

## **A child with earache**

### **Are antibiotics the best treatment?**

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**Background.** Conventional management of acute otitis media, deduced from pathophysiology, embodies scant regard to analgesia, but concentrates on the microbiological cure by the use of antibiotics.

**Objective.** A commonly encountered case of uncomplicated acute otitis media in a child of three is presented. An evidence based approach to management is offered.

**Results.** The search for empirical evidence of patient relevant benefits and harms challenges the conventional approach. A Cochrane review of the literature on the use of antibiotics for acute otitis media shows that the benefits of antibiotic use (reduced pain in those children who go on to suffer pain beyond 24 hours) are offset by adverse events from the antibiotics themselves (gastrointestinal and rashes). There is insufficient information to be sure about rare complications of not using antibiotics as well as using them, but it seems that in either case, catastrophe is very rare.

**Discussion.** Thinking in terms of a balance of harms and benefits would result in a decreased proportion of children prescribed antibiotics for acute otitis media.

Acute otitis media (AOM) comprises 2.2% of consultations in Australian general practice. Its management exemplifies the potential for harm from treatments. Acute otitis media is the condition for which antibiotics are most often prescribed.

### **Case**

Michael Fong is a three year old brought in by an anxious father. Michael has had a cold for six days. He seemed to be coping with the mild illness - sniffles and slight flushing, with anorexia and crotchiness. Yesterday he became very irritable, and stopped eating altogether, running high fevers. He was difficult to settle, even with paracetamol in appropriate doses. Last night the household's sleep was disturbed with Michael waking screaming and feverish. The father was about to insist they drive him to the hospital, when he settled in the small hours of the morning.

On examination Michael was fractitious and difficult to examine. He had mucopurulent nasal discharge, a slightly reddened throat, and a fever of 38.5°C. His chest was clear. It was difficult to visualise the tympanic membrane of the right ear because of wax, but a good glimpse of the left revealed a bulging, bright red, tympanic membrane. There was no mastoid bone

tenderness, and no hint of neck stiffness.

### **What is the appropriate management?**

The diagnosis of acute OM might appear straightforward with this presentation. The question is, what is the best management?

### **The pathophysiological focus**

Traditional views centre on the pathophysiology. A range of different organisms has been isolated from the middle ear cavity in children suffering AOM. This includes viruses, *Streptococci*, *Hemophilus* species and other organisms less commonly, including *Branhamella catarrhalis*. The pain results from pressure on the tympanic membrane, which is exquisitely sensitive. The pressure is exerted by pus filling the middle ear cavity. Normally empty of liquid, this space is ventilated usually by communication with the Eustachian tube into the pharynx. The upper respiratory tract clogged with mucus, or the inflammation of the respiratory mucosa causes enough swelling to obstruct the tube, or perhaps from direct spread of infection into the mucosa lining the middle ear cavity, may explain the mechanical and hydraulic causes of the illness.

By deduction the answer seems straightforward. Kill the organisms responsible, and the illness should resolve. First the inflammatory processes should settle, and then the pressure will be taken off the tympanic membrane, and the pain should disappear. The antibiotic, in addition, should prevent secondary infection.

Most discussion about the optimal treatment of middle ear infection has centred on the spectrum of organisms sensitive to the different antibiotics available to the GP.

### **Patient focused outcomes**

An evidence based medicine point of view that has patient focused outcomes has quite a different perspective. Here, as clinicians, we are concerned less on the mechanism - however interesting that might be, and how much it might inform new avenues of research - and more on simply the bottom line: is the treatment effective? If so by how much, and at what cost? The currency of cost should be seen as much in terms of adverse effects as in financial terms.

### **The evidence**

For interventions, the best evidence derives from systematic reviews of several well conducted randomised controlled trials. If (as in this case) there are several, then the best way of summarising the evidence is to combine them in a meta-analysis. If there are several of these (as in this case also), then the best are usually those exposed to the rigour of a Cochrane review (see end of article).

The Cochrane review of antibiotic use in AOM in children can be summarised as suggesting that the number needed to treat (NNT) with antibiotics is about 20 children for every one who derives any benefit from the treatment. The benefit is described in terms of the probability of the child experiencing less pain if given antibiotics, but which makes no significant difference to the hearing component.

### **Adverse effects**

The Cochrane review also suggests that adverse effects are attributable to antibiotics, most commonly rashes, abdominal pain, nausea and vomiting. The incidence of these is higher in children taking an antibiotic than not. We can estimate the chance of this occurring from the trials. The number needed to harm (NNH) is about 20 children treated with antibiotics for one to get a common side effect. This is about the same as the number to benefit.

### **Rare events**

A reasonable criticism of meta-analyses of trials is that there are not enough numbers to account for rare events. Complications of AOM might be more common among children not treated with antibiotic if the rate is less than could be detected among the more than 2,000 children combined for analysis in the trials. It is reasonable to be concerned about this. A report from the 1950s suggested that the rate of developing mastoiditis - the most common suppurative complication of AOM - was as high as 17%. This complication rate would be detectable from the numbers in these trials, but was not evident.

Luckily we have additional evidence to help us here. The 60 Gps from a district of southern Holland (Tilburg) resolved to treat most (97%) children with AOM only symptomatically (that is, without antibiotics). In 17 months they managed 4860 cases. Only 126 had a severe course (less than 3%), and these were satisfactorily managed with oral antibiotics as outpatients, used when their stormy course was established, (including only three cases of mastoiditis which were treated satisfactorily with oral amoxicillin in general practice). Delaying the use of antibiotics, and using them only for children who became seriously ill, was safe and led to no increase in complications needed referral to specialists. The disease seems to have changed in 50 years.

Of course we should also consider the rate of rare complications from antibiotic use. This is more difficult. There are few collections of data for these - we may not have enough information to make a quantitative estimate. Certainly catastrophe from antibiotic use (especially oral) is rare. But we must also think beyond the individual patient. Antibiotics are best regarded as a nonrenewable resource. Their use leads inevitably to resistance: what we use now will not be available for use in the future.

There are few instances in medical science where the harms of treatment so nearly balance out the good. We must therefore think very carefully before using such a double edged sword (Table 1).

## **Table 1. The rationale behind treatment**

- ▶ Treatments can prove useless or even harmful - despite expectations based on pathophysiology.
- ▶ It is important that assumptions about the efficacy of treatments are not based purely on pathophysiology.
- ▶ Information about treatments (like that of other medical information, including diagnostic, prognostic and aetiological) needs to be assessed for patient focused outcomes.
- ▶ Finding the best of such information is the purpose of evidence based medicine.
- ▶ If such information is not available it should become a priority for research.

### **Alternatives to antibiotics**

Unfortunately there is little evidence to guide us. One trial has compared paracetamol with a non-steroidal anti-inflammatory drug (ibuprofen), which showed they were both more effective than placebo, and ibuprofen more than paracetamol. However, there are several shortcomings of the trial and it is difficult to quantify the benefits.

There are also intriguing data from a trial of Xylitol, a commonly used sweetener which is effective in preventing dental caries and inhibits the growth of pneumococci. It was given to 857 healthy children as either chewing gum or as lozenges to such in younger children, over three months. The NNT to prevent an episode of AOM was about eight. Exactly how this could be translated into usual care (long term use of such gum seems unreasonable) is not clear. This seems to be an area ripe for more research.

More research generally seems needed in respect to alternative and novel ways of managing AOM. The main problem of the illness is the pain, and it is astonishing that more powerful analgesics have not been adequately trialed for this distressing condition.

### **Cochrane Collaboration**

This comprises centres in 15 countries, 50 topic based collaborative review groups and about 6000 members. The Collaboration members hand search journals in 19 countries, produce Cochrane reviews, moderate the feedback system, ensure that methodology, statistics and software used in the writing of reviews is state of the art and that consumers are represented.

The main output of the Cochrane Collaboration is systematic reviews of the effects of healthcare interventions. These systematic reviews are published electronically in successive issues of The Cochrane Library. There are currently 2.000 of these, and in addition, many other

systematic reviews and more than 300.000 trials listed in the Central Trials Register, many with abstracts.

The Cochrane Collaboration is an international organisation that commenced in 1993 in response to Archie Cochrane's call for systematic, up-to-date reviews in healthcare. Cochrane was an epidemiologist who observed that healthcare practice is not always based on good evidence, but that there is too much information for any individual to access and use.

[www.cochranelibrary.com](http://www.cochranelibrary.com)

### **Summary of Important Points**

- Conventional treatment of OM concentrates on microbiological cure by the use of antibiotics.
- Acute otitis media is the condition for which antibiotics are most often prescribed.
- The benefits of antibiotic prescribing are offset by the adverse effects of the antibiotics themselves.
- Delaying antibiotic use in OM and reserving them for seriously ill children does not appear to increase the complication rate.
- There is little research about alternative treatments to antibiotics, particularly adequate analgesia. This is surprising given that pain is the predominant symptom.