

# EAR, NOSE AND THROAT INFECTIONS

## Chapter

# 9

### INFECTIONS OF THE EAR

#### ACUTE OTITIS MEDIA

Viruses are responsible for up to 50% of acute otitis media (AOM), with bacterial co-infection in about 18–27% of cases.

#### BACTERIAL PATHOGENS

- Common: *Streptococcus pneumoniae*, non-typable *Haemophilus influenzae* and *Moraxella catarrhalis*
- Occasional: *Streptococcus pyogenes* and *Staphylococcus aureus*
- Special patient populations (newborn infants, immunosuppressed patients and patients with suppurative complications of chronic otitis media): Gram-negative enteric bacilli and methicillin-resistant *S. aureus* (MRSA)

Signs and symptoms include ear pain (otalgia), ear discharge, hearing loss, fever, lethargy or irritability. Vertigo, nystagmus and tinnitus may occur. Redness of the tympanic membrane is an early sign of otitis media, but erythema alone is not diagnostic of middle ear infection. In recurrent AOM, the use of tympanocentesis to identify the bacterial pathogen and susceptibility pattern may be necessary for choosing the most effective antibiotic.

Given the high rate of spontaneous resolution of AOM and the probable viral aetiology, the American Academy of Paediatrics guideline states that antibiotics should be deferred for at least 48 hours during which the patient is given analgesics and decongestants. A useful approach may be to dispense the antibiotic or provide a prescription with the instruction that it is to be given (or the prescription filled) if there has not been resolution by 48 hours. This approach is reasonable where good follow-up is possible.

#### ANTIBIOTICS ARE ESSENTIAL IF AOM IS DIAGNOSED IN THE FOLLOWING PATIENTS

- In children six months and older with severe signs and symptoms (moderate-severe otalgia or otalgia > 48 hours or temperature > 39°C).
- In children with bilateral AOM aged 6–23 months without severe signs and symptoms.

#### OTHER INDICATIONS FOR ANTIBIOTICS FOR AOM INCLUDE

- Recurrent AOM
- Immunocompromised patients
- Neonates
- Structural ENT or immunological abnormalities
- Day-care attendees or siblings of children attending day-care centres

The usual course of acute otitis media is spontaneous resolution for the majority of patients within one to two days. *Streptococcus pneumoniae* is the least likely cause to resolve spontaneously and therefore the most important target for antibiotic therapy. The routine use of antibiotics for AOM is based largely on a fear of complications if antibiotics are not used and also on limited access to healthcare.

Strains of *Streptococcus pneumoniae* throughout South Africa have shown rapid changes in their resistance patterns, and hence the recommendations in this guideline are based on surveillance data on antimicrobial susceptibilities, especially for penicillin. Of those strains showing resistance to penicillin, the vast majority are fully susceptible or partially/intermediately resistant on MIC testing. Therefore amoxicillin remains the preferred oral antimicrobial because it is highly effective against strains of *Streptococcus pneumoniae* which are both fully susceptible, and partially/intermediately resistant to penicillin, provided that it is administered in high doses (90 mg/kg/day).

Higher doses of amoxicillin (90 mg/kg/day divided in two or three doses) produce concentrations in the middle ear which are sufficient to treat penicillin intermediately susceptible strains of *Streptococcus pneumoniae*.



#### FIRST-LINE TREATMENT: ACUTE OTITIS MEDIA

Amoxicillin, 90 mg/kg/day PO into 2 or 3 divided doses for 5–7 days in children (adults 1 g PO 8 hourly). If the patient is < 2 years of age, has severe symptoms, a standard 10-day course of antibiotics is recommended.

Clinicians should prescribe an antibiotic with additional  $\beta$ -lactamase coverage for AOM when a decision to treat with antibiotics has been made and the child has received amoxicillin in the last 30 days or has concurrent purulent conjunctivitis, or has a history of recurrent AOM unresponsive to amoxicillin:

Amoxicillin-clavulanate (90 mg/kg/day of amoxicillin and a constant amount of clavulanate 6.4 mg/kg/day, amoxicillin-clavulanate ratio 14:1 in 2 divided doses) for 5–7 days (adults: 2 g sustained release PO 12 hourly).

Penicillin allergic patients: cefuroxime 30 mg/kg/day PO in 2 divided doses, cefpodoxime 16 mg/kg/day PO in 2 divided doses, ceftriaxone 50 mg IM/IV per day for 3 days.

### ACUTE OTITIS MEDIA WITH TYMPANOSTOMY TUBES

This is a common problem and the culture of otorrhoea fluid will often show significant growth of bacteria such as *Pseudomonas aeruginosa* and *Staphylococcus aureus* in addition to the more usual pathogens, namely *S. pneumoniae*, *H. influenzae* and *M. catarrhalis*. Oral treatment with  $\beta$ -lactams in the presence of the former pathogens would therefore be inappropriate, and in this regard, a topical otological formulation of ciprofloxacin is an efficacious therapeutic option for the antibiotic management, alleviating the need for oral treatment.

### OTITIS EXTERNA

Most are due to so-called 'swimmer's ear' and the pathogens involved are usually *Pseudomonas aeruginosa*, *Proteus mirabilis* or other Gram-negative bacteria. *Staphylococcus aureus* and *Streptococcus pyogenes* are also pathogens implicated in acute otitis externa. Rare causes of chronic otitis externa include tuberculosis, syphilis, yaws, leprosy and sarcoidosis.



#### TREATMENT: OTITIS EXTERNA

Clean the external ear canal with an acidic solution, such as acetic acid ear drops, or by mechanical suction, or dry-mopping with cotton wool on a thin carrier.

After cleaning the canal, initiate ototopical therapy, e.g. dexamethasone 0.5 mg **AND** framycetin 5 mg **AND** gramicidin 0.05 mg/mL (Sofradex® or otic ciprofloxacin/corticosteroid drops (CIPROBAY HC OTIC®))

Systemic antibiotics play little role in treating acute otitis externa; they are reserved for patients who have concomitant cellulitis of the auricle or periauricular structures, or invasive infections.

Otomycosis is a fungal infection of the external auditory canal, and a common reason for otitis externa treatment failure. It is usually caused by *Aspergillus niger* and *Candida* spp. As with otitis externa, the mainstay of treatment is meticulous cleaning of the ear canal. Ototopical medications include topical clotrimazole.

#### MALIGNANT OTITIS EXTERNA

Malignant otitis externa is an uncommon syndrome which usually occurs in elderly diabetic patients or debilitated patients, where *Pseudomonas aeruginosa* invades the soft tissue, cartilage and bone. This condition is best treated with parenteral antipseudomonal agents, e.g. piperacillin-tazobactam or ceftazidime or imipenem **AND** an aminoglycoside/quinolone, then followed with an oral quinolone, e.g. ciprofloxacin, when appropriate. Surgical debridement is often required. Urgent referral to an ENT surgeon is indicated.

#### MASTOIDITIS

Pathogens and treatment are as for otitis media. If the disease in the mastoid has had a prolonged course, coverage for *S. aureus* and Gram-negative enteric bacilli may be considered for initial therapy until the results of cultures become available. Cultures for bacteria from ear drainage fluid must be taken with care to distinguish fresh drainage fluid from material in the external canal. The canal must be cleaned and fresh pus obtained as it exudes from the tympanic membrane. If the tympanic membrane is not perforated, tympanocentesis should be performed to obtain material from the middle ear.

A mastoidectomy is performed when an abscess has formed in the mastoid bone. An urgent specialist ENT opinion is advisable, as surgery may be necessary.

#### INFECTIONS OF THE NOSE

##### ACUTE VIRAL RHINITIS: COMMON COLD

The common cold is a mild and self-limiting viral illness. Rhinoviruses account for approximately 50% of common colds. Other viruses include coronaviruses and respiratory syncytial virus (RSV). Influenza, parainfluenza and adenovirus may also produce upper respiratory tract symptoms. Human metapneumovirus has been isolated in about 5% of cases.

The average incidence of the common cold in preschool children is five to seven episodes per year, but this may be higher in children attending crèche. Symptoms include a 'scratchy throat', nasal obstruction and rhinorrhoea. In infants and young children, the symptoms usually peak on day two to three of the illness and then gradually improve over 10 to 14 days. In older children and adolescents, symptoms usually resolve in five to seven days. Re-evaluation may be warranted if the symptoms worsen or exceed the expected duration. Purulent nasal secretions are common, and do not necessarily signify bacterial infection.

Simple analgesics (e.g. paracetamol) relieve symptoms of fever, headache or sinus discomfort. In those over 12 years of age, oral or topical decongestants may provide relief of rhinorrhoea and nasal congestion. Use of decongestants for more than five days is not recommended as it may lead to *rhinitis medicamentosa*. Over the counter cough and cold medications should be avoided in children younger than six years old. Airway irritation contributing to cough may be relieved with oral hydration, warm fluids, honey or cough lozenges (in children who are not at risk of aspiration).

There is no evidence to support the use of antibiotics, antihistamines, antivirals, or vitamins and herbal remedies in the treatment of the common cold. Antibiotic treatment causes more harm than benefit.

## **ACUTE BACTERIAL RHINOSINUSITIS**

Acute bacterial rhinosinusitis (ABRS) is an extremely common condition and is usually preceded by a viral upper respiratory tract infection. Common bacterial pathogens associated with acute bacterial sinusitis include *Haemophilus influenzae*, *Streptococcus pneumoniae* and less commonly, *Staphylococcus aureus* and *Moraxella catarrhalis*. Anaerobes and atypical pathogens such as *Chlamydophila pneumoniae* play a significant role in adult sinusitis, especially if persistent – so-called 'chronic sinusitis'. Fungi may be seen in allergic sinusitis and in immunocompromised hosts.

As with acute otitis media, *Streptococcus pneumoniae* cause the most serious sequelae. Although *S. pneumoniae* and *H. influenzae* remain the predominant pathogens, the relative frequency between them may have been altered in adults by the use of the pneumococcal vaccine in children.

Sinus puncture and aspiration remain the gold standard for determining the aetiology of ABRS, but is rarely performed due to the invasive nature of sinus puncture. Most studies have shown poor correlation between nose and throat cultures with maxillary sinus aspirates (MSA), and these cultures are generally not recommended in patients with acute or chronic sinusitis. ABRS can be differentiated from viral aetiology by a sinus aspirate that shows the presence of  $> 10^4$  colony forming units of bacteria/mL or if polymorphonuclear cells in sinus fluid exceeds 5000 cells/mL. Lower quantities of bacteria may represent early stages of infection. Endoscopically directed middle meatus (EDMM) aspirates may be a reliable alternative to MSA for obtaining cultures from patients with suspected ABRS.

When antibiotic therapy is selected, amoxicillin is the first-line recommendation for the treatment of ABRS. In  $\beta$ -lactam allergic patients, a respiratory quinolone or doxycycline may be substituted. Second-line therapy using amoxicillin/clavulanic acid combinations or quinolones with enhanced Gram-positive activity should be used in patients where the risk of bacterial resistance is high, or where consequences of failure of therapy are greatest, as well as in those not responding to first-line therapy.

A careful history to assess the likelihood of resistance should be obtained, and should include exposure to antibiotics in the prior three months, exposure to day-care facilities and chronic symptoms. Bacterial resistance rates to penicillin and macrolide/streptogramin/licosamide families have increased rapidly over the past decade to the extent that penicillin and macrolide resistance is now common. Failure of therapy secondary to resistant organisms has led to poor clinical outcomes in several well-documented instances.

Traditional approaches to antimicrobial management of ABRS focus on courses of therapy of 10–14 days duration for paediatric patients. IDSA recommends five to seven days therapy for uncomplicated ABRS in adults.

**TREATMENT: ACUTE BACTERIAL RHINOSINUSITIS (FIRST-LINE)\*****FIRST-LINE TREATMENT**

Adults: Amoxicillin 1 g PO 8 hourly for 5–7 days

Children: Amoxicillin 80-90 mg/kg/day PO in 2 divided doses for 10 days

**ALTERNATIVE TREATMENT**

Adults: Amoxicillin-clavulanate SR 2 g PO 12 hourly for 5–7 days

Children: 90 mg/kg/day of the amoxicillin component PO in 2 or 3 divided doses for 10 days

OR

Adults: Cefuroxime axetil 1000 mg PO 12 hourly for 5–7 days

Children: 30 mg/kg/day PO in 2 divided doses (max. 250 mg per dose) for 10 days

OR

Adults: Cefpodoxime 400 mg PO 12 hourly for 5–7 days

Children: 16 mg/kg/day PO in 2 divided doses for 10 days

\*Dosing based on Brink *et al.* (2015)

If the patient responds poorly to your first choice of therapy, consider treatment which includes 'atypical bacteria' in its spectrum of activity. Alternative therapy includes the new fluoroquinolones (not ciprofloxacin, which does not provide adequate cover for *Streptococcus pneumoniae*) and telithromycin, which can be given for a shorter duration of treatment, i.e. five to seven days.

**TREATMENT: ACUTE BACTERIAL RHINOSINUSITIS (FOLLOWING FIRST-LINE FAILURE)\***

Moxifloxacin 400 mg PO once daily for 5–7 days

OR

Levofloxacin 500 mg PO 12 hourly or 750 mg PO daily for 5–7 days (children: 20 mg/kg/day PO once daily or in 2 divided doses)

OR

Telithromycin 800 mg PO once daily for 5–7 days

Azithromycin or clarithromycin are recommended agents for  $\beta$ -lactam allergic patients provided the pathogen is a macrolide-susceptible *Streptococcus pneumoniae* or *Moraxella catarrhalis*.

\*Dosing based on Brink *et al.* (2015)

Antibiotics may speed up time to resolution of symptoms in individuals with ABRS. However, overall response rates evaluated at 14 days are similar for both antibiotic-treated and untreated patients. Incidence of side effects, mainly digestive, increases with antibiotic administration.

The extension of disease beyond the confines of the sinuses is a medical emergency and requires aggressive assessment, medical therapy, and potential surgical drainage. Individuals with suspected complications should be urgently referred to a setting with appropriate imaging facilities and qualified specialty care. Red flags for urgent referral include: systemic toxicity, altered mental status, severe headache, and swelling of the orbit or change in visual acuity. Orbital and intracranial complications are the most-feared complications of both acute and chronic rhinosinusitis.

## CHRONIC RHINOSINUSITIS

In the few situations when deemed necessary, bacterial cultures in chronic rhinosinusitis (CRS) should be performed either via endoscopic culture of the middle meatus or maxillary tap but not by a simple nasal swab. Since all specimens are potentially contaminated to varying degrees, proper specimen collection, transport, storage, and processing are key. Most studies have shown poor correlation of nose and throat cultures with maxillary sinus aspirates and these cultures are generally not recommended in patients with acute or chronic sinusitis.

If invasive fungal sinusitis is suspected, prompt diagnosis and treatment are essential. Culture must be requested promptly because these infections are life-threatening and usually require emergency surgery. However, results of culture are rarely available to assist with decision-making, and diagnosis is most frequently made on the basis of Gram-staining and frozen sections demonstrating the characteristic branching hyphae arrangement. Biopsies for Gram stain and culture (aerobic and anaerobic bacterial culture plus fungal culture) and for histopathology and special stains are key.

The main pathogens recovered in chronic sinusitis include *S. aureus*, Enterobacteriaceae, *Pseudomonas* spp., and less commonly *S. pneumoniae*, *H. influenzae*, and  $\beta$ -haemolytic streptococci. It is thought that coagulase-negative staphylococci may be pathogenic when present in large amounts, and when seen with neutrophils on the Gram stain or on histopathology.

Antibiotic therapy should be broader spectrum than for ABRS. Empiric therapy should target enteric Gram-negative organisms, *S. aureus* and anaerobes in addition to the most common encapsulated organisms associated with an ABRS (*S. pneumoniae*, *H. influenzae*, *M. catarrhalis*). Use an antibiotic with broad-spectrum coverage such as amoxicillin-clavulanic acid or a respiratory fluoroquinolone. Antibiotic therapy duration tends to be slightly longer than for ABRS.

## INFECTIONS OF THE THROAT

### PHARYNGITIS AND TONSILLITIS

Acute pharyngitis is described as a triad of sore throat, fever and pharyngeal inflammation. Although usually a local infection, it may form part of a systemic illness such as an infectious mononucleosis.

Respiratory viruses are the major cause of pharyngitis (up to 45% of cases) with adenovirus being one of the most frequently identified causes. Other respiratory tract viruses such as rhinoviruses, influenza and parainfluenza viruses can also cause pharyngitis. Enteroviruses and herpes simplex type 1 and 2 may cause vesicular or ulcerative eruptions of the pharynx.

An infectious mononucleosis picture may be caused by Epstein-Barr virus, primary CMV infection and acute HIV seroconversion.

Bacteria, especially group A  $\beta$ -haemolytic streptococci (GABHS) (*S. pyogenes*), account for 5–30% of cases. It is difficult to distinguish clinically between the viral and bacterial causes of a sore throat. Patients with GABHS pharyngitis commonly present with a sore throat (of sudden onset), odynophagia and fever. Headache, nausea, vomiting and abdominal pain may also be present, especially in children. On examination, patients have tonsillopharyngeal oedema with enlarged anterior cervical lymph nodes. Other findings include a beefy, red, swollen uvula, petechiae on the palate and a scarlatiniform rash. If performed correctly, throat cultures have a 90–95% sensitivity to detect streptococcal pharyngotonsillitis. Antistreptolysin O titre (ASOT) may also be requested, however, this is not recommended in the routine diagnosis of a 'strep throat' as it may reflect past and not current infection (2012 IDSA Clinical Practice Guidelines, Group A Streptococcal Pharyngitis).

Although GABHS tonsillitis is usually self-limiting in the majority of cases, antibiotics are recommended to prevent the suppurative and non-suppurative sequelae of *Streptococcus pyogenes* infection (e.g. acute rheumatic fever and glomerulonephritis). Other less common causes include *Fusobacterium necrophorum*, *Arcanobacterium haemolyticum* and *Corynebacterium diphtheriae*. *Neisseria gonorrhoeae* may also cause an exudative pharyngitis. *Mycoplasma* and *Chlamydomphila* have also been implicated as possible causes of pharyngitis. Non-infective causes of pharyngitis include allergy and exposure to irritating substances.

*Streptococcus pyogenes* remains highly susceptible to penicillin and hence penicillin remains the antibiotic of choice. A 10-day course of penicillin is recommended by the Infectious Disease Society of America (IDSA) and the American Academy of Pediatrics (AAP) for the treatment of pharyngitis caused by GABHS.

### TREATMENT: GROUP A STREPTOCOCCAL PHARYNGITIS

#### USE ONE OF THE FOLLOWING OPTIONS

 ANTIBIOTIC	ADULT AND ADOLESCENT DOSE	PAEDIATRIC DOSE
Penicillin VK (should be given 30 minutes before a meal)	500 mg PO 12 hourly for 10 days	250 mg PO 12 hourly daily for 10 days (< 27 kg) 500 mg PO 12 hourly for 10 days (> 27 kg)
Benzathine penicillin	1.2 MU IMI as a single dose	< 27 kg: 600 000 U IMI > 5 years: 1.2 MU IMI
Amoxicillin	500-1000 mg PO 12 hourly for 10 days Alternatively, 50 mg/kg/day PO once daily (max 3000 mg) for 10 days	50 mg/kg PO once daily (max 1000 mg) for 10 days Alternatively, 25 mg/kg PO (max 500 mg) 12 hourly for 10 days
Azithromycin	500 mg PO once daily for 5 days	10–20 mg/kg PO once daily for 5 days (max 500 mg)
Clarithromycin	250 mg PO 12 hourly for 10 days	15 mg/kg/day in 2 divided doses for 10 days (max 250 mg/dose)

Dosing based on Shulman *et al.* (2012), as well as Brink *et al.* (2015).



#### NOTE

Amoxicillin is an alternative to penicillin VK and has the advantage of no food restrictions. However, a rash can occur where pharyngotonsillitis is due to Epstein-Barr virus infection. This can lead to an erroneous diagnosis of penicillin allergy or, rarely, a severe skin reaction. Therefore, amoxicillin should preferably only be used when GABHS has been identified by culture.

A 10-day course of an oral cephalosporin is recommended for most penicillin-allergic individuals.

## ORAL THRUSH (OROPHARYNGEAL CANDIDIASIS)



### TREATMENT: OROPHARYNGEAL CANDIDIASIS\*

#### FOR MILD DISEASE

Swish mouth with 4–6 mL of oral nystatin suspension (100 000 U/mL) four times per day OR 1–2 nystatin pastilles (200 000 U/mL) 4 times daily for 7–14 days.

#### FOR MODERATE TO SEVERE DISEASE

Treat with oral fluconazole 100-200 mg PO daily for 7–14 days.

#### FOR OESPHAGEAL CANDIDIASIS

Treat with oral fluconazole 200-400 mg PO daily for 14–21 days.

\*Based on Pappas *et al.* (2016).

## REFERENCES

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Pappas PG, et al. 2016. Clinical practice guideline for the management of candidiasis: Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*.

Shulman ST, et al. 2012. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*.