Upper respiratory tract infections collectively encompass a range of syndromes with various aetiologies. Our Drug review considers the common URTIs and their diagnosis and management, including when to prescribe antibiotics, followed by sources of further information in Resources.

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.

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

In 2008, the National Institute for Health and Clinical Excellence (NICE) produced guidelines for the prescription of antibiotics and this review article

URTIs: recommended diagnosis and treatment in general practice

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will consider the diagnosis and treatment of URTIs within the framework of those guidelines.

**Common cold**

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 coronavirus, respiratory syncytial virus (RSV), influenza virus, parainfluenza virus and adenovirus may also cause the same syndrome. Recently, human metapneumovirus and human bocavirus have been identified, two agents that may contribute to acute URTIs.

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.

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.

**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 common assertion that antibiotics have no role in treatment. Steam inhalation and increasing oral fluid intake did not demonstrate any benefit either. Additionally, there is insufficient evidence that would support the routine use of complementary or alternative therapies, such as Chinese medicinal herbs, vitamin C, garlic or *Echinacea* preparations. NSAIDs have been shown to alleviate some of the symptoms of colds but have no effect on disease course. Generally treatment is symptomatic only.
Influenza
Infection with an influenza virus is most often associated with a self-limiting illness, usually manifesting as fever, malaise and cough; however, serious pneumonic infection may occur and this can become complicated by bacterial infection. The emergence in 2009 of a pandemic strain of an influenza A (H1N1) virus of swine lineage can have escaped few healthcare professionals.

In the UK a number of control measures were enacted for the duration of the epidemic, including an immunisation programme for at-risk groups, the development of a swine flu clinical package and the widespread availability of antiviral therapy. At the current time, however, the pandemic measures have been relaxed and the management of suspected influenza has reverted to NICE guidelines.

Oseltamivir (Tamiflu) or zanamivir (Relenza) – both neuraminidase inhibitors – are the recommended antivirals, and one of these is indicated where the following criteria are satisfied: national surveillance schemes indicate that influenza virus A or B is circulating, the person is in an at-risk group, and the person presents with an influenza-like illness and can start treatment within 48 hours of the onset of symptoms. Diagnosis may be made on the basis of polymerase chain reaction (PCR) tests on respiratory specimens, or retrospectively by serological methods.

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 The most important of the bacterial infections of the pharynx are those due to group A beta-haemolytic streptococci (GAS), also known as *Streptococcus pyogenes*. This is due to the possibility of postinfectious sequelae; these may be supplicative, eg local abscess formation, or nonsupplicative. The nonsupplicative 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.

Gonococcal infections The incidence of gonococcal infections of the pharynx has increased in recent years, and may cause occasional cases of mild pharyngitis.

Pharyngitis associated with the common cold Mild to moderate pharyngeal discomfort is frequent. The symptom is characterised as soreness, scratchiness or irritation.

Pharyngoconjunctival fever is a syndrome caused by adenovirus and is usually more severe than pharyngitis associated with colds. A feature distinguishing adenovirus pharyngitis from streptococcal infections is the presence of conjunctivitis, which occurs in a third to half of cases.

Herpangina is an uncommon type of pharyngitis caused by Coxsackie virus (an enterovirus) and is distinguished by the presence of small vesicles on the soft palate, uvula and anterior tonsillar pillars.

Epstein-Barr virus (EBV) induces a broad spectrum of illness in humans. Primary EBV infection in children is often asymptomatic. In young children, the typical infectious mononucleosis syndrome is an acute illness characterised clinically by sore throat, fever and lymphadenopathy. Due to previously acquired immunity the disease is less common in older patients.

Rare causes Although uncommon, diphtheria still occurs in unimmunised populations. The characteristic membrane varies in colour from light to dark grey and is firmly adherent to the tonsils and pharyngeal...
mucosa. Other rare causes of pharyngitis include infections with *Arcanobacterium haemolyticum*, *Yersinia enterocolitica*, *Chlamydia pneumoniae*, or *Mycoplasma 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 (IM), 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 where the Paul-Bunnell test is negative, but the clinical syndrome and peripheral blood film are consistent with IM. 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 (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.

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.

**Acute laryngitis**

This is a common illness characterised by inflammation of the larynx. It presents as hoarseness of the voice, often in the presence of coryzal symptoms. 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, although the rates of antibiotic prescription vary significantly with geography: perhaps as low as 31 per cent in the Netherlands and up to 98 per cent in Australia and the USA. 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, and these demonstrate *Streptococcus pneumoniae* in 23–28 per cent, *H. influenzae* in 25–36 per cent, *Moraxella catarrhalis* in 3–4 per cent and viruses in 25 per cent of patients. Complications may include mastoiditis (addressed later in this review) and intracranial spread of infection.

**Diagnosis**

AOM may present nonspecifically, for example with fever or irritability, or with specific symptoms such as ear pain, discharge or decreased hearing. On examination there is erythema of the tympanic membrane, and fluid is present in the middle ear.

It is important to distinguish AOM from chronic otitis media with effusion (OME), in which otalgia and fever are usually absent. The latter disease is likely to require closer follow-up and, depending on severity and disability, may require surgical intervention.

**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. It is difficult to know whether withholding antibiotics contributes to an increased risk of complications as these are generally rare. 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.

If an antibiotic is prescribed, it should have activity against *Strep. pneumoniae* and *H. influenzae* – amoxicillin is commonly employed. However, virtually all isolates of *M. catarrhalis* possess a beta-lactamase, conferring resistance to amoxicillin; in this case co-amoxiclav may be used. 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.

Adjunctive measures such as decongestants and antihistamines are unlikely to be of benefit, and offer the potential for unwanted side-effects.

Recurrent 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; it would, therefore, 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 they may be beneficial in reducing episodes, but no evidence indicating improvement in long-term outcome was available. Additionally, the effect of long-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. Zinc supplements are unlikely to be helpful in the prevention of AOM.

An alternative approach might be to attempt to reduce the patient’s exposure to modifiable risk factors; for example, parental smoking (where this occurs) is an obvious choice, although there is no evidence to support this intervention.

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 and therapy should be changed; a broad-spectrum antibiotic such as co-amoxiclav may be used as a second-line agent.

**Mastoiditis**

Infection in the mastoid bone generally occurs subsequent to middle ear infection; for this reason, the signs are symptoms are initially indistinguishable. As the disease progresses, postauricular erythema, swelling and tenderness develop.

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 *Staphylococcus 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)**

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.

| Infection      | Drug                     | Duration of treatment |
|----------------|--------------------------|-----------------------|
| Pharyngitis/tonsillitis | phenoxymethylpenicillin erythromycin | 10 days 7 days |
| Otitis media | amoxicillin erythromycin | 5 days 5 days |
|                | second line co-amoxiclav | 5 days |
| Rhinosinusitis | amoxicillin erythromycin | 7 days 7 days |
| Influenza      | zanamivir oseltamivir   | 5 days 5 days |

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

Common symptoms include nasal congestion, a reduced sense of smell, facial pressure/pain, rhinorrhoea 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. 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.

There is also only limited evidence supporting the use of antibiotics in the management of chronic sinusitis, 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.

The NICE guidelines on antibiotic prescribing in respiratory tract infections summarise recommendations for therapy: no antibiotic or delayed antibiotic prescribing strategy is appropriate for the common cold, acute pharyngitis/tonsillitis, acute otitis media and acute rhinosinusitis. However, the guideline does state that immediate prescription might be appropriate for bilateral acute otitis media in children younger than two years, acute otitis media 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 comorbidity.

References
1. Royal College of General Practitioners, Office of Population Censuses and Surveys, Department of Health. Morbidity statistics from general practice – fourth national study 1991-1992. London: HMSO, 1995.
2. National Institute for Health and Clinical Excellence. Respiratory tract infections – antibiotic prescribing. CG069. London: NICE, 2008.
3. Turner RB. The common cold. In Mandell GL, et al. Principles and practice of infectious diseases. 7th ed. Philadelphia: Churchill Livingstone, 2010.
4. Arroll B, et al. Antibiotics for the common cold and acute purulent rhinitis. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD000247.
5. Singh M. Heated, humidified air for the common cold. Cochrane Database of Systematic Reviews 2006, Issue 3. Art. No.: CD001728.
6. Guppy MPB, et al. Advising patients to increase fluid intake for treating acute respiratory infections. Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD004419.
7. Zhang X, et al. Chinese medicinal herbs for the common cold. Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.: CD004782.
8. Hemilä H, et al. Vitamin C for preventing and treating the common cold. Cochrane Database of Systematic Reviews 2007, Issue 3. Art. No.: CD000980.
9. Lissiman E, et al. Garlic for the common cold. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD006206.
10. Linde K, et al. Echinacea for preventing and treating the common cold. Cochrane Database of Systematic Reviews 2006, Issue 1. Art. No.: CD000530.
11. Kim SY, et al. Non-steroidal anti-inflammatory drugs for the common cold. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD006362.
12. Treanor JJ. Influenza viruses, including avian influenza and swine influenza. In Mandell GL, et al. Principles and practice of infectious diseases. 7th ed. Philadelphia: Churchill Livingstone, 2010.
Amantadine, oseltamivir and zanamivir for the treatment of influenza. TA168. London: NICE, 2009.
14. Alcaide ML, et al. Infect Dis Clin N Am 2007;21:449–69.
15. Bisno AL, et al. Streptococcus pyogenes. In Mandell GL, et al. Principles and practice of infectious diseases. 7th ed. Philadelphia: Churchill Livingstone, 2010.
16. Bisno AL, et al. Clinical Infectious Diseases 2002;35:113–25.
17. Hurt C, et al. The American Journal of Medicine 2007;120:911.e1–911.e8.
18. van Driel ML, et al. Different antibiotic treatments for group A streptococcal pharyngitis. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD004406.
19. McIsaac WJ, et al. JAMA 2004;291:1587–95.
20. Caserta MT. Acute laryngitis. In Mandell GL, et al. Principles and practice of infectious diseases. 7th ed. Philadelphia: Churchill Livingstone, 2010.
21. Reveiz L, et al. Antibiotics for acute laryngitis in adults. Cochrane Database of Systematic Reviews 2007, Issue 2. Art. No.: CD004783.
22. Scottish Intercollegiate Guidelines Network. Diagnosis and management of childhood otitis media in primary care. Edinburgh: SIGN, 2003.
23. Klein JO. Otitis externa, otitis media, and mastoiditis. In Mandell GL, et al. Principles and practice of infectious diseases. 7th ed. Philadelphia: Churchill Livingstone, 2010.
24. Subcommittee on Management of Acute Otitis Media. Pediatrics 2004;113:1451–65.
25. Sanders S, et al. Antibiotics for acute otitis media in children. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.: CD000219.
26. Petersen I, et al. BMJ 2007;335:982.
27. Coleman C, et al. Decongestants and antihistamines for acute otitis media in children. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD001727.
28. Leach AJ, et al. Antibiotics for the prevention of acute and chronic suppurative otitis media in children. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD004401.
29. Jansen AGSC, et al. Pneumococcal conjugate vaccines for preventing otitis media. Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD001480.
30. Abba K, et al. Zinc supplements for preventing otitis media. Cochrane Database of Systematic Reviews 2010, Issue 2. Art. No.: CD006639.
31. Kerstein R. Br J Gen Pract 2008;58:364–5.
32. Leibovitz E. Vaccine 2008;26 Suppl 7:G16–G19.
33. Al-see KW, et al. BMJ 2007;334:358–61.
34. Ahovuo-Saloranta A, et al. Antibiotics for acute maxillary sinusitis. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD00243.
35. Williamson IG, et al. JAMA 2007;298:2487–96.
36. Arroll B, et al. Br J Gen Pract 2003;53:871–7.

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Resources

Further reading
BMJ collected resources. All articles published in the BMJ since January 1998. www.bmj.com/collections.

Clinical Knowledge Summaries. Topics include: common cold, otitis media – acute, sinusitis, sore throat – acute. cks.library.nhs.uk.

NICE. Respiratory tract infections – antibiotic prescribing. Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. Clinical guideline 69. July 2008.

NICE. Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza. Technology appraisal TA158. September 2008.

NICE. Amantadine, oseltamivir and zanamivir for the treatment of influenza. Technology appraisal TA168. February 2009.

SIGN. Management of sore throat and indications for tonsillectomy. SIGN publication no. 117, April 2010.

SIGN. Diagnosis and management of childhood otitis media in primary care. SIGN publication no. 66, February 2003.

Websites
www.commoncold.org. This site provides a comprehensive, updated and referenced source of information on the common cold to help inform decisions about medical care for the common cold.

www.patient.co.uk. Information leaflets include: URTI, coughs and cold in children, flu-like illness, common cold – adults and older children, sore throat, ear infection (otitis media), laryngitis, scarlet fever, tonsillitis and on other related illnesses.