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**Review of essential medicine priorities in ear, nose  
and throat conditions in children**

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## **1. Intent of the review**

The intent of this review is to:

- identify the priority ear, nose and throat (ENT) conditions in children ( up to 12 years)
- based on good quality treatment guidelines, to identify the essential medicines necessary for treating these conditions
- to review the existing EMLc and highlight those medicines that are already included that are indicated in the management of the identified priority ENT conditions
- to identify the medicines that need to be added to the EML for these conditions.

## 2. Identification of priority conditions

The South African Standard Treatment Guidelines and Essential Drugs List (STG/EDL) for paediatric care at hospital level<sup>1</sup> (last updated in 2006) includes the following ENT conditions:

- 17.1 Abscess, retropharyngeal
- 17.2 Tonsillitis, complicated (peritonsillar cellulitis, peritonsillar abscess)
- 17.3 Epistaxis
- 17.4 Mastoiditis
- 17.5 Otitis externa
- 17.6 Otitis media, acute
- 17.7 Otitis media, chronic, suppurative
- 17.8 Rhinitis, allergic
- 17.9 Sinusitis, acute
- 17.10 Sinusitis, chronic
- 17.11 Sinusitis, complicated

The corresponding STG/EDL for primary health care (for both adults and children; last updated in 2003)<sup>2</sup> lists the following ENT conditions:

- 17.01 Allergic rhinitis
- 17.02 Epistaxis
- 17.03 Otitis
- 17.03.1 Otitis externa
- 17.03.2 Otitis media, acute
- 17.03.3 Otitis media, chronic, suppurative
- 17.04 Sinusitis, acute
- 17.05 Tonsillitis and pharyngitis
- 17.05.1 Pharyngitis, viral
- 17.05.2 Tonsillitis, bacterial

These were considered to be an effective priority list of ENT conditions for which medicines were specifically indicated.<sup>a</sup> The list was also reviewed with an ENT surgeon who has post-graduate training in pharmacology,<sup>b</sup> in order to identify whether any other priority conditions could be listed. Two additional conditions were suggested:

- Acute croup
- Acute epiglottitis

The WHO handbook on Hospital Care for children only lists a single ENT condition – children presenting with stridor (viral croup, diphtheria).<sup>3</sup>

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<sup>a</sup> The South African documents are different from many other EDLs developed by national authorities. A list of priority conditions was first developed, followed by standard treatment guidelines (STGs), from which the essential drugs list (EDL) was abstracted. The first primary health care (PHC) document was developed in 1998 and then updated in 2003. Hospital level documents were first issued in 1998 and then updated in 2006. All of these documents can be downloaded from <http://www.doh.gov.za/docs/facts-f.html>

<sup>b</sup> Dr P Desmarais. Durban, South Africa – personal communication.

The Integrated Management of Childhood Illness (IMCI) handbook (updated in 2005) was also reviewed.<sup>4</sup> Recommendations for the child presenting with a acute ear infections, “runny nose”, and “sore throat and cough” were identified. In the latter case, the advice is as follows: “To soothe the throat or relieve a cough, use a safe remedy. Such remedies can be homemade, given at the clinic, or bought at a pharmacy. It is important that they are safe. Home-made remedies are as effective as those bought in a store” However, a few warnings are also given: “Harmful remedies may be used in your area. ... Never use remedies that contain harmful ingredients, such as atropine, codeine or codeine derivatives, or alcohol. These items may sedate the child. They may interfere with the child’s feeding. They may also interfere with the child’s ability to cough up secretions from the lungs. Medicated nose drops (that is, nose drops that contain anything other than salt) should also not be used.” For the diagnosis “NO PNEUMONIA: COUGH OR COLD”, the advice is that such a child “does not need an antibiotic. The antibiotic will not relieve the child’s symptoms. It will not prevent the cold from developing into pneumonia. Instead, give the mother advice about good home care. A child with a cold normally improves in one to two weeks. However, a child who has a chronic cough (a cough lasting more than 30 days) may have tuberculosis, asthma, whooping cough or another problem.”

In addition, the Technical updates of the guidelines on the IMCI from 2005 included a review of the management of acute and chronic ear infections.<sup>5</sup>

The following list of priority conditions (or groups of conditions) was thus used:

- Acute croup
- Epiglottitis
- Epistaxis
- Otitis externa
- Otitis media (acute and chronic)
- Rhinosinusitis
- Sore throat

### **3. Search for suitable guidelines**

The following sources were searched in order to identify suitable evidence-based treatment guidelines:

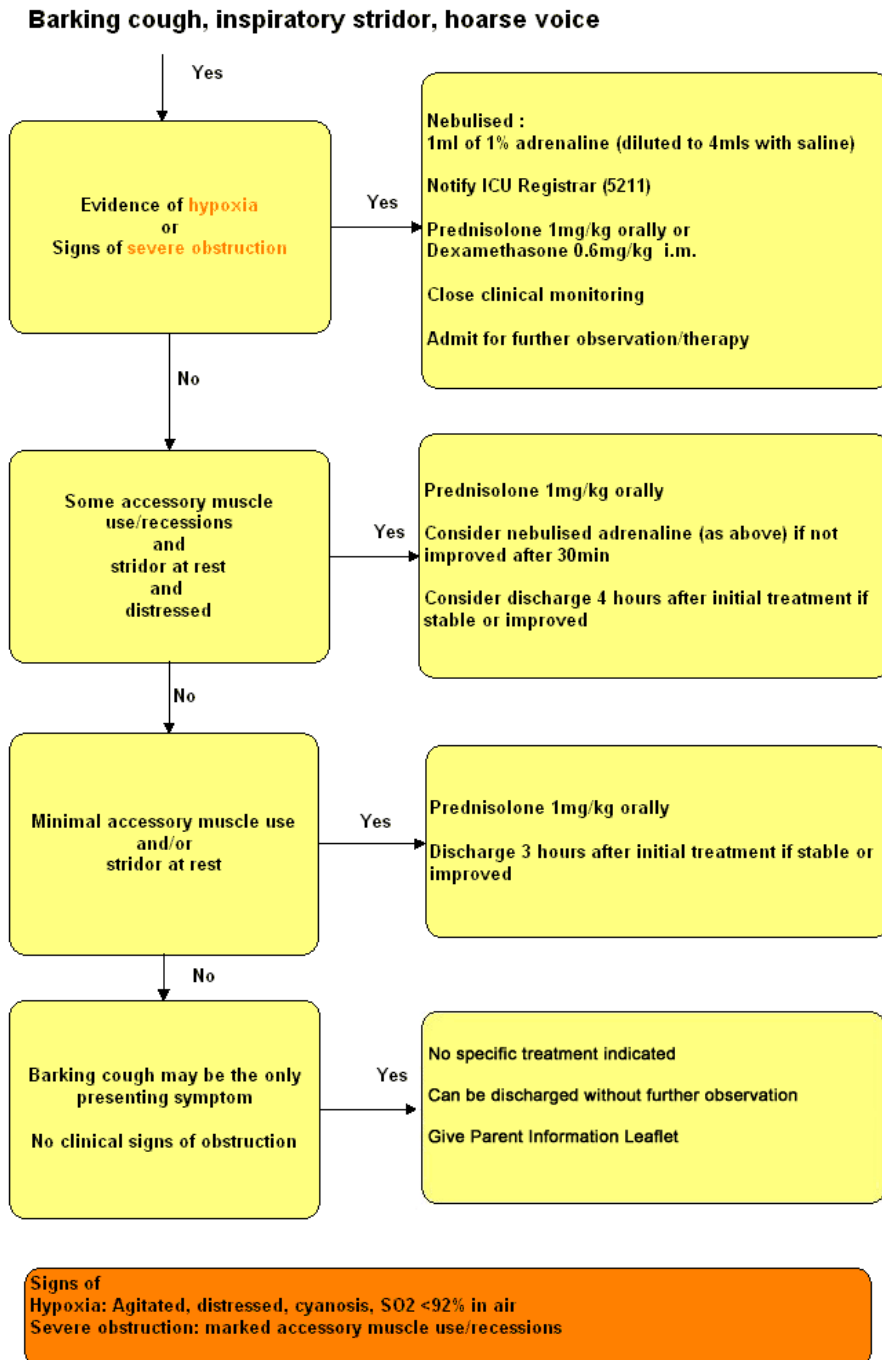
- National Institute for Health and Clinical Excellence (<http://www.nice.org.uk/>)
- Scottish Intercollegiate Guidelines Network (<http://www.sign.ac.uk/>)
- National Guideline Clearinghouse (<http://www.guideline.gov/>)
- Agency for Healthcare Research and Quality (<http://www.ahrq.gov/>)
- Bandolier (<http://www.jr2.ox.ac.uk/bandolier/booth/booths/ent.html>)
- Canadian Paediatric Society (<http://www.cps.ca/english/index.htm>)
- American Academy of Pediatrics (<http://www.aap.org/>)
- The Royal Children's Hospital, Melbourne (<http://www.rch.org.au/>)

In addition, the clinical query facility of PubMed (Medline) was used to identify suitable systematic reviews (including Cochrane Reviews) in relation to the priority conditions chosen. The contents of the International Journal of Pediatric Otorhinolaryngology were also searched.

## 4. Identified guidelines

### 4.1 Acute croup

The Royal Children's Hospital has a guideline on the management of acute croup<sup>6</sup>  
The Main differential diagnoses are listed as epiglottitis, bacterial tracheitis and laryngeal foreign body. The flowchart for management is as shown



The specific medications listed are nebulised adrenaline, prednisolone 1mg/kg orally and dexamethasone 0.6mg/kg IM. The Monash University web site provides similar advice, but with no evidence referenced for the specific details on steroid dosing (<http://www.med.monash.edu.au/paediatrics/resources/uao.html#croup>).

The South African STG/EDL for PHC also lists the following specific treatment:

- paracetamol, oral, 4–6 hourly, when required to a maximum of four doses daily.
- “If the child requires referral - while awaiting transfer:
  - adrenaline, 1:1000, nebulised, immediately using a nebuliser. If there is no improvement, repeat every 15 minutes, until the child is transferred. Dilute 1 mL of 1:1000 adrenaline with 1 mL sodium chloride 0.9%. nebulise the entire volume with oxygen at a flow rate of 6-8 L/minute
  - prednisone, oral, 2 mg/kg, single dose”.

## **4.2 Epiglottitis**

The South African STG/EDL only provides advice for antibiotic therapy in acute epiglottitis in children, as follows: cefotaxime, IV, 50 mg/kg/dose, 8 hourly for 7 days (or, in cases of penicillin allergy - chloramphenicol, IV, 25 mg/kg/dose, 6 hourly for 7 days).

The American Academy of Pediatrics provides guidance on the referral for surgical management (“The following patients are preferably managed by a pediatric otolaryngologist: Infants and children with complicated infections that may require surgery involving the ear (eg, otitis media with effusion and hearing change), the nose and paranasal sinuses (eg, chronic rhinosinusitis), the pharynx (eg, recurrent adenotonsillitis), the airway (eg, epiglottitis), and the neck (eg, retropharyngeal abscess).<sup>7</sup>

## **4.3 Epistaxis**

The Royal Children’s Hospital has a guideline on the management of epistaxis.<sup>8</sup> Some medications are mentioned:

- petroleum gel, if dry cracked mucosa are found to be a contributing factor
- vasoconstrictors applied via spray or cotton wool to Little’s area, for persistent bleeding (the example cited being a branded product – Co-phenylcaine forte®, which contains lignocaine hydrochloride 50mg/ml and phenylephrine hydrochloride 5mg/ml in a aqueous spray formulation – <http://www.enttech.com.au/downloads/Co-Phenylcaine%20Product%20Information.pdf>)

The South African STG/EDL suggests an alternative vasoconstrictor, as follows: oxymetazoline 0.025%, nose drops, 1–2 drops instilled into the affected nostril(s) and repeat digital pressure as above. No evidence for the efficacy of this measure is, however, provided.

A Cochrane Review has covered the issue of recurrent epistaxis in children.<sup>9</sup> Three studies were retrieved, involving a total of 256 participants. One randomised

controlled trial (RCT) compared Naseptin® antiseptic cream (containing chlorhexidine hydrochloride 1mg and neomycin sulphate 3250IU/g) with no treatment. Another RCT compared petroleum jelly with no treatment and a controlled clinical trial compared Naseptin® antiseptic cream with silver nitrate cautery. The authors found that: “Overall, results were inconclusive, with no statistically significant difference found between the compared treatments. No serious adverse effects were reported from any of the interventions, although children receiving silver nitrate cautery reported that it was a painful experience (despite the use of local anaesthetic)”. They concluded: “The optimal management of children with recurrent idiopathic epistaxis is unknown. High quality randomised controlled trials comparing interventions either with placebo or no treatment, and with a follow-up period of at least a year, are needed to assess the relative merits of the various treatments currently in use”.

The question of “cautery or cream” had also been addressed in a previous short review article.<sup>10</sup> On the basis of two papers, the authors concluded that: “Cautery and naseptin are equally effective. Given the ease of application naseptin is the treatment of choice.”

#### **4.4 Otitis externa**

The South African STG/EDL suggests the use of acetic acid 2% in alcohol, instilled 3–4 drops 4 times daily into the cleaned and dried ear.

Evidence-based guidelines were published by American Academy of Otolaryngology-Head and Neck Surgery Foundation in 2006.<sup>11</sup> The recommended flowchart for management of acute otitis externa is as shown below.

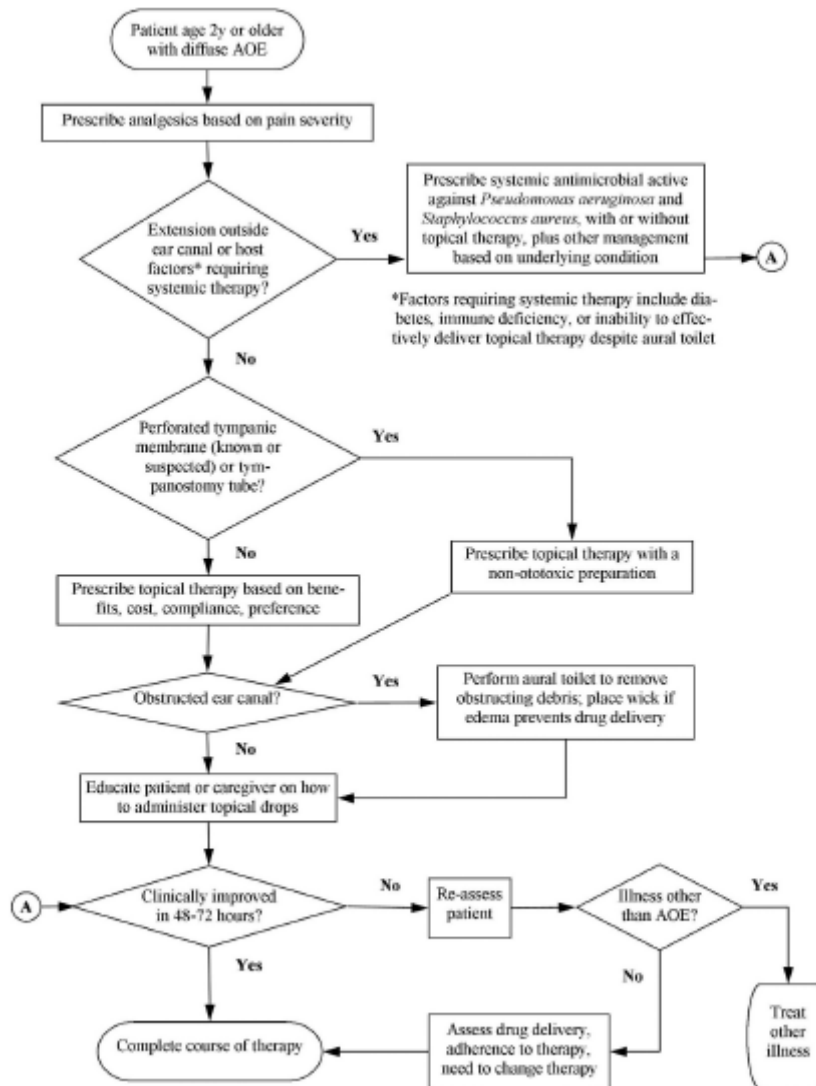


Figure 1 Flowchart for managing acute otitis externa.

The review noted that available topical preparations contained an antibiotic (an aminoglycoside, polymyxin B, a quinolone, or a combination of these agents), a steroid (such as hydrocortisone or dexamethasone) or a low pH antiseptic (such as aluminum acetate solution or acetic acid). The authors “found no significant differences in clinical outcomes ..... for antiseptic vs antimicrobial, quinolone antibiotic vs nonquinolone antibiotic(s), or steroid-antimicrobial vs antimicrobial alone” They stated that “[r]egardless of topical agent used, about 65% to 90% of patients had clinical resolution within 7 to 10 days”. A specific systematic review of the role of antimicrobials was published in the same supplement.<sup>12</sup> It provided the detailed evidence for the stance that “Topical antimicrobial is highly effective for acute otitis externa with clinical cure rates of 65% to 80% within 10 days of therapy. Minor differences were noted in comparative efficacy, but broad confidence limits containing small effect sizes make these of questionable clinical significance”. This was based on 20 trials, of which 18 provided data suitable for pooling. The detailed findings were as follows: “Topical antimicrobials increased absolute clinical cure rates over placebo by 46% (95% confidence interval [CI], 29% to 63%) and bacteriologic cure rates by 61% (95% CI, 46% to 76%). No significant differences were noted in clinical cure rates for other comparisons, except that steroid alone increased cure rates by 20% compared with steroid plus antibiotic (95% CI, 3% to

38%). Quinolone drops increased bacteriologic cure rates by 8% compared with nonquinolone antibiotics (95% CI, 1% to 16%), but had statistically equivalent rates of clinical cure and adverse events.

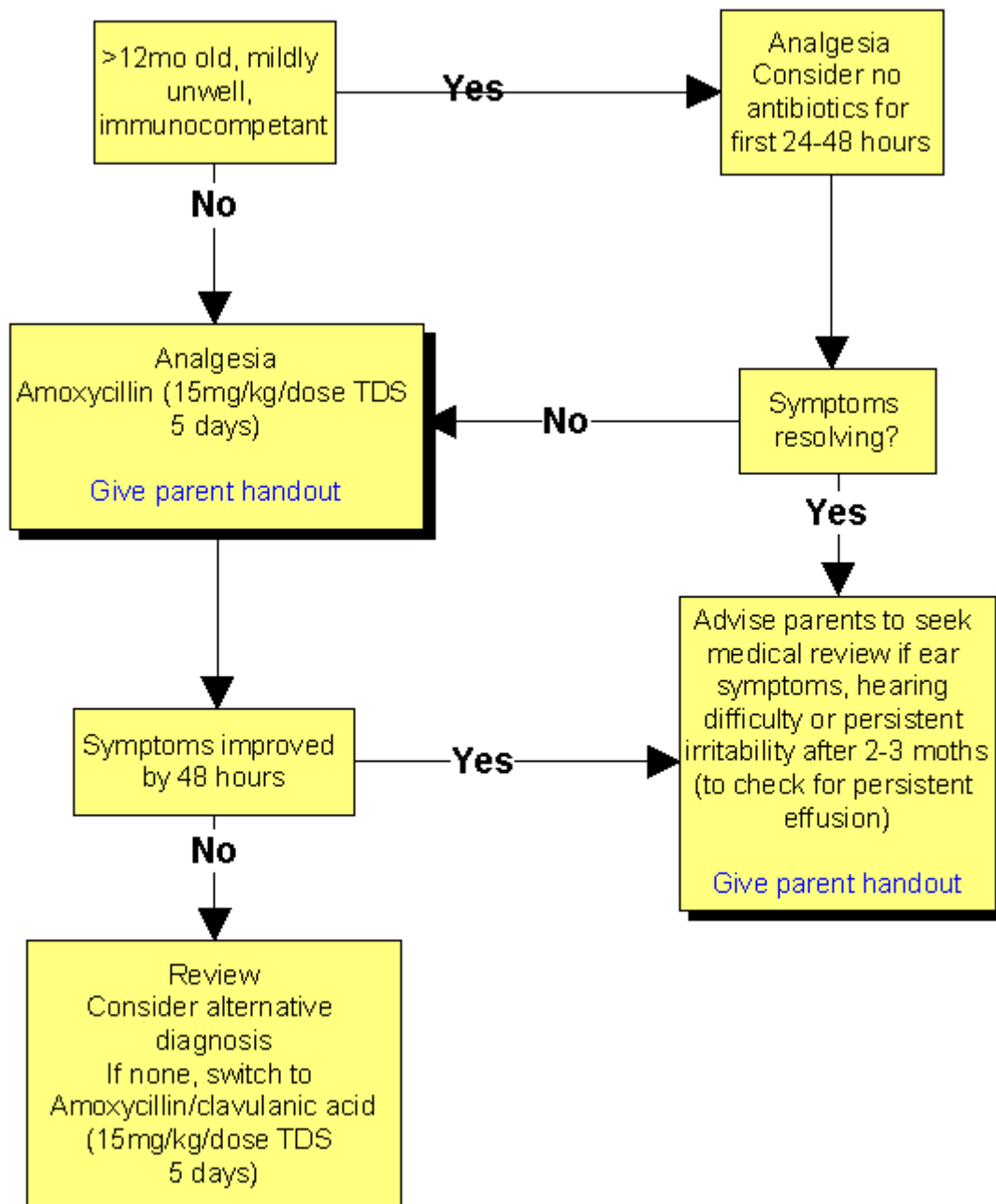
Bandolier noted a 2006 review on the role of antibiotics (RM Rosenfeld et al. Systematic review of topical antimicrobial therapy for acute otitis externa. *Otolaryngology – Head and Neck Surgery* 2006 134:S24-S48), concluding that “we have a paucity of data to guide therapy for a relatively common condition”.<sup>13</sup>

A protocol for a Cochrane review has been registered, with the following intentions: “[t]o determine the effectiveness of different methods of managing acute diffuse otitis externa. Methods of management to be considered include topical antibiotics, topical astringents, topical alcohol, topical antiseptics, topical steroids, combination topical treatments, systemic antibiotics, and aural toilet”.<sup>14</sup>

#### **4.5 Otitis media (acute and chronic)**

The drug therapy mentioned in South African STG/EDL for acute otitis media (AOM) is amoxicillin, oral, 30 mg/kg/dose 8 hourly for 5–10 days. For chronic, suppurative otitis media, the recommended antimicrobial treatment is a fluoroquinolone eardrop (such as ofloxacin drops, 2 drops 8 hourly instilled in the affected ear after dry mopping for 4 weeks).

The Royal Children’s Hospital flowchart is as shown overleaf.<sup>15</sup> It offers co-amoxiclav as a second-line choice antimicrobial. No specific analgesic is preferred. However, a link is provided to an analgesia flowchart at [http://www.rch.org.au/clinicalguide/cpg.cfm?doc\\_id=5144](http://www.rch.org.au/clinicalguide/cpg.cfm?doc_id=5144). The RCH guideline makes some important points: “Most cases of AOM in children resolve spontaneously. Antibiotics provide a small reduction in pain beyond 24 hours in only about 5% of children treated. The modest benefit must be weighed against the potential harms related to antibiotic use, both for the individual patient (adverse effects) and at a population level (resistance pressure). It has been shown that not using antibiotics for otitis media is acceptable to parents if the reasons are explained clearly. Pain is often the main symptom, so adequate analgesia is very important. Paracetamol 20-30 mg/kg for 2-3 doses/day should be given if pain is significant. Short-term use of topical 1% lignocaine drops applied to the tympanic membrane seems anecdotally to be very effective for severe acute ear pain. Decongestants, antihistamines and corticosteroids have not been shown to be effective in AOM.” No evidence for the use of topical anaesthetic drops is provided.



RCH flowchart - [http://www.rch.org.au/clinicalguide/cpg.cfm?doc\\_id=5284](http://www.rch.org.au/clinicalguide/cpg.cfm?doc_id=5284)

The AHRQ site provides access to Evidence Report/Technology Assessment No. 15 “Management of Acute Otitis Media”.<sup>16</sup> Medicine selection-related findings were as follows:

- “Meta-analysis demonstrated a reduction in the clinical failure rate within 2 to 7 days of 12.3 percent (95 percent confidence intervals, 2.8 percent and 21.8 percent) in favor of ampicillin or amoxicillin therapy compared with placebo or observational treatment. This result was generally robust to sensitivity analysis. Eight children with AOM would need to be treated with ampicillin or amoxicillin rather than no antibiotic treatment to avoid a case of clinical failure.”

- “Previous meta-analyses have demonstrated minimal to modest benefits of antibiotics compared with observational intervention without antibiotics during the initial treatment of AOM for the following outcomes: pain and fever resolution at 2 days, pain resolution at 2 to 7 days, contralateral otitis media and 7- to 14-day clinical resolution rate. The following outcomes did not appear to be affected by antibiotic use: pain resolution at 24 hours, pain and fever resolution at 4 to 7 days, tympanic membrane perforation, vomiting/diarrhea/rash, 1-month tympanometry, or recurrent AOM.”
- “Meta-analyses did not demonstrate a significant rate difference in clinical failure rates in children with AOM treated with ampicillin or amoxicillin compared with children treated with penicillin, cefaclor, or cefixime.”
- “Meta-analysis did not demonstrate a significant difference in clinical failure rates in children treated with trimethoprim-sulfamethoxazole compared with children treated with cefaclor for AOM.”
- “Meta-analysis demonstrated that children treated with cefixime had an 8.4 percent greater rate of diarrhea than children treated with ampicillin or amoxicillin. Twelve children with AOM would need to be treated with ampicillin or amoxicillin rather than cefixime to avoid a case of diarrhea.”

A 2003 AHRQ report focused only on the late effects of OME, not on treatment or management.<sup>17</sup>

The Scottish Intercollegiate Guidelines network published guidelines for otitis media in 2003.<sup>18</sup> While supporting a standard dose, 5-day course of antibiotics where needed, it provided this level “A” statement on other medication: “Children with otitis media should not be prescribed decongestants or antihistamines”. Similar advice (including mucolytics and both topical and systemic steroids) was offered for otitis media with effusion.

Both acute otitis media and otitis media with effusion have been the subject of guidelines published by the American Academy of Pediatrics.<sup>19,20</sup> The initial choice of antimicrobial, when used, is amoxicillin 80-90mg/kg/day. In relation to otitis media with effusion (OME), the AAP offered the following guidance:

- “Watchful waiting: clinicians should manage the child with OME who is not at risk with watchful waiting for 3 months from the date of effusion onset (if known) or diagnosis (if onset is unknown)”
- “Medication: antihistamines and decongestants are ineffective for OME and are not recommended for treatment; antimicrobials and corticosteroids do not have long-term efficacy and are not recommended for routine management”

In the case of the latter advice, it was stated that “This recommendation is based on systematic review of randomized, controlled trials and the preponderance of harm over benefit.”

A review of the Canadian Paediatric Society guidelines (currently at <http://www.cps.ca/english/statements/ID/id97-03.htm>) is underway. The 1998 guideline stated that “because of its excellent ‘track record’ (for infections due to penicillin-susceptible and -resistant bacteria), low cost, safety and acceptability to patients, amoxicillin remains the drug of choice for uncomplicated AOM.” It also states that “In patients with documented allergy to penicillin, an alternative to

amoxicillin is required. Although there is a risk of cross-reaction to other beta-lactam agents, this occurs rarely and therapy with a cephalosporin is generally safe. ... The choice should be guided by various considerations including cost, frequency of adverse side-effects and patient tolerability. A reasonable choice is either trimethoprim/sulfamethoxazole or erythromycin/sulfisoxazole.”

The choice of antimicrobial for otitis media is, of course, affected by local resistance patterns. A 2005 review of the evidence suggested the following potential choices:

- “When antibiotic therapy is considered necessary, according to these guidelines, amoxicillin (high-dose in most cases) represents the first-line treatment for AOM.”
- “In patients who present with a severe illness (moderate to severe otalgia or fever  $\geq 39^{\circ}\text{C}$ ) therapy may also be initiated with high-dose Amoxicillin clavulanate (Augmentin) in 2 divided doses for 10 days.”
- “If the patient is allergic to penicillin and the allergic reaction was not a associated with urticaria or anaphylaxis (Type I), cefdinir (14 mg/kg/day in 1 or 2 doses), cefpodoxime (10 mg/kg/day once daily), or cefuroxime (30 mg/kg/day bid) can be used. In cases of Type I hypersensitivity reactions, azithromycin (10 mg/kg/day on day 1, followed by 5 mg/kg/day for 4 days as a single daily dose) or clarithromycin (15 mg/kg/day bid) can be used.”
- “In a patient who is vomiting or cannot otherwise tolerate oral medication, a single dose of parental ceftriaxone (50 mg/kg) may be used for the treatment of AOM.”
- “Patients who failed to improve after a 48—72 h initial management with antibiotic agents should be treated with ceftriaxone (50 mg/kg/day for 3 days) or high dose augmentin. A diagnostic tympanocentesis should be performed in order to identify the etiologic organisms responsible for the failure of the first-line therapy and their susceptibility to antibiotics.”
- “Alternative therapy in penicillin allergic is clindamycin (30—40 mg/kg/day) in three divided doses.”<sup>21</sup>

Although not guidelines *per se*, a number of Cochrane Reviews on the subject of otitis media have been published.

The need for antibiotics in the management of acute otitis media in children was the subject of a meta-analysis, based on 8 trials (including 2 287 children).<sup>22</sup> Notably, all the trials included were conducted in developed countries. The findings were as follows: “The trials showed no reduction in pain at 24 hours, but a 30% relative reduction (95% confidence interval 19% to 40%) in pain at two to seven days. Since approximately 80% of patients will have settled spontaneously in this time, this means an absolute reduction of 7% or that about 15 children must be treated with antibiotics to prevent one child having some pain after two days. There was no effect of antibiotics on hearing problems of acute otitis media, as measured by subsequent tympanometry. However, audiometry was done in only two studies and incompletely reported. Nor did antibiotics influence other complications or recurrence. There were few serious complications seen in these trials: only one case of mastoiditis occurred in a penicillin treated group.” The authors’ conclusions – that “[a]ntibiotics provide a small benefit for acute otitis media in children” and that “[a]s most cases will resolve spontaneously, this benefit must be weighed against the possible adverse reactions” was, however, balanced by this statement: “Antibiotic treatment may play an

important role in reducing the risk of mastoiditis in populations where it is more common”.

A previous Cochrane Review had focused on the issue of short courses of antibiotics in AOM.<sup>23</sup> It was concluded that the data “suggests that five days of short-acting antibiotic is effective treatment for uncomplicated ear infections in children”.

The question of whether to use topical analgesic ear drops in AOM has also been addressed by a Cochrane Review.<sup>24</sup> The authors concluded that: “The evidence from these four randomised controlled trials, only one of which addresses the most relevant question of primary effectiveness, is insufficient to know whether ear drops are effective or not”.

A Cochrane Review on the question of whether decongestants or antihistamines have a role in the management of AOM in children, last updated in 2004, was removed from the web site in 2007.<sup>25</sup> The reason cited was that “the review authors were unable to work on any further updates due to other work commitments”. An update was planned for 2007.

A Cochrane Review that looked at the role of pneumococcal vaccination as a preventative strategy concluded that evidence for this was still lacking.<sup>26</sup>

The technical report accompanying the 2005 IMCI updates included this decision in relation to the management of chronic suppurative otitis media: “Daily instillation of topical antiseptics or topical antibiotics after meticulous aural toilet for at least 2 weeks is the most cost-effective treatment for the short-term resolution of otorrhoea. Intravenous antibiotics, particularly the anti-pseudomonal drugs, are highly effective but too expensive.”<sup>5</sup> A 2005 Cochrane Review provided these detailed findings: “Topical quinolone antibiotics can clear aural discharge better than no drug treatment or topical antiseptics; non-quinolone antibiotic effects (without steroids) versus no drug or antiseptics are less clear. Studies were also inconclusive regarding any differences between quinolone and non-quinolone antibiotics, although indirect comparisons suggest a benefit of topical quinolones cannot be ruled out. Further trials should clarify non-quinolone antibiotic effects, assess longer-term outcomes (for resolution, healing, hearing, or complications) and include further safety assessments, particularly”.<sup>27</sup> These conclusions were based on 14 trials, including 1 724 “analysed participants or ears”. The same group also concluded, the following year, that: “Topical quinolone antibiotics can clear aural discharge better than systemic antibiotics; topical non-quinolone antibiotic (without steroids) or antiseptic results are less clear”.<sup>28</sup> This conclusion was reached on the basis of data from 9 trials (833 randomised participants; 842 analysed participants or ears). The authors also noted that the definitions of chronic suppurative otitis media (CSOM) and the severity of cases varie, that some trials included mastoid cavity infections, and that “[m]ethodological quality varied”. From a selection point of view, it is worth noting the finding that “[a]dverse events reported were generally mild, although hearing worsened by ototoxicity (damaging auditory hair cells) was seen with chloramphenicol drops (non-quinolone antibiotic)”.

Other Cochrane reviews have addressed the prevention of OM using antibiotics in high risk children (“For children at risk, antibiotics given once or twice daily will

reduce the probability of AOM while the child is on treatment. Antibiotics will reduce the number of episodes of AOM per year from around three to around 1.5.”),<sup>29</sup> and the use of oral or intranasal steroids in OME (“Both oral and topical intranasal steroids alone or in combination with an antibiotic lead to a quicker resolution of OME in the short term, however, there is no evidence of longer term benefit.”).<sup>30</sup> The use of decongestants and/or oral antihistamines in OME has also been reviewed and no benefit found (“Because the pooled data demonstrate no benefit and some harm from the use of antihistamines or decongestants alone or in combination in the management of OME, we recommend against their use”).<sup>31</sup>

The South African STG/EDL for paediatric hospital care provides specific antibiotic and analgesia advice for the management of mastoiditis. No additional guidelines in this regard were sought, as the management is fairly standard.

#### **4.6 Rhinosinusitis**

The South African STG/EDL for paediatric hospital care provides the following advice in respect of the drug treatment of allergic rhinitis:

- chlorpheniramine, oral, 0.1 mg/kg/dose three times daily
- corticosteroid aqueous nasal solution, 2 sprays into each nostril twice daily

For acute sinusitis in children, the recommended drug treatment is:

- amoxicillin, oral, 30 mg/kg/dose 8 hourly for 5 days
- paracetamol, oral, 10–15 mg/kg/dose 6 hourly as required
- oxymetazoline 0.025%, nose drops, 2 drops instilled into each nostril, 6–8 hourly for not more than 5 days continuously.

For chronic sinusitis, the recommended approach is to “identify and treat the underlying cause, e.g. nasal allergy”, with the following suggestions:

- “hypertonic sodium chloride, 3.5% drops, may improve outcome”
- “There is no clear evidence that antibiotics improve the outcome. If non-medicine treatment fails, a trial of antibiotics may be tried in unresponsive cases” (the suggested regimen being amoxicillin, oral, 30 mg/kg/dose 8 hourly for 5 days)
- For analgesia, paracetamol, oral, 10–15 mg/kg/dose 6 hourly as required.

Lastly, the South African STG/EDL provides advice for complicated sinusitis, as follows:

- ceftriaxone, IV, 80–100 mg/kg as a single daily dose; followed once there is improvement with amoxicillin/clavulanic acid, oral, 25–30mg/kg/dose of amoxicillin component, 8 hourly (in the case of penicillin allergy, substituting clindamycin, IV, 10 mg/kg/dose, 8 hourly or erythromycin, oral, 6.25–12.5 mg/kg/dose, 6 hourly for 7 days)
- for pain, paracetamol, oral, 10–15 mg/kg/dose 6 hourly as required.

The Royal Children’s Hospital Clinical Practice Guidelines combines advice for “rhinosinusitis”, defined as “inflammation of the epithelial lining in the paranasal sinuses” and noting that this is “common in children”, “probably under-diagnosed”, but that “it resolves spontaneously in the majority of cases”.<sup>32</sup> Links are provided to

guidelines for the management of complications, such as orbital cellulitis ([http://www.rch.org.au/clinicalguide/cpg.cfm?doc\\_id=5164](http://www.rch.org.au/clinicalguide/cpg.cfm?doc_id=5164)). The specific drug treatment of acute bacterial sinusitis is as follows:

- “1st line - amoxicillin (15mg/kg/dose tds) for 10days (Cephalexin if penicillin allergic)”
- “2nd line - amoxicillin/clavulanic acid (if pt has had amoxicillin in the last month)”
- “If orbital / intracranial signs - IV flucoxacillin (50mg/kg/dose 6 hourly) and IV cefotaxime (50mg/kg/dose 6 hourly) and refer to ophthalmology/neurosurgery”.

The following strong statement is made: “The addition of steroid sprays, decongestants, or antihistamines to antibiotic treatment has been shown to have no benefit in sinusitis”.

The Agency for Healthcare Research and Quality lists a May 2002 guideline for the management of allergic and non-allergic rhinitis.<sup>33</sup> Although this was an exhaustive effort, it noted that “There were no specific studies of the pediatric population. Even though some studies may have enrolled patients in pediatric ranges, separate data were not reported for this subgroup. Therefore, no specific conclusions could be drawn for the pediatric population.” Despite this important caveat, the following findings are worth noting in respect of non-allergic rhinitis:

- “Antihistamines (all classes) versus placebo: Only one study which examined the role of antihistamines in the treatment of nonallergic rhinitis met the inclusion criteria. However, because the antihistamine used an ingredient in an antihistamine-decongestant combination product, the outcomes related to the antihistamine component of this drug cannot be separately identified. The Food and Drug Administration (FDA) recently approved a nasal topical product –azelastine (an H1 antihistamine) – for the treatment of vasomotor rhinitis.”
- “Nasal corticosteroids: Two of three identified studies employed budesonide and the other used beclomethasone. One study indicated that the symptoms of nasal congestion were improved by budesonide without alteration in other symptoms of nonallergic rhinitis. In the other two studies, comparison was made between the nasal corticosteroid and nasal ipratropium bromide. One study favored the nasal corticosteroid but the other failed to differentiate between the two interventions on the basis of symptom relief. Intranasal corticosteroids have been recommended for long-term therapy in nonallergic rhinitis and the two are approved by the FDA.”
- “Sympathomimetics versus placebo: Only two randomized controlled studies were identified which examined the role of oral decongestants (phenylpropranolamine) in treatment of nonallergic rhinitis. In both studies emphasis was placed on relief of symptoms of nasal congestion. However, the FDA has urged companies marketing phenylpropranolamine to voluntarily withdraw the drug from the market while the FDA initiated regulatory actions to mandate such withdrawals. The only currently available orally active decongestant, pseudoephedrine, was not identified in any clinical trial concerning management of nonallergic rhinitis.”
- “Leukotriene modifiers versus placebo: No studies were identified looking at the efficacy of leukotriene modifiers in the treatment of nonallergic rhinitis.”

- “Anticholinergics versus placebo: Each of these five trials studied intranasal ipratropium bromide and each study demonstrated the efficacy of ipratropium in reducing nose blowing frequency and rhinorrhea.”
- “Cromoglycate versus placebo: Two randomized controlled trials identified as looking at the effects of cromoglycate in nonallergic rhinitis recorded improvement in symptoms of rhinitis with active treatment compared to placebo.
- “Side effects/adverse effects: There were no side effects or adverse events reported in the studies of antihistamines or nasal corticosteroids. There is a report on the suppressive effect of beclomethasone nasal spray on bone growth in children and all nasal steroid preparations in the United States now warn of this adverse event. In the two studies comparing cromoglycate, there were no significant adverse effects associated with its use. In only one of the two studies involving sympathomimetics were adverse events such as drowsiness, nausea and headache described. Significant side effects of nasal dryness and nasal irritation were recorded in three of the five studies looking at ipratropium.”

In relation to allergic rhinitis:

- “Antihistamines vs. nasal corticosteroids: One published systematic review reported that for six individual nasal symptoms studied, as well as for overall nasal symptoms, nasal corticosteroids produced significantly greater relief than did oral antihistamines. The search identified eight new studies that were not included in this meta-analysis. Seven of the studies favored intranasal corticosteroids over antihistamines both in respect to improvement in global nasal symptoms as well as in most individual nasal symptoms. One study showed better symptom improvement with cetirizine alone over fluticasone alone. Thus, the overwhelming majority of studies clearly favour the use of intranasal corticosteroids over either sedating or nonsedating antihistamines for relief of symptoms of nasal allergy. These results are true for both seasonal allergic rhinitis and perennial allergic rhinitis.”
- “Antihistamines vs. immunotherapy: No randomized controlled trials were identified directly comparing immunotherapy with antihistamines in the treatment of seasonal and/or perennial allergic rhinitis. Immunotherapy is generally considered as a long-term disease-modifying treatment measure requiring months to years of treatment, whereas antihistamines are most often used for immediate symptom relief. Therefore, direct comparisons with respect to effectiveness/efficacy are not likely to be undertaken.”
- “Nasal corticosteroids versus immunotherapy: No randomized controlled trials were identified which directly compared immunotherapy with intranasal corticosteroids in the treatment of seasonal and/or perennial allergic rhinitis.”
- “Sedating versus nonsedating antihistamines: With respect to symptom alleviation in seasonal and perennial allergic rhinitis, study results indicate no consistent benefit of sedating antihistamines over nonsedating antihistamines. However, the side-effect profile favors use of nonsedating antihistamines.”

- Other agents (cromolyn, leukotriene modifiers, sympathomimetics, ipratropium): Studies provide strong support for the beneficial effect of cromoglycate in the management of both seasonal and perennial allergic rhinitis. Two clinical trials were identified which looked at the effects of decongestant drugs in allergic rhinitis and suggest some benefit in relief of nasal congestion but not other symptoms. The trial of ipratropium showed no significant differences between dosages of ipratropium but there was significant reduction in rhinorrhea and postnasal drip.”
- “Side effects/adverse events: A majority of the studies reported no major adverse events associated with the use of antihistamines. In those studies where major adverse events were reported, somnolence, dry mouth, dizziness and headache were identified most frequently. These symptoms were seen almost exclusively with the sedating antihistamines. Epistaxis, headache and pharyngitis were the most frequently reported side effects of nasal corticosteroids. None of the studies reported systemic side effects from intranasal corticosteroids in the short-term treatment studies. There is a report on the suppressive effect of beclomethasone nasal spray on bone growth in children and all nasal steroid preparations in the United States now warn of this adverse event. No major adverse events were reported in studies of cromolyn; among the minor reported side effects were high frequency of nasal irritation, headache and nasal congestion.”

A 2005 update focused on antibiotic choices only.<sup>34</sup>

A similar document, prepared for the University of Michigan Health System (and updated in November 2007) was obtained from the National Guidelines Clearinghouse.<sup>35</sup> While not specifically directed at paediatric care, it listed the following preferred medications:\

- “The over-the-counter (OTC), non-sedating antihistamine loratadine (Claritin) should be tried initially, as it will provide relief in most cases.”
- “Intranasal corticosteroids are considered the most potent medications available for treating allergic rhinitis [A]. They control itching, sneezing, rhinorrhea, and stuffiness in most patients, but do not alleviate ocular symptoms. They have a relatively good long-term safety profile.” (a local note stated that “Mometasone (Nasonex AQ) is preferred for children”).
- “Oral, non-sedating antihistamines prevent and relieve itching, sneezing, and rhinorrhea, but tend to be less effective for nasal congestion [A].”
- “Oral decongestants decrease swelling of the nasal mucosa which, in turn, alleviates nasal congestion [A]. However, they are associated with appreciable side effects, especially in geriatric patients, and should only be considered when congestion is not controlled by other agents. They are contraindicated with monoamine oxidase inhibitors (MAOIs), in uncontrolled hypertension and in severe coronary artery disease.”
- Leukotriene inhibitors are less effective than intranasal corticosteroids [A] but may be considered for patients that cannot tolerate the first line agents or have co-morbid asthma.”
- “Intranasal cromolyn (OTC) is less effective than intranasal corticosteroids [A]. Cromolyn is a good alternative for patients who are not candidates for

corticosteroids. It is most effective when used regularly prior to the onset of allergic symptoms.”

- “Intranasal antihistamines (Astelin), while effective in treating the nasal symptoms associated with seasonal and perennial rhinitis and nonallergic vasomotor rhinitis, offer no therapeutic benefit over conventional treatment [A].”
- “Ocular preparations should be considered for patients with allergic conjunctivitis who are not adequately controlled with or can not tolerate an oral antihistamine.”

The National Guidelines Clearinghouse does provide a more recent review, as part of a larger review of the diagnosis and treatment of respiratory illness in children and adults by the Institute for Clinical Systems Improvement.<sup>36</sup> An algorithm for allergic rhinitis can be downloaded at [http://www.guideline.gov/algorithm/6369/NGC-6369\\_3.pdf](http://www.guideline.gov/algorithm/6369/NGC-6369_3.pdf) and one for sinusitis at [http://www.guideline.gov/algorithm/6369/NGC-6369\\_4.pdf](http://www.guideline.gov/algorithm/6369/NGC-6369_4.pdf). The same medications are listed.

A specific review of the management of acute bacterial sinusitis in children 1-18 years of age is also provided on the National Guidelines Clearinghouse site, prepared by the Cincinnati Children's Hospital Medical Center.<sup>37</sup> While symptomatic treatment of cough or congestion was noted as “considered but not recommended”, the following antibiotics were recommended:

- “High-dose amoxicillin or amoxicillin-clavulanate (with high-dose amoxicillin component)
- Cefuroxime, cefpodoxime, or cefdinir (2nd-line treatment or for patients with non-type I allergies to penicillin)
- Alternative agent (e.g., ceftriaxone) or combination therapy (e.g., clindamycin and cefixime)
- Clarithromycin or azithromycin (for patients with type I allergies to penicillin)”.

The American Academy of Pediatrics published a guideline on the management of sinusitis in 2001.<sup>38</sup> Apart from recommending suitable antibiotics, at that point the Academy made the following recommendation in relation to other medication:

“Adjuvant therapies used to supplement the effect of antimicrobials have received relatively little systematic investigation. Available agents include saline nasal irrigation (hypertonic or normal saline), antihistamines, decongestants (topical or systemic), mucolytic agents, and topical intranasal steroids.” The technical report on this subject can be accessed at

<http://pediatrics.aappublications.org/cgi/content/full/108/3/e57>. A more recent review came to the same conclusions.<sup>39</sup> Much attention has been paid to the problem of over-use of antibiotics for this condition. However, a contemporaneous publication in the International Journal of Pediatric Otorhinolaryngology has highlighted the extent to which adjunctive medication is used, claiming level “A” evidence for the following in children:

- Oral antihistamines
- Intranasal H1 antihistamines
- Intranasal corticosteroids
- Intranasal chromones

- Specific immunotherapy.<sup>40</sup>

The most recent guidelines have been issued by the British Society for Allergy and Clinical Immunology.<sup>41,42</sup> Both are intended for adult and paediatric application. The following advice is offered in relation to rhinitis:

- “Saline douching reduced symptoms in children and adults with seasonal rhinitis (Grade of recommendation= A). It is a safe, inexpensive treatment.”
- Oral and nasal antihistamines – “First-line therapy for mild to moderate intermittent and mild persistent rhinitis. Additional to intranasal steroids for moderate/severe persistent rhinitis uncontrolled on topical intranasal corticosteroids alone”.
- Intranasal corticosteroids – “Meta-analysis shows that intranasal corticosteroids (INS) are superior to antihistamines”; “Reduce all symptoms of rhinitis by about 17% greater than placebo, with a variable effect on associated allergic conjunctivitis”; “Systemic absorption negligible with mometasone and fluticasone, modest for the remainder and high for betamethasone and dexamethasone – these should be used short term only”; “Long-term growth studies in children using fluticasone, mometasone and budesonide have reassuring safety data, unlike beclomethasone”.
- Anti-leukotrienes – “less effective than topical nasal corticosteroids”; “May have a place in patients with SAR and asthma”.
- Intranasal decongestants – “ $\alpha$ 1-agonist ephedrine (as nasal drops) and  $\alpha$  2-agonist xylometazoline (available as nasal drops or spray for adults and children over 3 months of age) are sympathomimetics that increase nasal vasoconstriction and are effective for nasal obstruction in both allergic and non-AR”; “Brief use of <10 days is advised in order to avoid rebound effect \_ for \* eustachian tube dysfunction when flying, \* in children with acute otitis media to relieve middle ear pain/pressure, \* post-URTI to reduce nasal/sinus congestion, \* to increase nasal patency before intranasal administration of nasal steroids”.
- Oral decongestants (pseudoephedrine) – “Weakly effective in reducing nasal obstruction”; “Do not cause a rebound effect on withdrawal but are less effective than topical preparations for nasal obstruction”.
- Chromones – “Children and adults with mild symptoms only and sporadic problems in season or on limited exposure”.

In short, for children, first-line treatments are antihistamines (“Compliance with once-daily administration of a long-acting antihistamine is likely to be better than medication that requires multiple daily doses. Antihistamines are useful if the main symptoms are rhinorrhoea and sneezing, or if there are symptoms outside the nose such as conjunctivitis or rash. Desloratadine, cetirizine, levocetirizine and fexofenadine may also be beneficial for symptoms of nasal congestion. For optimal results, they should be given continuously or prophylactically as opposed to ‘as required’”) and nasal steroids (“Nasal steroid with low systemic bioavailability should be used at the lowest possible dose to control symptoms and are useful for nasal congestion and obstruction. Intermittent use may be beneficial due to the rapid vasoconstrictor effect of corticosteroids. Compliance and efficacy is improved if the child is taught how to use the nasal spray”). Second-line treatments are as follows:

- “For relief of nasal congestion, short-term use (<14 days) of corticosteroid nose drops (e.g. betamethasone or fluticasone) and a topical decongestant may

be helpful”; “A short course of oral steroids may be required to relieve nasal congestion with systemic symptoms in SAR”.

- “For refractory rhinorrhoea, ipratropium bromide 0.03% may be helpful.”
- “For SAR, saline nasal irrigation during the pollen season may improve symptoms and reduce antihistamine requirement”
- “Leukotriene receptor antagonists may have a role if there is concomitant asthma”.

For rhinosinusitis in children:

- “Medical treatment including douching should be instigated, with surgery reserved for acute severe problems or for those patients with severe chronic symptoms not responding to medical therapy” (this review also pointed to a previous guideline: Clement PA, Bluestone CD, Gordts F, Lusk RP, Otten FW, Goossens H, Scadding GK, Takahashi H, van Buchem FL, van Cauwenberge P, Wald ER. Management of rhinosinusitis in children. *Int J Pediatr Otorhinolaryngol.* 1999 Oct 5;49 Suppl 1:S95-100).

The role of rhinitis in asthma has also been the subject of intense scrutiny.<sup>43</sup> In terms of paediatric management, the following comment was offered: “The principles of treatment for children are the same as for adults, but special care has to be taken to avoid the side effects typical in this age group. A Cochrane meta-analysis was recently published concerning the efficacy of intranasal glucocorticosteroids in children with IAR and PER but the papers analysed may not be totally adequate.” (see reference 47 below)<sup>c</sup>

There have been a number of Cochrane Reviews looking at different treatment modalities:

- Antibiotics in the common cold and acute purulent rhinitis – “There is insufficient evidence of benefit to warrant the use of antibiotics for upper respiratory tract infections in children or adults. Antibiotics cause significant adverse effects in adults. The evidence on acute purulent rhinitis and acute clear rhinitis suggests a benefit for antibiotics for these conditions but their routine use is not recommended”.<sup>44</sup>
- Allergen injections for seasonal rhinitis – “This review has shown that specific allergen injection immunotherapy in suitably selected patients with seasonal allergic rhinitis results in a significant reduction in symptom scores and medication use. Injection immunotherapy has a known and relatively low risk of severe adverse events. We found no long-term consequences from adverse events.”<sup>45</sup>
- Sublingual immunotherapy for allergic rhinitis – “SLIT is a safe treatment which significantly reduces symptoms and medication requirements in allergic rhinitis. The size of this benefit compared to that of other available therapies, particularly injection immunotherapy, is not clear, having been assessed directly in very few studies. Further research is required concentrating on optimising allergen dosage and patient selection”.<sup>46</sup>
- Topical nasal steroids for intermittent and persistent allergic rhinitis in children – “The three included trials provided some weak and unreliable

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<sup>c</sup> The ARIA process offered a new classification for allergic rhinitis which was subdivided into “intermittent” (IAR) or “persistent” (PER) disease

evidence for the effectiveness of Beconase® and flunisolide used topically intranasally for the treatment of intermittent and persistent allergic rhinitis in children. The reduction of severity in symptoms as assessed by the trialists could not be confirmed with the data provided and decisions on the use of these medications should, until such time as more robust evidence is available, be guided by the physician's clinical experience and patients' individual circumstances and preferences".<sup>47</sup>

- Nasal saline irrigations for the symptoms of chronic rhinosinusitis – “Saline irrigations are well tolerated. Although minor side effects are common, the beneficial effect of saline appears to outweigh these drawbacks for the majority of patients. The use of topical saline could be included as a treatment adjunct for the symptoms of chronic rhinosinusitis”.<sup>48</sup>

A Cochrane Review on the subject of antibiotics for persistent nasal discharge (rhinosinusitis) in children has, unfortunately, been withdrawn.<sup>49</sup>

#### **4.7 Sore throat (and common cold)**

The South African STG/EDL for paediatric hospital care provides specific antibiotic advice for “tonsillitis, complicated (peritonsillar cellulitis, peritonsillar abscess)”.

The National Guidelines Clearinghouse document, “Diagnosis and treatment of respiratory illness in children and adults”, prepared by the Institute for Clinical Systems Improvement also provides a recommendation for the medical management pharyngitis in children:

- “Penicillin
- Cephalosporins, erythromycin, and clindamycin for patients allergic to penicillin (Note: Sulfonamides and tetracyclines were considered but not recommended.)
- Patient education regarding home remedies for sore throats (e.g., acetaminophen or ibuprofen, salt water gargle, throat lozenges, hard candies, cool beverages or warm liquids) and callback instructions”.<sup>36</sup>

An algorithm for pharyngitis can be downloaded at [http://www.guideline.gov/algorithm/6369/NGC-6369\\_2.pdf](http://www.guideline.gov/algorithm/6369/NGC-6369_2.pdf)

A Cochrane Review on the role of antibiotics in “sore throat” concluded that “Antibiotics confer relative benefits in the treatment of sore throat. However, the absolute benefits are modest. Protecting sore throat sufferers against suppurative and non-suppurative complications in modern Western society can only be achieved by treating many with antibiotics, most of whom will derive no benefit. In emerging economies (where rates of acute rheumatic fever are high, for example), the number needed to treat may be much lower for antibiotics to be considered effective. Antibiotics shorten the duration of symptoms by about sixteen hours overall”.<sup>50</sup> That difference is clearly shown in the South African STG/EDL for PHC, which specifically indicates antibiotic treatment, and the Scottish Intercollegiate Guidelines Network document from 199, which states “The limited information available is insufficient to support a recommendation on the routine use of antibiotics in acute sore throat”.<sup>51</sup>

Although not strictly-speaking only an ENT condition, the guidelines for the common cold are also considered here. The South African PHC advice is as follows:

- “Antibiotics are of no value for the treatment of the common cold and influenza”
- For analgesia – “ paracetamol, oral, 4–6 hourly, when required to a maximum of four doses daily”
- In infants – “sodium chloride 0.9%, instilled into each nostril”.

Guidelines on cough and the common cold have been issued by the American College of Chest Physicians.<sup>52</sup> The advice offered is as follows:

- Patients with acute cough (as well as PND and throat clearing) associated with the common cold can be treated with a first-generation A/D preparation (brompheniramine and sustained-release pseudoephedrine). Naproxen can also be administered to help decrease cough in this setting. Level of evidence, fair; benefit, substantial; grade of recommendation, A
- In patients with the common cold, newer generation non-sedating antihistamines are ineffective for reducing cough and should not be used. Level of evidence, fair; benefit, none; grade of recommendation, D
- In patients with cough and acute URTI, because symptoms, signs, and even sinus-imaging abnormalities may be indistinguishable from acute bacterial sinusitis, the diagnosis of bacterial sinusitis should not be made during the first week of symptoms. (Clinical judgment is required to decide whether to institute antibiotic therapy.) Level of evidence, fair; benefit, none; grade of recommendation, D”.

## 5. Medications identified

The following medications were identified as indicated for priority ENT conditions.

ENT condition	Medicine recommended in guidelines	Appearing in EMLc	Appearing in WHO Model EML 15	Possible candidate for application
Acute croup	Adrenaline nebulisation (injectable form, diluted with saline)	epinephrine (adrenaline) Injection: 1 mg (as hydrochloride or hydrogen tartrate) in 1ml ampoule (section 3 and section 25.1).	epinephrine (adrenaline) Injection: 1 mg (as hydrochloride or hydrogen tartrate) in 1ml ampoule (sections 3, 12.2 and 25.1).	No
	Prednisolone oral	Prednisolone Oral liquid: 5mg/ml; tablet 5mg; 25mg (sections 3 and 8.3)	Prednisolone tablet 5mg; 25mg (sections 3 and 8.3)	No
Epiglottitis	Cefotaxime IV	No	No	No (alternative would be ceftriaxone); could be left to national choice
	Chloramphenicol IV	Powder for injection: 1 g (sodium succinate) in vial. (section 6.2.2)	Powder for injection: 1 g (sodium succinate) in vial. (section 6.2.2)	No
Epistaxis	Petroleum jelly	No	No	No (home remedy)
	Lignocaine + phenylephrine nasal spray	No	No	Questionable
	Oxymetazoline 0.025% nasal drops	No	No	Could be considered (alternative could be xylometazoline)
	Chlorhexidine + neomycin nasal cream	No (only neomycin + bacitracin ointment)	No (only neomycin + bacitracin ointment)	Questionable
Otitis externa	Acetic acid 2% in alcohol ear drops	No	No	Could be considered; commercial availability could be a problem
	Steroid ear drops (hydrocortisone or dexamethasone)	No	No	Could be considered
	Steroid + antibiotic	No	No	Could be

	combination ear drops			considered
	Antibiotic ear drops (quinolone)	No	No	Could be considered
	Antibiotic ear drops (non-quinolone, such as aminoglycoside, polymixin B)	No	No	Could be considered
Otitis media (acute and chronic)	Amoxicillin oral	Capsule or tablet: 250 mg; 500 mg (anhydrous); Powder for oral liquid: 125 mg (anhydrous)/5 ml; 250 mg (anhydrous)/5 ml. (section 6.2.1)	Capsule or tablet: 250 mg; 500 mg (anhydrous); Powder for oral liquid: 125 mg (anhydrous)/5 ml; (section 6.2.1)	No
	Amoxicillin-clavulanic acid oral	Oral liquid: 125 mg amoxicillin + 31.25 mg clavulanic acid/5 ml AND 250 mg amoxicillin + 62.5 mg clavulanic acid/5 ml.; Tablet: 500 mg + 125 mg.	Tablet: 500 mg + 125 mg (section 6.2.1)	No
	Trimethoprim + sulphamethoxazole oral	Oral liquid: 200 mg + 40 mg/5 ml. Tablet: 100 mg + 20 mg; 400 mg + 80 mg. (section 6.2.2)	Oral liquid: 200 mg + 40 mg/5 ml. Tablet: 100 mg + 20 mg; 400 mg + 80 mg. (section 6.2.2)	No
	Erythromycin + sulfisoxazole oral	No	No	No (could be left to national choice)
	Paracetamol oral	Syrup: 125 mg/5 ml. Tablet: 100 mg to 500 mg.(section 2.1 and 7.1)	Syrup: 125 mg/5 ml. Tablet: 100 mg to 500 mg.(section 2.1 and 7.1)	No
	Lignocaine 1% ear drops	No (but Lidocaine 2% to 4% hydrochloride) is listed as a topical form in section 1.2).	No (but Lidocaine 2% to 4% hydrochloride) is listed as a topical form in section 1.2).	Questionable
	Antibiotic ear drops (quinolone)	No	No	Yes (as per ICMI guidance on chronic suppurative otitis media)
Rhinosinusitis	Chlorpheniramine oral	Chlorphenamine Oral liquid: 2	Chlorphenamine Tablet: 4 mg	EMLc noted "Review of

		mg/5 ml. Tablet: 4 mg (hydrogen maleate). (section 3)	(hydrogen maleate). (section 3)	diphenhydramine to assess comparative efficacy and safety with chlorphenamine as a possible preferable alternative. Could also consider comparison with non-sedating antihistamines.
	Amoxicillin oral	Capsule or tablet: 250 mg; 500 mg (anhydrous); Powder for oral liquid: 125 mg (anhydrous)/5 ml; 250 mg (anhydrous)/5 ml. (section 6.2.1)	Capsule or tablet: 250 mg; 500 mg (anhydrous); Powder for oral liquid: 125 mg (anhydrous)/5 ml; (section 6.2.1)	No
	Paracetamol oral	Syrup: 125 mg/5 ml. Tablet: 100 mg to 500 mg.(section 2.1 and 7.1)	Syrup: 125 mg/5 ml. Tablet: 100 mg to 500 mg.(section 2.1 and 7.1)	No
	Ceftriaxone IV	<b>Powder for injection:</b> 250 mg, 1 g (as sodium salt) in vial. (section 6.2.1)	<b>Powder for injection:</b> 250 mg, 1 g (as sodium salt) in vial. (section 6.2.1)	No (note, square box for class)
	Cefalexin oral (and newer cephalosporins, such as cefuroxime, cefpodoxime, cefixime and cefdinir	No	No	No (could be left to national choice)
	Amoxicillin-clavulanic acid oral	Oral liquid: 125 mg amoxicillin + 31.25 mg clavulanic acid/5 ml AND 250 mg amoxicillin + 62.5 mg clavulanic acid/5 ml.; Tablet: 500 mg + 125 mg.	Tablet: 500 mg + 125 mg (section 6.2.1)	No
	Clindamycin IV	Injection: 150 mg (as phosphate)/ml. (section 6.2.2)	Injection: 150 mg (as phosphate)/ml. (section 6.2.2)	No
	Erythromycin oral (and newer macrolides, such as	Capsule or tablet: 250 mg	Capsule or tablet: 250 mg	EMLc noted: Review

	azithromycin and clarithromycin)	(as stearate or ethyl succinate). Powder for oral liquid: 125 mg (as stearate or ethyl succinate). (section 6.2.2) Azithromycin Capsule: 250 mg or 500 mg. Oral liquid: 200 mg/5 ml. * Only listed for trachoma.	(as stearate or ethyl succinate). Powder for oral liquid: 125 mg (as stearate or ethyl succinate). (section 6.2.2)	macrolides used in children for specific indications and whether erythromycin is the appropriate listed medicine. Review to consider use in neonates (risk of pyloric stenosis with erythromycin), relative toxicity and dosing compared to other macrolides. Include consideration of use of other macrolides for rheumatic fever.
	Flucloxacillin IV	Cloxacillin Powder for injection: 500 mg (as sodium salt) in vial. (section 6.2.1)	Cloxacillin Powder for injection: 500 mg (as sodium salt) in vial. (section 6.2.1)	No (square box)
	Cefotaxime IV	No	No	No (alternative would be ceftriaxone); could be left to national choice
	Antihistamine oral	Chlorphenamine Oral liquid: 2 mg/5 ml. Tablet: 4 mg (hydrogen maleate). (section 3)	Chlorphenamine Tablet: 4 mg (hydrogen maleate). (section 3)	EMLc noted "Review of diphenhydramine to assess comparative efficacy and safety with chlorphenamine as a possible preferable alternative. Could also consider comparison with non-sedating antihistamines.
	Antihistamine intranasal	No	No	No
	Decongestant nasal drops or sprays (ephedrine or xylometazoline)	No	No	Could be considered (alternative could be oxymetazoline)
	Nasal corticosteroid	No	No	Yes
	Leukotriene antagonist oral	No	No	Questionable

	Cromoglycate intranasal	No	No	Questionable
	Saline nasal irrigation/douche	No	No	No (home remedy)
Sore throat (and common cold)	Suitable antibiotics	See above	See above	No
	First-generation antihistamine/decongestant oral preparation (such as brompheniramine and sustained-release pseudoephedrine)	No	No	Questionable

Priority preparation in respect of which applications could be invited or reviews commissioned would be (in order):

1. an antibiotic ear drop (with consideration of quinolone vs. non-quinolone options) for chronic suppurative otitis media
2. a nasal corticosteroid for allergic rhinitis
3. an antiseptic or antimicrobial ear drop (with consideration of whether inclusion of a steroid would be necessary) for otitis externa
4. an oral antihistamine (with consideration of whether chlorphenamine is the appropriate first-line choice, and whether non-sedating agents were needed)
5. an appropriate first-line oral macrolide (with consideration of whether erythromycin is the appropriate first-line choice, and whether longer-acting versions were needed)
6. a decongestant nasal spray/nose drop (such as oxymetazoline or xylometazoline)

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