiply.

The aetiology of AOM has been defined by specimens obtained via tympanocentesis demonstrating that Strep. pneumoniae and H. influenzae are the most commonly isolated bacterial pathogens followed by Moraxella catarrhalis, with Staphylococcus aureus and group A streptococcus being rare. Combined viral and bacterial infections are frequent.\(^\text{27}\)

Complications may include mastoiditis (addressed below) and intracranial spread of infection.

**Diagnosis**\(^\text{28}\)

Signs on otoscopic examination include a bulging tympanic membrane with loss of the normal landmarks, erythema and poor mobility, and fluid is present in the middle ear. Routine bacterial cultures are not indicated as the causative organisms are predictable; tympanocentesis is reserved for complicated cases (persistent symptoms despite repeated courses of antibiotics) that need to be referred to ENT.

It is important to distinguish AOM from chronic otitis media with effusion (OME), which is defined as the presence of fluid in the middle ear without signs or symptoms of acute ear infection. The latter disease can lead to hearing loss and contribute to developmental delay and is therefore likely to require closer follow-up; depending on severity and disability, it may require surgical intervention.\(^\text{29}\)

**Treatment**

*Acute otitis media* Although there are difficulties in interpreting the literature on the condition, the consensus view is that, in most children, antibiotics have only marginal benefits that must be balanced against a small potential for harm.\(^\text{28-30}\) It is difficult to know whether withholding antibiotics contributes to an increased risk of complications as these are generally rare.\(^\text{31}\) It is therefore a reasonable approach to not routinely prescribe antibiotics initially in uncomplicated, nonsevere AOM.

An alternative approach that has been proposed is delayed antibiotic therapy: the patient, or more frequently the parents, may be given the opportunity to collect antibiotics if improvement has not occurred in a 72-hour period after initial consultation.\(^\text{28}\)

If an antibiotic is prescribed, it should have activity against Strep. pneumoniae and H. influenzae – amoxicillin is commonly employed. In patients intolerant of penicillins, erythromycin may be prescribed but a significant proportion of H. influenzae will not be susceptible to this regimen. A five-day course length is recommended.\(^\text{28}\)

Resistant bacterial otitis media is recognisable by the persistence of signs and symptoms after three or more days of antibiotic therapy. In this circumstance bacteria resistant to the empirical regimen may be implicated,\(^\text{32}\) eg isolates of M. catarrhalis that possess a beta-lactamase conferring resistance to amoxicillin. In these cases therapy should be changed;\(^\text{29}\) a broad-spectrum antibiotic such as co-amoxiclav may be used as a second-line agent, or azithromycin for penicillin-allergic patients.\(^\text{33}\)

*URTls* | **DRUG REVIEW**

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Table 3. Antimicrobial prescribing for URTIs

<table>
<thead>
<tr>
<th>Infection</th>
<th>Drug</th>
<th>Duration of treatment</th>
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<tbody>
<tr>
<td>Pharyngitis/tonsillitis</td>
<td>phenoxymethylpenicillin, erythromycin</td>
<td>10 days 7 days</td>
</tr>
<tr>
<td>Otitis media</td>
<td>amoxicillin, erythromycin</td>
<td>5 days 5 days</td>
</tr>
<tr>
<td></td>
<td>second line co-amoxiclav, azithromycin</td>
<td>5 days 5 days</td>
</tr>
<tr>
<td>Rhinosinusitis</td>
<td>amoxicillin, erythromycin</td>
<td>7 days 7 days</td>
</tr>
<tr>
<td>Influenza</td>
<td>zanamivir, oseltamivir</td>
<td>5 days 5 days</td>
</tr>
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Adjunctive measures such as decongestants and antihistamines are unlikely to be of benefit and have the potential for unwanted side-effects.34

Recurrence otitis media is defined as three or more episodes of otitis media in six months. It has been associated with hearing loss and consequent speech delay; therefore, to be desirable to limit episodes of AOM for this reason, the associated morbidity notwithstanding. A review of the use of long-term antibiotics to prevent otitis media indicated that they may be beneficial in reducing episodes, but no evidence indicating improvement in long-term outcome was available.35 Additionally, the effect of longer-term systemic therapy on promoting antibiotic resistance was not addressed, so long-term therapy might be cautiously recommended only where benefit is likely to outweigh risk.

Other interventions have been evaluated. The immunisation of infants against Strep. pneumoniae with conjugate vaccine may reduce AOM overall, but is unlikely to be of benefit as secondary prevention of the disease in older children.36 Zinc supplements are unlikely to be helpful in the prevention of AOM.37

An alternative approach might be to attempt to reduce the patient’s exposure to modificable risk factors; parental smoking38 is an obvious choice, although there is no evidence to support this intervention.

Otitis media with effusion While there may be a short-term benefit of antibiotic treatment, it has not been demonstrated to be effective in long-term resolution of OME. The incidence of side-effects and development of resistant strains of organisms are considerable and therefore blanket prescription of antibiotics is not recommended.28,29 There is no evidence to support the routine use of antihistamines, decongestants, mucolytics and steroids in these patients either.28

Mastoiditis27

Infection in the mastoid bone generally occurs subsequent to middle-ear infection; for this reason, the signs and symptoms are initially indistinguishable. As the disease progresses, postauricular erythema, swelling and tenderness develop. Radiological imaging can confirm the diagnosis, and carefully taken ear drainage fluid should be sent for bacterial culture.

The causative organisms, and therefore the antibiotic therapy, of acute mastoiditis are similar to those of AOM. However, in cases of mastoiditis associated with chronic middle-ear disease, additional coverage for Staph. aureus and Gram-negative enteric bacilli may be required. Surgical intervention may be necessary in cases where complications, such as abscess formation, supervene.

Sinusitis (see Figure 3)39

Sinusitis is inflammation of the mucosa of the paranasal sinuses; it also usually involves the nasal mucosa, so might be more correctly termed rhinosinusitis. Acute sinusitis of infectious origin is generally viral in aetiology, with only a minority complicated by bacterial infection. Generally this is a self-limiting disease, even when bacterial in origin. However, complications may rarely occur in nearby structures, such as the orbit, eg orbital cellulitis, or the brain, eg cerebral abscess.

Persistent or repeated episodes of acute sinusitis may lead to chronic sinusitis (symptoms > 12 weeks). The bacteria involved in sinus infections differ between acute (generally Strep. pneumoniae or H. influenzae) and chronic sinusitis (where anaerobes, Gram-negative bacteria and Staph. aureus predominate).

Common symptoms include nasal congestion, a reduced sense of smell, facial pressure/pain, rhinorrhea and fever/malaise. Also, occasionally, toothache of the upper teeth may be a complaint. Radiological tests, such as plain X-ray and computed tomography, may aid the diagnosis but are infrequently available in the primary-care setting.

Treatment

A Cochrane review of antibiotics for acute sinusitis found only a very small treatment effect, with the majority (80 per cent) of patients not receiving antibiotics improving within two weeks.40 The use of antibiotics is therefore generally discouraged. If an antibiotic is to be prescribed, then amoxicillin, co-amoxiclav, cephalosporins and macrolides have been used previously, with similar resolution rates. Although sometimes used, there is little evidence supporting the use of nasal decongestants.41

Treatment options for chronic sinusitis include topical nasal steroids.39 There is only limited evidence supporting the use of antibiotics,30 so they should not play a role in the initial management of this condition.

Conclusion

In most cases of URTI antibiotics have only marginal benefits, but it is often difficult to recognise those patients who will go on to develop serious complications. Delayed antibiotic prescription may offer a strategy, both as a safety net to avoid development of severe disease and to manage patient expectations, while avoiding inappropriate antibiotic use.42

The NICE guidelines on antibiotic prescribing in respiratory tract infections summarise recommendations for therapy:24 a no-antibiotic or delayed-antibiotic prescribing strategy is appropriate...
for the common cold, acute pharyngitis/tonsillitis, AOM and acute rhinosinusitis.

However, the guideline does state that immediate prescription might be appropriate for bilateral AOM in children younger than two years, AOM in children with otorrhoea, and acute pharyngitis/tonsillitis where three or more Centor criteria are present. Furthermore, immediate antibiotic prescription is indicated if the patient is systemically very unwell, if there is evidence of serious illness and/or complications, or if the patient is at high risk of serious complications because of co-morbidity.

References
Figure 3. Sinusitis: most patients improve after two weeks without antibiotics being prescribed

15. www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Influenza/
22. van Driel ML, et al. Different antibiotic treatments for group A strepto-

Declaration of interests
None to declare.

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