

"Just say no" - reducing the use of antibiotics for colds, bronchitis and sinusitis

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The use of antibiotics to treat infection can be miraculously beneficial or foolish and wasteful. Antibiotics save lives when used to treat endocarditis, meningitis and pneumonia, and restore health and prevent complications in many other infections (Figure 1). However, antibiotics provide no benefit for the common cold and in some other common respiratory tract infections their risk of adverse effects, cost, and contribution to the selection of resistant organisms outweigh their relatively trivial health benefits. Colds, upper respiratory tract infections and bronchitis are among the most common reasons to visit a doctor.¹ Despite a widespread appreciation that viruses are the overwhelmingly predominant causes of these illnesses, antibiotics are prescribed surprisingly frequently. Any reduction in the use of antibiotics for these illnesses is therefore likely to make a major contribution to reducing the overall use of antibiotics in our community without placing patients at risk of adverse health outcomes.

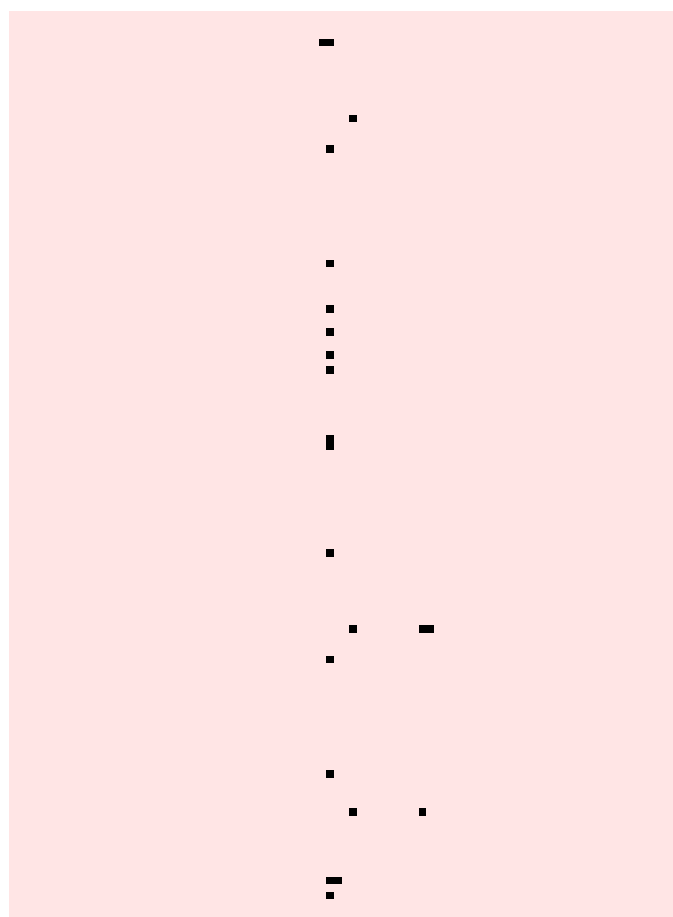


Figure 1. Schematic representation of the health effects of antibiotic treatment.

Colds - no benefit from antibiotic treatment

The cold is among the most common of human ailments. On average, children suffer six to eight episodes and adults two to four episodes per year. The usual duration is one week but symptoms including cough and nasal discharge can

persist for as long as two weeks. Contrary to common perception, involvement of the para-nasal sinuses is the rule rather than the exception.² Consequently, the common cold should be thought of as an episode of viral rhinosinusitis. Another widely believed fallacy is that clear nasal discharge indicates viral infection while mucopurulent discharge is due to a bacterial super-infection. In fact, the change to a thick, coloured nasal discharge which commonly occurs after one to three days of illness is due to the presence of increased numbers of desquamated epithelial cells and neutrophils.³

A variety of viruses (rhinoviruses, corona viruses, respiratory syncytial virus, adenoviruses etc) may be responsible for the common cold. In a minority of patients, bacterial respiratory pathogens (ie *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*) can be cultured from swabs of nasal mucus but these patients cannot be distinguished on clinical grounds.⁴ A recent meta-analysis of seven placebo-controlled studies involving 2056 patients aged over six months found no benefit in terms of cure or improvement from antibiotic treatment of the common cold.⁵ A significantly increased incidence in side effects (usually gastrointestinal) was found in the patients treated with antibiotics. Another reason sometimes given for the prescription of an antibiotic for an illness acknowledged to be viral in origin is to prevent the progression to secondary bacterial infection. There is however, no evidence to support such prescribing. A meta-analysis⁶ which reviewed five randomised controlled trials involving a total of 2520 children found no evidence that antibiotic therapy of upper respiratory tract infections (URTIs) prevented the subsequent development of pneumonia.

Acute bronchitis - trivial, brief benefit from antibiotics

The diagnosis of bronchitis is usually made in patients with an acute cough (or an exacerbation of a pre-existing cough) and scattered abnormal chest sounds such as wheeze and coarse or moist sounds.⁷ The illness may be difficult to differentiate from the common cold in which cough may also be a prominent feature. Acute bronchitis occurs most frequently in children aged less than four years and in the elderly. It is almost always preceded by symptoms of a cold and there is significant overlap between the viral causes of these two syndromes. In a minority of patients bronchitis is caused by bacterial pathogens such as *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Bordetella pertussis*. Cough frequently persists for two weeks, although production of sputum usually resolves within one week.⁸

The effects of antibiotic therapy for acute bronchitis or cough have been studied in four recent systematic reviews of randomised placebo-controlled trials.⁹⁻¹² Antibiotic treatment tended to provide modest beneficial effects which reached statistical significance for some of the variables evaluated eg. 'congestion', 'feeling unwell', 'number of patients taking cough or cold medications'. In those studies which found a benefit from antibiotic treatment, the effects were greatest between four and eight days after starting treatment and were no longer apparent at ten days.¹¹ The overall benefit of antibiotic treatment, in terms of days of purulent sputum,

days of cough or time off work was never more than half a day.¹² This clinical benefit was offset by a 6% risk of adverse events of which the most common were nausea and vomiting.¹¹ The authors of these reviews concluded that “the benefit from antibiotics, where present, was modest”,¹¹ and “may be outweighed by the side-effects of treatment”.¹⁰

Chronic bronchitis - modest benefit from antibiotics may be useful in sickest patients

Chronic obstructive pulmonary disease (COPD), or chronic bronchitis, affects approximately 10% of the adult population. The relationship between infection of the large airways and clinical symptoms is difficult to unravel. In approximately 50% of patients oropharyngeal flora, *S.pneumoniae* and *H.influenzae* persistently colonise the bronchi. Acute exacerbations of COPD are characterised by increased cough, sputum volume, sputum purulence and breathlessness. While increased numbers of bacteria (especially *H.influenzae*, *S.pneumoniae* and *M.catarrhalis*) and neutrophils are present in sputum during acute exacerbations of COPD, the role of infection in the causation of these exacerbations remains unclear and treatment of infection appears to provide only modest benefit.

A recent meta-analysis of nine randomised placebo controlled trials conducted between 1957-1992 found that antibiotic treatment provided a small but statistically significant benefit.¹³ The average improvement in peak expiratory flow rate attributable to antibiotic therapy was 11 L/min (95% CI 5-17 L/min). The beneficial effect of antibiotic therapy in outpatients was approximately half of that seen in hospitalised patients. In the best designed study,¹⁴ the mean peak flow on day six was approximately 212 L/min for antibiotic treated patients and 200 L/min for placebo treated patients. At the other times when peak flow was measured (days three, nine, twelve and fifteen), the mean difference in peak flow between patients treated with an antibiotic or placebo was always less than 7 L/min. The mean duration of each exacerbation of COPD was 14.1 ± 6.3 days for antibiotic treated patients and 15.5 ± 6.1 days for placebo treated patients. These short-lived modest benefits of antibiotic therapy may be clinically beneficial in the most frail patients, such as those who are over 60 years or in patients with poor underlying lung function (FEV1 < 50% predicted) and/or significant concurrent medical illnesses.¹⁵ However, there is little evidence that antibiotic treatment of patients with less severe disease provides any significant clinical benefit.

Sinusitis - modest benefit from antibiotics

Sinusitis is a common reason to consult a doctor and is widely regarded by doctors and patients as an illness requiring antibiotic therapy. However, as the sinuses are involved in most episodes of the common cold, it is likely that most episodes of sinusitis are viral in origin. Acute bacterial sinusitis complicates approximately 2% of episodes of the common cold and is usually caused by *S.pneumoniae*, *H.influenzae* or *M.catarrhalis*. Differentiation of viral rhinosinusitis from bacterial sinusitis is difficult but predominantly unilateral facial pain, unilateral purulent rhinorrhoea, poor response to decongestants, and maxillary toothache have all been found to be associated with bacterial infection.^{16,17} Demonstration of an air-fluid level, complete opacification or mucosal thickening on sinus X-rays or CT scanning will confirm the presence of sinus disease but cannot be taken as proof of a bacterial aetiology.

There have been conflicting results from placebo controlled trials of antibiotic therapy in acute sinusitis. Some studies have

failed to find a significant benefit from antibiotic therapy,^{18,19} while others have shown a modest but significant benefit.²⁰⁻²² Taken together, the studies show that the proportion of patients who are improved or cured by day ten is approximately 60-80% for placebo treated patients and 80-90% for those treated with an antibiotic.²³ Overall it seems likely that antibiotics offer a small benefit to those patients most likely to have bacterial infection ie those with symptoms present for more than ten days (and who have radiological evidence of sinus disease). While concern has been expressed that the increasing prevalence of beta-lactamase producing organisms (especially *H.influenzae* and *M.catarrhalis*) may render older regimens less effective, there is no evidence that newer agents provide any improvement in clinical outcome compared with amoxycillin.^{17,23} Treatment is traditionally given for ten to fourteen days but shorter treatment courses, eg three days, may provide similar efficacy.¹⁷

Adverse consequences of antibiotic therapy for URTI

The evidence suggests that antibiotic treatment provides no benefit in patients with colds, trivial benefit in patients with acute bronchitis, trivial benefit in all but a minority of patients with acute exacerbations of COPD and modest benefit in patients with sinusitis. These conclusions will not be surprising for most doctors or their patients, and yet antibiotics are commonly prescribed for these conditions. Studies of the prescribing patterns of doctors in New Zealand²⁴ and abroad^{25,26} show that antibiotics are prescribed for the majority of patients who present with an upper respiratory tract infection. The consequences of this continued overuse of antibiotics include rapidly increasing antimicrobial resistance, which will inevitably lead to failures of antimicrobial therapy in the future. For example following recent antibiotic therapy, children have an increased (two to five times) prevalence of nasopharyngeal carriage of *S.pneumoniae* with reduced penicillin susceptibility^{27,28} and a similar increase (two to nine times) in the risk that otitis media, pneumonia, bacteraemia or meningitis is caused by infection with these non-susceptible strains of *S.pneumoniae*.²⁸ Unfortunately, the genes for penicillin resistance in *S.pneumoniae* are frequently associated with genes for resistance to other unrelated antibiotics such as erythromycin, cotrimoxazole and tetracycline.²⁹ The effects of this linkage are firstly, that treatment with any one of a wide range of antibiotics can select for penicillin resistant *S.pneumoniae* and secondly, that a limited range of agents is available to treat the infections due to these multi-resistant organisms. It is for this reason that a recent British working party has suggested we should exhort our patients to “cherish their normal bacterial flora” and not needlessly assault it with unnecessary courses of antibiotic therapy.³⁰

These adverse consequences of antibiotic prescribing, need to be explained to our patients so that they are our partners in reducing antimicrobial use. However, it is reasonable to expect the medical profession to lead the community in this matter. For patients in whom antibiotic therapy can be expected to have only a net negative effect, maybe the admonition applied to another drug taking context, “Just say no”, is applicable. In those patients for whom antibiotics might provide some benefit, the use of a delayed (contingent) prescription can allow reduced antibiotic use without a significant increase in patient morbidity. For example, patients with sinusitis might be given a prescription for amoxil (or an equivalent agent) and advised to have it dispensed if they had not experienced spontaneous improvement within two to three days of the consultation. A UK study which examined the use of delayed prescription for patients with sore throats found that this approach reduced the proportion of prescriptions which were dispensed from 99% to

31%.³¹ Unless strategies such as these result in a reduction in antimicrobial use we can expect to see an inexorable increase in the prevalence of multi-resistant bacteria followed by an increase in the number of patients who fail to respond to conventional therapy.

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