Our Drug review discusses the diagnosis and current recommended management of common URTIs, followed by sources of further information and the Datafile.

A cute cough and respiratory tract infection are terms used to describe a wide variety of clinical syndromes. Symptoms range from cough without sputum to an illness characterised by expectoration of mucopurulent sputum, fever, general malaise and dyspnoea. Therefore, although the terms acute bronchitis, upper respiratory tract infection (URTI), common cold and chest infection are used in a clinical context to define separate disease entities, they represent a range of respiratory tract infections whose symptoms, causative agents and resolution vary.

This review will consider the diagnosis and treatment of common URTIs. The fourth National Morbidity Survey in the UK found that the overall consultation rate for acute URTI was 772 per 10 000 person years at risk.¹

Common cold
As a clinical entity, the common cold is a mild, self-limiting, catarrhal syndrome that is the leading cause of acute morbidity and visits to GPs. A small proportion of colds are complicated by bacterial infections of the paranasal sinuses and the middle ear, and these require antimicrobial therapy. The major respiratory...
viruses causing colds and similar URTIs are rhinovirus, coronavirus, parainfluenza, influenza, adenovirus and respiratory syncytial virus (RSV).

Possible means of transmission include direct contact with infectious secretions on skin and environmental surfaces, large particles of respiratory secretions that are briefly transported in air, and infectious droplet nuclei suspended in air.

The incubation period of the common cold varies with different viruses but is usually between 12 and 72 hours. The cardinal symptoms are nasal discharge, nasal obstruction, sneezing, sore throat, cough and fever. The clinical picture of common cold is similar in children and adults; however, in young children parainfluenza virus and RSV infections may lead to viral pneumonia, croup and bronchiolitis, whereas in adults these viruses usually cause only ‘colds’.

The combination of a first-generation antihistamine such as chlorphenamine maleate and an NSAID may reduce rhinorrhoea, sneezing and amount of nasal secretions; from personal experience, this has shown minimal effect on other cold symptoms. Sore throats can be relieved with saline gargle. Antibiotics have no place in the treatment of uncomplicated colds.

### Pharyngitis

**Syndromes**

Acute pharyngitis is an inflammatory syndrome of the pharynx caused by several different groups of microorganisms (see Table 1). Most cases are of viral aetiology and occur as part of common colds and influenza syndromes.

The most important of the bacterial infections is that due to *Streptococcus pyogenes*, because of the possibility of poststreplococcal sequelae such as acute rheumatic fever or acute glomerulonephritis. Acute *Strep. pyogenes* pharyngitis has certain characteristic epidemiological and clinical features (see Table 2). The disorder is primarily a disease of children 5-15 years of age, and usually occurs in the winter and early spring.

In *pharyngitis associated with a common cold*, mild-to-moderate pharyngeal discomfort is frequent. The symptom is characterised as soreness, scratchiness or irritation. Rhinorrhoea and postnasal discharge are usually present. Most patients recover within a week.

*Streptococcal pharyngitis* In severe cases of streptococcal pharyngitis, there is marked pharyngeal pain, odynophagia and a temperature. The clinical features of pharyngeal infection with strains of group C and group G streptococci are similar to those of *Strep. pyogenes*, including the occurrence of purulent exudates, fever and anterior cervical adenopathy.

An *aerobic pharyngitis* is caused by a mixture of anaerobic bacteria and spirochaetes, a purulent exudate coats the membrane and there may be a foul odour to the breath. It may lead to complications like peritonsillar abscess and Lemierre’s disease.

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

*Pharyngococonjunctival fevers* caused by adenovirus is usually more severe than pharyngitis associated with the common cold. A feature distinguishing adenovirus pharyngitis from streptococcal infections is conjunctivitis, which occurs in a third to half of cases.

*Herpangina* is an uncommon type of pharyngitis caused by Coxsackie viruses 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 in children is often asymptomatic. In young children typical infectious mononucleosis is an acute illness characterised clinically by sore throat, fever and lymphadenopathy.

| Pathogen | Associated disorders/symptoms |
|----------|-------------------------------|
| Viral | • rhinovirus/coronavirus | • tonsillitis and scarlet fever |
| | • adenovirus | • tonsillitis and scarlatiniform rash |
| | • herpes simplex virus types 1 & 2 | • anaerobic pharyngitis |
| | • parainfluenza virus | • pharyngitis |
| | • Coxsackie virus A | • diphtheria |
| | • Epstein-Barr virus | • scarlatiniform rash |
| | • influenza A and B virus | |
| Mycoplasmal | *Mycoplasma pneumoniae* | • pneumonia and bronchitis |
| Chlamydial | • *Chlamydia psittaci* | • acute respiratory disease |
| | • *Chlamydia pneumoniae* | • pneumonia |

Table 1. Microbial aetiology of acute pharyngitis

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Because of previously-existing immunity the disease is less common in older patients. Rare causes Although uncommon, diphtheria still occurs in unvaccinated populations. The characteristic tonsillar or pharyngeal membrane varies in colour from light to dark grey and is firmly adherent to the tonsils and pharyngeal mucosa. Arcanobacterium haemolyticum, Yersinia enterocolitica, Chlamydia pneumoniae and Mycoplasma pneumoniae are other rare causes of pharyngitis.

Diagnosis Diagnosis of acute pharyngitis is important to distinguish cases of common viral aetiology from those due to Streptococcus pyogenes, and to detect and identify the occasional case due to unusual or rare cause for which treatment is available. The development of rapid antigen detection tests (RADTs) for streptococcal pharyngitis with a specificity of over 90 per cent and sensitivity of 60-95 per cent has been used in clinical practice. However, these near-patient tests are rarely used in the UK, where the primary method employed is throat swab for culture. Investigations are rarely necessary for viral causes of URTIs, as most are self-limiting.

Treatment Treatment of patients with pharyngitis due to Streptococcus pyogenes is a 10-day course of penicillin or erythromycin (see Table 3). In patients with multiple, recurrent episodes of group A beta-haemolytic Streptococcus infection proven by culture or RADT testing, oral clindamycin (Dalacin C) or co-amoxiclav (Augmentin) for 10 days might be helpful. Oral penicillin is still recommended for the treatment of anaerobic pharyngitis.

Warm saline gargles and supportive measures such as rest, analgesics and liquids are sufficient in most cases of viral pharyngitis.

Zanamivir (Relenza) and oseltamivir (Tamiflu) are recommended by the National Institute for Health and Clinical Excellence (NICE) for the treatment of at-risk adults who present with influenza-like illness (see Table 4). Amantadine (Lysovir) has been used in the prevention and treatment of influenza (activity against influenza A only), but is not recommended for treatment by NICE (see Table 4).

Acute laryngitis This is a common clinical syndrome encountered by GPs in patients of all ages. The symptoms are hoarseness of voice with voice breaks or episodes of aphonia. All the major respiratory viruses like rhinovirus, influenza, parainfluenza, adenovirus and coronavirus may cause laryngitis. Also, M. pneumoniae, C. pneumoniae and bacterial respiratory infections have been associated with laryngitis. Treatment needs to be directed at the underlying infectious cause of hoarseness but, in general, as the aetiology is usually viral, treatment is symptomatic in nature, with voice rest and humidification.

Otitis media Also known as inflammation of the middle ear, this is the most common reason for the prescription of antibiotics in children. The diagnosis of otitis is usually followed by antibiotic treatment despite ‘a woeful lack of substantial evidence on the question of antibiotic therapy’ for this condition.

Acute otitis media usually follows a viral infection of the nasopharynx which disrupts the function of the eustachian tubes. In patients with colds, bacteria and viruses from the nasopharynx that reach the middle ear during pressure equilibration may be cleared by the mucociliary system less effectively than usual. Bacteria may replicate in the fluid of the middle ear, and respiratory viruses may infect the mucosa of the middle ear.

Typanocentesis has revealed Streptococcus pneumoniae in 20-35 per cent of patients, nontypable Haemophilus influenzae in 20-30 per cent, Moraxella catarrhalis in 20 per cent, no bacteria in 20-30 per cent, and viruses with or without bacteria in 17-44 per cent of patients.
Diagnosis
Acute otitis media can be diagnosed by the presence of inflammation and fluid in the middle ear (see Figure 1). Inflammation of the middle ear may be signified by local or systemic findings such as ear pain, erythema of the tympanic membrane, fever and cold symptoms.

Treatment
Once acute otitis media has been diagnosed, the central issue is whether antibiotic therapy will be in the child’s best interest. A meta-analysis of randomised, placebo-controlled trials found that acute otitis had resolved at one week in 81 per cent of placebo recipients as compared with 94 per cent of those given antibiotics.\textsuperscript{7} In general, the rate of clinical resolution was similar in placebo and antibiotic recipients on the first day of therapy, but slightly higher at three to five days and at seven days among those who received antibiotic therapy.\textsuperscript{8,9}

Amoxicillin is as effective as any other drug, even though at least a quarter of \textit{Strep. pneumoniae} strains have increased resistance to penicillin and amoxicillin, a quarter to a third of \textit{H. influenzae} strains are resistant \textit{in vitro} to amoxicillin (beta-lactamase positive) and virtually all strains of \textit{M. catarrhalis} are resistant to amoxicillin (beta-lactamase positive). The clinical effect of a single dose of ceftriaxone (Rocephin) or five days of azithromycin (Zithromax) was not different from that of 7-10 days of amoxicillin.\textsuperscript{10}

Whether antibiotic therapy reduces the risk of prolonged illness in children six months to two years of age was examined in a trial comparing amoxicillin and placebo in 240 children in the Netherlands, where the background rates of resistance to amoxicillin are 1 per cent for \textit{Strep. pneumoniae} and 6 per cent for \textit{H. influenzae}.\textsuperscript{11} Antibiotic therapy had a limited effect, reducing the incidence of persistent symptoms by 13 per cent on day 4 and shortening the duration of fever by one day.

\textit{Recurrent otitis media} is usually defined as three or more episodes of acute otitis within six months, or four episodes within 12 months. One strategy for the prevention of recurrent acute otitis media is the use of antibiotic prophylaxis with co-trimoxazole (Septrin) or amoxicillin, but a meta-analysis of antibiotic prophylaxis showed an average decrease of 0.11 episodes per child-month, or about one episode of acute otitis per year, in qualifying children.\textsuperscript{12} This small benefit is generally outweighed by the disadvantage of promoting antibiotic resistance. Also, the indications for use of co-trimoxazole are restricted in the UK due to its side-effect profile.

\textit{Resistant bacterial otitis media} is recognisable by the persistence of fever, otalgia and bulging red tympanic membranes or by persistent otorrhoea after three or more days of antibiotic therapy.\textsuperscript{13,14} Culture of purulent fluid yielded bacteria that were resistant to the prescribed antibiotic in only one-third of cases.\textsuperscript{13,15} In the absence of data on the efficacy of antibiotics for resistant bacterial otitis, one expert panel recommended high-dose co-amoxiclav, cefuroxime axetil (Zinnat) or intramuscular ceftriaxone for three days.\textsuperscript{14}

\textit{Delayed antibiotic therapy} is used in the Netherlands. Children under two years of age are closely monitored, and a seven-day course of antimicrobial therapy is begun only when there is no improvement in symptoms within one to two days in children younger than two and within three days in children who are two years of age or older.

The effectiveness in general practice of this delayed prescribing strategy was assessed in a randomised trial involving 315 children six months to 10 years of age with acute red ear (41 per cent were three years of age or younger).\textsuperscript{9} The parents of only 36 of the 150 children in the delayed-antibiotics group (24 per cent) picked up the antibiotic prescription, reflecting the fact that the parents recognised that the symptoms were resolving on their own within three days in the majority of children.

\begin{table}[h]
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\begin{tabular}{|l|l|l|}
\hline
\textbf{Illness} & \textbf{Drug} & \textbf{Duration of treatment} \\
\hline
Pharyngitis/tonsillitis & phenoxymethylpenicillin & 10 days \\
& erythromycin & 7 days \\
Otitis media & amoxicillin & 5 days \\
& erythromycin & 5 days \\
& \textit{second line} co-amoxiclav & 5 days \\
Rhinosinusitis & phenoxymethylpenicillin & 7 days \\
& amoxicillin & 7 days \\
& erythromycin & 7 days \\
& \textit{second line} co-amoxiclav & 7 days \\
& ciprofloxacin + metronidazole & 7 days \\
Influenza & zanamivir & 5 days \\
& oseltamivir & 5 days \\
\hline
\end{tabular}
\caption{Antimicrobial prescribing for URTIs}
\end{table}
Vaccination

Influenza vaccination reduces the occurrence of acute otitis in young children while the virus is circulating in the community, but does not have an effect during the remainder of the year.16

Evidence of the ability of a bacterial vaccine to prevent acute otitis media, on the other hand, is not as promising. In two trials, immunisation of infants up to the age of two years with a seven-valent conjugate pneumococcal vaccine (CRM197) was not very effective in preventing acute otitis during an 18-month follow-up.6,17 However, it is highly effective in reducing the prevalence of invasive pneumococcal disease caused by the seven serotypes included in the vaccine.

Mastoiditis

The proximity of the mastoid to the middle ear cleft means that most cases of suppurative otitis media are associated with inflammation of the mastoid air cells. During early stages, the signs are those of acute otitis media with hearing loss, otalgia and fever. Subsequently, swelling, redness and tenderness are present over the mastoid bone.

The antimicrobial drugs of choice for acute infection are similar to those for acute otitis media. If the disease in the mastoid has had a prolonged course, coverage for Staphylococcus aureus and Gram-negative enteric bacilli including Pseudomonas species may be considered for initial therapy until the results of cultures become available.

Epiglottitis

Acute epiglottitis is a cellulitis of the epiglottis and adjacent structures that has the potential for causing abrupt complete airway obstruction. Tachycardia, fever, inspiratory stridor and hoarseness may occur. The diagnosis is confirmed by an oedematous ‘cherry-red’ epiglottis. H. influenzae, pneumococci, staphylococci and streptococci have been isolated from cultures of blood or epiglottis. The incidence of epiglottitis due to H. influenzae has decreased dramatically since the introduction of H. influenzae type b (Hib) vaccination.

The role of viruses in epiglottitis has not been established.

A child even suspected of having acute epiglottitis should be handled as a medical emergency because of the potential for complete respiratory obstruction.

Sinusitis

Acute sinusitis is an infection of one or more of the paranasal sinuses that usually complicates a common cold or other viral infections of the upper respiratory tract. Sinusitis in turn may be complicated by serious intracranial infections such as bacterial meningitis and epidural, subdural and brain abscesses.

The microbial aetiology of acute sinusitis is Strep. pneumoniae (31 per cent), H. influenzae (21 per cent), anaerobic bacteria (6 per cent), Gram-negative bacteria (9 per cent) and viruses (20 per cent). This information comes from studies in which specimens for culture were obtained by direct sinus puncture and aspiration to avoid contamination by nasopharyngeal flora.

Prolonged and repeated episodes of infection may lead to irreversible changes in the mucosal lining of the sinus, resulting in chronic sinus disease. Cultures of surgical specimens obtained from patients with chronic sinus disease have grown a wide variety of Gram-positive and -negative bacteria.

Common symptoms include purulent nasal and postnasal discharge (see Figure 2), headache, and

Table 4. NICE guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza

| 1. Zanamivir and oseltamivir are not recommended for the treatment of influenza in children or adults unless they are considered to be ‘at risk’. |
| 2. At-risk adults and children are defined for the purpose of this guidance as those who are in at least one of the following groups. People who: |
| • have chronic respiratory disease (including asthma and chronic obstructive pulmonary disease) |
| • have significant cardiovascular disease (excluding people with hypertension only) |
| • have chronic renal disease |
| • are immunocompromised |
| • have diabetes mellitus |
| • are aged 65 years or older. |
| 3. Amantadine is not recommended for the treatment of influenza. |
| 4. Within their licensed indications, zanamivir and oseltamivir are recommended for the treatment of at-risk adults who present with influenza-like illness (ILI) and who can start therapy within 48 hours of the onset of symptoms. |
| 5. Within its licensed indications, oseltamivir is recommended for the treatment of at-risk children who present with ILI and who can start therapy within 48 hours of the onset of symptoms. |
| 6. Community-based virological surveillance schemes, such as those organised by the RCGP and the Health Protection Agency, should be used to indicate when influenza virus is circulating in the community. Such schemes should ensure that the onset of the circulation of influenza virus (A or B) within a defined area is identified as rapidly as possible. |
disorder of smell. In a small number of patients ery-thema and tenderness of the involved sinus are present.

Sinus X-rays and CT (computed tomography) scans may be used to diagnose acute sinusitis.

**Treatment**

Although viruses may play a role in the initiation of acute sinusitis, the disease should be treated as a bacterial infection. Treatment should be directed against the known sinus pathogens. A 10-day course of treatment with one of the antimicrobials such as co-amoxiclav is recommended. Nasal decongestants should be used in supportive treatment. Patients with severe sinus infection may require early surgical drainage.

Once sinusitis has reached a chronic state, bacterial colonisation of the sinus cavity is usual, but the condition no longer responds to antimicrobial treatment.

**Conclusion**

There is no single course of action that will suit all patients when treating URTIs. The evidence must be applied in different ways according to different local conditions; these will include environmental, historical and social factors. GPs put as much weight on social factors as on the physical examination in deciding whether or not to use antibiotics.

Recently, there has been much discussion as to the appropriateness of prescribing antibiotics for patients with uncomplicated URTI. According to a recent paper there has been a fall of 50 per cent in antibiotics prescribing for children with URTIs, without an accompanying increase in hospital admission for peritonsillar abscess or rheumatic fever. This rapid decline in antibiotic usage appears to be a combination of fewer prescriptions and ‘delayed prescribing’ – a strategy documented in 1994. So should GPs stop prescribing antibiotics in uncomplicated URTI completely? Clearly no, as it is impossible on the first consultation to decide who will develop rare but important infective complications. However, delayed prescribing could provide a safety net.

We know that the way of presenting evidence-based information can greatly influence the decisions people make. The challenge is for us to learn more about how to apply this science.
novirus, respiratory syncytial virus, and corona virus infections in acute otitis media by reverse transcriptase polymerase chain reaction. Pediatr 1998;102:291-5.
6. Eskola J, Kilpi T, Palmu A, et al. Efficacy of a pneumococcal conjugate vaccine against acute otitis media. N Engl J Med 2001;344:403-9.
7. Rosenfeld RM, Vertrees JE, Carr J, et al. Clinical efficacy of antimicrobial drugs for acute otitis media: meta-analysis of 5400 children from thirty-three randomised trials. J Pediatr 1994;124:355-67.
8. Del Mar C, Glasziou P, Hayen M, et al. Are antibiotics indicated as initial treatment for children with acute otitis media? A meta-analysis. BMJ 2000;320:350-4.
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10. Sharland M, Kendall H, Veates D, et al. Antibiotic prescribing in general practice and hospital admissions for pharyngitis, mastoiditis and rheumatic fever in children: time trend analysis. BMJ 2005;331:328-9.
11. Dr Virginica is consultant in microbiology at the Royal Berkshire Hospital, Reading, and Dr Spencer is consultant in microbiology at Bristol Royal Infirmary

Resources

Guidelines
Scottish Intercollegiate Guidelines Network (SIGN). Guideline No 34. Management of sore throat and indications for tonsillectomy. Website: www.sign.ac.uk/guidelines/published/numlist.html.

PRODIGY. Guidance on sinusitis, acute sore throat and acute otitis media. Website: www.prodigy.nhs.uk.

National Institute for Health and Clinical Excellence. Guidance on prophylaxis and treatment of influenza. Website: www.nice.org.uk/cattal.asp?c=153.

Further reading
BMJ Collected Resources. All articles published in the BMJ since January 1998. http://bmj.bmjjournals.com/collections.

Useful websites
Health Protection Agency. Antibiotic prescribing guidance for primary care. Web-based guidance at www.hpa.org.uk/infections/topics_az/antimicrobial_resistance/guidance.htm.

A virtual hospital site gives useful guidelines for treatment at www.vh.org.

www.generalpractice.co.uk has many links including the Medical Algorithms Project, which displays treatment algorithms for all conditions including infectious diseases.

Patient information
www.netdoctor.co.uk includes extensive health information for patients.