Evidence for antibiotic use for sore throat and URTI in general practice

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There is a common misconception among many people that antibiotics are necessary for common colds and their symptoms. Evidence-based medicine can provide a rational approach to this problem.

Sore throat and upper respiratory tract infections (URTIs) are among the commonest presenting complaints in general practice, especially in the paediatric population.[1,2] Each year children have about five such infections, and adults two or three. Most are self-limiting and caused by viruses, but approximately 15% of sore throats reflect group A ß-haemolytic streptococcal (GABS) infections (also commonly referred to as 'strep throat') and may benefit from antibiotic treatment. Antibiotic use comes at a cost, not only of the medicine itself, but of side-effects and of promoting ever-growing bacterial resistance to antibiotics. Given the widespread use of antibiotics for these conditions (60% for adults with the common cold in the USA[3]), the costs are considerable. This article attempts to follow a rational approach to the antibiotic management of URTIs. We start by considering a common clinical problem.

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CASE 1

A 2-year-old child presents to a general practitioner with a 2-day history of fever, runny nose and cough. He has not been feeding as well as usual. On examination, his temperature is 38°C, he has a clear nasal discharge and a slightly red throat. The rest of the examination is normal.

What are the questions?

Before starting with an antibiotic we must ask what we hope to gain for the patient by doing so. We suggest that in this child we could aim at reducing the degree and duration of discomfort, and caregiver's time off work, and at preventing complications. Any such benefits would have to be balanced against the cost and harmful effects of the treatment. To balance benefits and adverse effects we need to know not only whether the antibiotic helps and/or harms, but how much it does of either.

We might phrase some of the questions as follows:

- Do antibiotics reduce the severity or duration of important symptoms in a 2-year-old child with an URTI? If so, by how much?
- Do antibiotics prevent complications of URTI?
- Do antibiotics have harmful effects? If so, how severe and how often?

Will antibiotics reduce the severity and duration of his symptoms?

The best evidence for the effectiveness of interventions comes from randomised controlled trials (RCTs), and good quality systematic reviews of RCTs generally offer the highest level of all. A systematic review differs from a traditional review article. It aims to collect and synthesise information from all applicable research in a prospective systematic manner.

A recent systematic review of 9 RCTs of antibiotics for the common cold did not find a significant impact on general or specific nasopharyngeal symptoms (odds ratio (OR) 0.80, 95% confidence interval (CI) 0.59 - 1.08).[4] A second systematic review in children found no change in clinical outcomes (relative risk (RR) 1.01, 95% CI 0.90 - 1.13).[5]

However, one RCT found that, in the 20% of people who had positive sputum cultures (for *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pneumoniae)*, antibiotics increased the proportion who had recovered by 5 days (27% v. 4% with placebo).[6] Therefore, why not culture the sputum of all patients, and only treat those who are positive? If approximately one-quarter of culture-positive people (27% minus 4%) will benefit, we shall need to treat approximately 4 people in order for one of them to benefit. Considering that only 1 in 5 people will be culture-positive, we would need to culture the sputum of 20 people to identify 4 people to treat, so that 1 person will benefit. If the cost, hassle and side-effects of 20 sputum cultures and 4 courses of antibiotics are worth 1 additional person benefiting, then this approach is worth it. It is up to the patient and practitioner to decide. This so-called 'number needed to treat' (NNT) is one tool of an evidence-based approach that helps provide a more intuitive idea of how much an intervention will help in a specific situation.

Will antibiotics prevent complications?

A systematic review[5] of 12 RCTs in children found no significant difference in the rate of development of otitis media or the progression of respiratory symptoms (RR 0.71, 95% CI 0.45 - 1.12).

Do antibiotics cause harm?

In the systematic reviews mentioned above, adverse effects of antibiotics, such as gastrointestinal disturbances, were 3 or 4 times more common in adults when treated with antibiotics, but not in children.

The current evidence therefore indicates that the main impact of antibiotics for the common cold is to produce adverse effects. The systematic reviews do not examine the impact of antibiotic use on the development of bacterial resistance, which is an additional very important reason not to prescribe antibiotics.

CASE 2

An 8-year-old girl from an outlying area comes to town with her mother on a once-a-day bus to see the nearest general practitioner. She has a fever and follicles on swollen, red tonsils. The general practitioner diagnoses tonsillitis, possibly due to GABS.

What are the questions?

Here the questions are similar to those in case 1, but the answers may be very different. The tonsillitis may be due to GABS and seems more likely to benefit from an antibiotic, and the potential complications of the condition, such as rheumatic fever and glomerulonephritis, are more severe.

Will antibiotics reduce the severity and duration of her symptoms?

A systematic review of 25 RCTs of antibiotics for sore throat found that antibiotics had their greatest effect at 3.5 days, by which time 50% of untreated patients had recovered (OR 0.41, 95% CI 0.36 - 0.48).[7] In other words, antibiotics shorten the duration of illness by an average of about 16 hours, and one would need to treat approximately 5 people for 1 additional person to have benefited at 3 days. In deciding whether an antibiotic is worth while for reducing symptoms, one must decide whether these modest benefits are worth the cost, adverse effects and promotion of bacterial resistance, remembering that analgesics are also effective for reducing symptoms.[8]

Will antibiotics prevent complications?

In addition to relieving symptoms there are of course other reasons for treating this child with a sore throat. The main one is to prevent rheumatic fever. A systematic review has found that antibiotics reduce the development of rheumatic fever by about two-thirds (OR 0.30, 95% CI 0.20 - 0.45).[7] So, how many people does one need to treat to prevent 1 case of rheumatic fever? This number will vary greatly, depending on the setting. It has been estimated that it would have taken 12 GP lifetimes to encounter 1 new case of rheumatic fever in Western Scotland in the 1980s.[9]

Unfortunately, in developing countries there is little evidence regarding the risk of rheumatic fever from a specific episode of sore throat in a specific setting, and this will vary greatly with age and socio-economic setting. Poor socio-economic circumstances greatly increase the risk. Therefore, in the

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absence of adequate information, it seems prudent to treat children from poor socio-economic circumstances who are at the age of greatest risk of streptococcal infection and acute rheumatic fever (5 - 15 years). It does not make sense to treat children under 3 years because rheumatic fever is very rare at this age. Incidentally, the argument that the introduction of antibiotics led to the reduction of rheumatic fever is not very convincing. In Denmark the incidence of rheumatic fever was steadily declining from 1900, and was largely unaffected by the arrival of antibiotics.

AN ALTERNATIVE DIAGNOSTIC APPROACH?

Would it be helpful to perform a throat swab culture in this patient, and delay treatment until the result is available? This is the standard approach in the USA. Apart from the cost and organisational difficulties (prohibitive in many situations) the throat swab is not a good test. There is a high carrier rate of group A b-haemolytic streptococci in people without symptoms, and cultures from the surface of the tonsil agree poorly with those from deep in the tonsillar crypts.[10] From published data (using the antistreptolysin o titre (ASOT) as the 'gold standard'), the sensitivity and specificity of throat swab culture are 26 - 30% and 73 - 80%, respectively.[11] In other words, in a group of patients of whom 30% have a streptococcal infection, we would miss approximately 70% of all these infections, and the positive predictive value of a positive throat swab would be 40%, i.e. more than 60% of those treated with an antibiotic would not have had a streptococcal infection. Despite the widespread use of throat swabs, when feasible, there seems little reason to recommend them.

Several studies have examined the accuracy of clinical examination in detecting streptococcal infections. Generally, the accuracy has been low, but these findings are difficult to assess because most research has used the throat swab as the 'gold standard'.

This case of tonsillitis illustrates a common and important element of an evidence-based approach. Good evidence is not always available. The size of the benefit of antibiotics in preventing rheumatic fever is uncertain, and a particular patient's risk of developing rheumatic fever after a particular infection is at best an educated guess. We have to find and use the best available evidence, taking its limitations into account. This requires judgement. Different people (both doctors and patients) with different perspectives, personalities and values will arrive at different decisions in some specific cases. This is not necessarily bad. People's needs and values differ. An evidence-based approach enables the best use of the limited available evidence, and makes more explicit the values underlying the decision. This can help to ensure that the patient's values, and not the doctor's, are influencing the decision. Put another way, an evidence-based approach does not replace clinical judgement. It is merely a tool to improve that judgement and the well-being of the patient.

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FURTHER READING

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IN A NUTSHELL

Sore throat and URTI are common presenting problems in general practice, and antibiotics are commonly used.

Antibiotic resistance is a major cost of widespread antibiotic use.

The main impact of antibiotics for people with the common cold is financial cost and adverse clinical effects.

In one-half of patients with sore throat, symptoms have improved by day 3 of the illness, with or without the use of antibiotics.

For sore throat, antibiotics shorten the average duration of symptoms by hours only, and analgesics are an effective alternative for pain.

A throat swab culture is a poor test for active streptococcal infection.

There is little reliable evidence regarding the accuracy of clinical signs for diagnosing 'strep throat'.

Antibiotic treatment for sore throat reduces the risk of rheumatic fever.

Antibiotic treatment to reduce the risk of rheumatic fever is pointless in people with a very low risk, e.g. children under 3 years and perhaps people in good socio-economic circumstances.