Diagnosis and recommended treatment of common URTIs

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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.

Acute 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 infections 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, adenovirus and respiratory syncytial virus (RSV).

Human metapneumovirus and human bocavirus are more commonly associated with lower respiratory tract infections, but do have coryzal features and can often be found as mixed infection with RSV.

Colds are frequent because of the large number of different causative viruses and also because reinfections may occur with the same virus type. Adults have an average of two to four episodes annually and young children may have as many as six to eight episodes.

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. Symptoms usually peak around day 3 or 4 and begin to resolve by day 7.2

The clinical picture of the 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’.

Treatment
A Cochrane review showed that there is a lack of good evidence to determine the effectiveness of any over-the-counter product at reducing the frequency or severity of cough in children or adults.3 Despite these conclusions, two studies included in the Cochrane review suggest that dextromethorphan provides a modest clinical benefit in adults.

Although a combination of a first-generation oral antihistamine and a decongestant may reduce rhinorrhoea, sneezing and amount of nasal secretions in adults, it has not been shown to benefit young children.4,5

Complementary and alternative therapies like Echinacea, vitamin C and zinc are not recommended for treating common cold symptoms.6,7 Sore throats can be relieved with saline gargle, and fluid intake may be useful. Antibiotics have no place in the treatment of uncomplicated colds.

Figure 1. An inflamed pharynx; pharyngitis is typically of viral aetiology, coincides with cold and flu, and is primarily a disease of childhood

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 Strep. pyogenes (also known as group A beta-haemolytic streptococci) because of the possibility of poststreptococcal sequelae – although increasingly uncommon in the UK – 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. Symptoms develop after a short incubation period of 24 to 72 hours.

Pharyngitis associated with common cold Mild to moderate pharyngeal discomfort is frequent. The symptom is characterised as soreness, scratchiness or irritation. Rhinorrhaea 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 beta-haemolytic streptococci are similar to those of Strep. pyogenes, including the occurrence of purulent exudates, fever and anterior cervical adenopathy.
**Gonococcal infections** The incidence of gonococcal infections of the pharynx has increased in recent years, and may cause an occasional case of mild pharyngitis.

**Pharyngoconjunctival fever** is a syndrome caused by adenoviruses and 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. 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.

Other rare causes of pharyngitis include infection with *Arcanobacterium haemolyticum*, *Yersinia enterocolitica*, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*.

**Diagnosis** Diagnosis of acute pharyngitis is important to distinguish cases of common viral aetiology from those due to *Strep. pyogenes*, and to detect and identify the occasional case due to an 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.

When the clinical scenario suggests the presence of infectious mononucleosis, the diagnosis may be obtained by the presence of a positive heterophil antibody test (monospot test) for EBV. This test is more than 80 per cent sensitive in the second week of illness. Also IgM antibody test to the viral capsid antigen should be considered.

Investigations are rarely necessary for viral causes of URTIs, as most are self-limiting.

| Pathogen | Associated disorders/symptoms |
|----------|-------------------------------|
| **Bacterial** | | |
| • *Strep. pyogenes* | • tonsillitis and scarlet fever |
| • streptococci group C and G | • tonsillitis and scarlatiniform rash |
| • mixed anaerobes | • anaerobic pharyngitis |
| • *Neisseria gonorrhoeae* | • pharyngitis |
| • *Corynebacterium diphtheriae* | • diphtheria |
| • *Arcanobacterium haemolyticum* | • scarlatiniform rash |
| **Viral** | | |
| • rhinovirus/coronavirus | • common cold |
| • adenovirus | • pharyngoconjunctival fever and acute respiratory disease |
| • herpes simplex virus types 1 and 2 | • gingivostomatitis |
| • parainfluenza virus | • cold and croup |
| • *Coxsackie virus A* | • herpangina and foot and mouth disease |
| • *Epstein-Barr virus* | • infectious mononucleosis |
| • influenza A and B virus | • influenza |
| **Mycoplasmal** | | |
| • *Mycoplasma pneumoniae* | • pneumonia and bronchitis |
| **Chlamydial** | | |
| • *Chlamydia psittaci* | • acute respiratory disease |
| • *Chlamydia pneumoniae* | • pneumonia |

Table 1. Microbial aetiology of acute pharyngitis

**Treatment**

Treatment of patients with pharyngitis due to *Strep. pyogenes* is a 10-day course of penoxymethylpenicillin or erythromycin (see Table 3). In patients with multiple, recurrent episodes of group A beta-haemolytic *Streptococcus* infections proven by culture or RADT testing, oral clindamycin or co-amoxiclav for 10 days might be helpful.

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. Amantadine (Lysovir) has been used in the prevention and treatment of influenza (activity against influenza A only), but is not recommended by NICE.

**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.9

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. Epiglottitis was a disease of childhood, although it is increasingly recognised in adults as most children have been vaccinated with *Haemophilus influenzae type B* (HiB).

The diagnosis is confirmed by visualising an oedematous ‘cherry-red’ epiglottis (although this is inadvisable unless facilities to secure the airway are at hand). *H. influenzae* is the usual aetiologic agent, isolated from cultures of blood or epiglottis, although pneumococci, staphylococci and streptococci have occasionally been isolated. The role of viruses in epiglottitis has not been established. The incidence of epiglottitis due to *H. influenzae* has decreased dramatically since the introduction of the HiB vaccination.

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

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.10

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 that usual. Bacteria may replicate in the fluid of the middle ear, and respiratory viruses may infect the mucosa of the middle ear.

Tympanocentesis has revealed *Strep. pneumoniae* in 20-35 per cent of patients, *H. influenzae* in 20-30 per cent, *Moraxella catarrhalis* in 20 per cent and viruses in 20-40 per cent of patients.11-13

Diagnosis
Acute otitis media can be diagnosed by the presence of inflammation and fluid in the middle ear. 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.14 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.15,16

Amoxicillin is as effective as any other drug, although virtually all strains of *M. catarrhalis* are resistant to amoxicillin (beta-lactamase positive). The clinical effect of a single dose of ceftriaxone (Rocephin)

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**Features suggestive of Strep. pyogenes**
- sudden onset
- sore throat
- fever, headache
- nausea, vomiting and abdominal pain
- inflammation of pharynx and tonsils
- patchy discrete exudate
- tender, enlarged anterior cervical nodes
- patient aged 5-15 years
- presentation in winter and early spring
- history of exposure

**Features suggestive of viral aetiology**
- conjunctivitis
- coryza
- cough
- diarrhoea

**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.
or five days of azithromycin was not different from that of 7-10 days of amoxicillin.\textsuperscript{17}

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{18} 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 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{19} 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{20,21} Culture of purulent fluid yielded bacteria that were resistant to the prescribed antibiotic in only one-third of cases.\textsuperscript{20,22} In the absence of data on the efficacy of antibiotics for resistant bacterial otitis, one expert panel recommended high-dose co-amoxiclav, cefuroxime axetil or intramuscular ceftriaxone for three days.\textsuperscript{22}

\textit{Delayed antibiotic therapy} is used in the Netherlands. Children under two years 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{16} 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.

Although this approach is reasonable, a recent Cochrane review suggested that patient and parent satisfaction was reduced using this method. Similarly, although there is a pragmatic belief that there is no harm done by delaying, or no, antibiotics, there may be social and financial implications that are not considered in the trials. A reduction in fever time by 24 hours would allow the child back to school sooner and the carer to go back to work.

\textit{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.\textsuperscript{23}

There is also evidence of the ability of a bacterial vaccine to prevent acute otitis media. Since the introduction of the heptavalent conjugate vaccine in the USA in 2000, the incidence of otitis media has reduced by 246 per 1000 children, representing a 20 per cent reduction in visits.\textsuperscript{24}

\textbf{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.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
\textbf{Infection} & \textbf{Drug} & \textbf{Duration of treatment} \\
\hline
\textit{Pharyngitis/tonsillitis} & \textit{phenoxymethylpenicillin} & 10 days \\
& \textit{erythromycin} & 7 days \\
\hline
\textit{Otitis media} & \textit{amoxicillin} & 5 days \\
& \textit{erythromycin} & 5 days \\
& \textbf{second line} & 5 days \\
& \textit{co-amoxiclav} & \\
\hline
\textit{Rhinosinusitis} & \textit{phenoxymethylpenicillin} & 7 days \\
& \textit{amoxicillin} & 7 days \\
& \textit{erythromycin} & 7 days \\
& \textbf{second line} & 7 days \\
& \textit{co-amoxiclav} & 7 days \\
& \textit{ciprofloxacin + metronidazole} & 7 days \\
\hline
\textit{Influenza} & \textit{zanamivir} & 5 days \\
& \textit{oseltamivir} & 5 days \\
\hline
\end{tabular}
\caption{Antimicrobial prescribing for URTIs}
\end{table}
The antimicrobial drugs of choice for acute infections 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 and *Pseudomonas aeruginosa* may be considered for initial therapy until the results of cultures become available.

**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, headache and disorder of smell. In a small number of patients erythema and tenderness of the involved sinus are present.

Sinus X-ray and CT scan 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 likely 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.

**Peritonsillar, retropharyngeal and parapharyngeal abscesses**

Peritonsillar, retropharyngeal and parapharyngeal abscesses are the most common deep cervical fascial space infections.

Peritonsillar abscess is the most common of these infections. Most develop secondary to an oropharyngeal or dental infection. Additional factors such as smoking and periodontal disease may also contribute to the formation of a peritonsillar abscess.

These abscesses develop in distinct anatomical fascial spaces. Their clinical presentation, however, can be very similar and present challenges to accurate diagnosis. Pain on swallowing is the most common initial symptom of each of these infections. Progression of the disease leads to drooling, dysphagia, neck immobility and interference in the airway as well as general systemic effects of infection. In peritonsillar abscesses the tonsil usually moves to the midline with erythema and oedema seen on the anterior tonsillar pillar and soft palate.

Radiologic imaging is routinely used in evaluating the abscesses; CT scan is used to confirm the presence of deep neck abscesses.

The most common organisms isolated in peritonsillar, retropharyngeal and parapharyngeal abscesses are group A streptococci, *Staph. aureus*, *H. influenzae*, *Prevotella spp.*, *Porphyromonas spp.*, *Fusobacterium spp.* and *Peptostreptococcus spp.*

Treatment consists of admission to hospital for parenteral antibiotics like co-amoxiclav, clindamycin (Dalacin C) or cefuroxime (Zinacef) and metronidazole, hydration, pain control and surgical drainage. However, in selected cases medical therapy...
alone can resolve parapharyngeal and hypopharyngeal abscesses.

**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.²⁷

Recently, there has been much discussion as to the appropriateness of prescribing antibiotics for patients with uncomplicated URTIs.²⁸ According to a recent paper there has been a fall of 50 per cent in antibiotic prescribing for children with URTIs, with an accompanying increase in hospital admission for peritonsillar abscess or rheumatic fever.²⁹ This rapid decline in antibiotic usage appears to be a combination of fewer prescriptions and ‘delayed prescribing’ – a strategy documented in 1994.³⁰

So should GPs stop prescribing antibiotics in uncomplicated URTIs 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.

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**Resources**

**Further reading**

BMJ collected resources. All articles published in *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. Flu treatment – zanamivir (review), amantadine and oseltamivir. Technology appraisal 58, February 2003. www.nice.org.uk/nicemedia/pdf/58_Flu_fullguidance.pdf.

NICE. The clinical effectiveness and cost effectiveness of amantadine and oseltamivir for the prophylaxis of influenza. Technology appraisal 67, September 2003. www.nice.org.uk/nicemedia/pdf/67_Flu_prophylaxis_guidance.pdf.

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.

**Patient resources**

*Colds, Flu and Antibiotics*. Self-care booklet on managing colds and flu symptoms at home including flu jab advice, information on pandemic flu and advice on the effective use of antibiotics. Campaign package can be ordered from DPP: www.dpp.org.uk /en/1/ camcfa.qxml or tel. 020 7383 6824.