

# Appropriate antibiotic use must be addressed now before resistance levels render them obsolete

The wide use of antibiotics — sometimes inappropriately prescribed — has led to the evolution of antibiotic-resistant bacterial strains, which are increasing at a worrying rate. To maximise the effect and prolong the ‘lifetime usage’ of currently active antibiotics it is imperative that they are prescribed appropriately, as described by Catherine Lowe and Adrian Penney.

## Introduction

Managing infections appropriately and effectively in primary care is a major challenge facing prescribers. Many common infections encountered are viral, not bacterial, in origin which makes antibiotic use inappropriate. Despite this antibiotics have been used widely giving rise to increasing antibacterial resistance. Unfortunately, few new drugs are currently being developed and treatment options are narrowing. This means that the antibiotics currently available need to be used appropriately to limit the spread of resistance and ensure that effective therapies are available for those who need them.

In 1998 the Standing Medical Advisory Committee (SMAC) highlighted this problem in their report *The path of least resistance*,<sup>1</sup> which included recommend-



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ations for prescribing in primary care. More recently NICE have published a report<sup>2</sup> making recommendations for the appropriate prescribing of antibiotics in

respiratory tract infections. In a recent *BMJ* article<sup>3</sup> Cars and colleagues expressed matters very starkly, stating: ‘The growing phenomenon of bacterial resistance, caused by the use and abuse of antibiotics and the decline of research and development of new medicines, is now threatening to take us back to the pre-antibiotic era’. This apocalyptic vision is one that should be of the greatest concern to all health care professionals and demand their action. However, attempts in recent years to address the issues of appropriate prescribing of antibiotics have been met with limited success. Clearly, action is required at all levels from individual prescribers through to Government.

This is the first of two articles in which we consider what can be done to improve the appropriate use of antibiotics. We will give a brief overview of current guidelines on when to treat common infections in primary care (listed in Table 1). When antibiotics are indicated to manage infections readers are also directed to local policies for specific guidance on which antibiotic is recommended in their area. Guidelines alone do not change prescribing behaviour and in our second article we will consider the dilemmas prescribers face when managing infections and suggest practical ways of resolving these.

## Prescribing for infections

The rate of antibiotic resistance is increasing

and depends, among other things, on how widely an antibiotic is used. Reducing antibiotic use may reduce the rate at which new resistance accumulates. Given the absence of new drugs for treating infections it is a priority to prescribe antibiotics carefully and so limit the spread of resistance. Antibiotics should be prescribed for those patients who are most likely to benefit from therapy. This includes the following:

- infections that are bacterial
- self-limiting infections that have not resolved
- infections where antibiotics significantly shorten the duration or severity of the illness
- patient is at high risk of complications.

General Practitioners (GPs) are usually more interested in the clinical decision to prescribe rather than the scientific

**Table 1. Common infections in general practice considered in this article**

- Respiratory tract
- Sore throat
- Otitis media
- Sinusitis
- Acute bronchitis
- Urinary tract
- Cellulitis
- Conjunctivitis

## Infection management

The antibiotics currently available need to be used appropriately to limit the spread of resistance and ensure that effective therapies are available for those who need them.

evidence detailing the specifics of antibiotic sensitivities. There is a critical hierarchy between medical emergencies, medically important diagnoses and those which are social. Medical emergencies and inappropriate requests to prescribe antibiotics are easy to identify. It is the area in between these two extremes which is difficult to manage. This middle ground is modified by the long-term narrative relationship that doctors have with patients. This relationship profoundly influences the negotiation that the doctor makes during a consultation.

Decisions to prescribe should be based upon a face-to-face consultation, where a problem needs an answer and satisfactory conclusion for patient, perhaps their carer and for the doctor. The patients and carers bring certain expectations about the role of antibiotics with them to their GP. Many GPs perceive that patients will be unhappy if they are not given an antibiotic for an infection and can sometimes prescribe one even if they consider it inappropriate. This area is explored in more detail in our second article. The role of a carer is particularly important to consider when prescribing for both children and older vulnerable adults.

### Respiratory tract infections

Antibiotics are commonly prescribed for respiratory tract infections (RTIs) in general practice and account for 60% of all antibiotic prescribing. Each year one quarter of the population visit their GP because of a RTI. Many upper RTIs are viral in origin and so prescribing an antibiotic is inappropriate. NICE recently published a guideline with recommendations on the management of RTIs. The guidance made suggestions for the management of acute otitis media, acute sore throat or acute

pharyngitis or acute tonsillitis. It suggests that a clinical assessment should be made together with an assessment of patient concerns and expectations. One of three strategies are proposed: 1. no prescribing, 2. delayed prescribing or 3. immediate prescribing. It is important that patients understand the natural time-course of infections and information provided in Table 2 can be useful for communicating this.

### Acute sore throat

The vast majority of sore throats are viral and do not require antibiotics. Symptoms usually take about eight days to resolve regardless of treatment.

A Cochrane review evaluated the evidence for antibiotics.<sup>4</sup> Symptoms of headache, throat soreness and fever were reduced by antibiotics by half-a-day at day three but about 90% of treated and untreated patients were symptom-free at one week.

In an open pragmatic trial<sup>5</sup> patients were randomised to receive either: prescription for 10 days, no prescription or delayed prescription (three days plus relevant advice pack). Nearly 70% of patients who had delayed prescription did not collect it. There was little difference between the groups for outcome. The main reason for attendance at surgery was to legitimise the illness, for example to take days off work or school. One year later more patients in the antibiotic prescription group returned requesting advice and treatment for a subsequent sore throat.<sup>6</sup> The authors concluded that doctors should avoid medicalising a self-limiting illness by giving antibiotics. Although they could be considered appropriate for patients who have a streptococcal throat infection a Dutch study<sup>7</sup> found that even if a streptococcal infection was present antibiotics made no difference to those who were not severely ill.

One of the reasons that some doctors prescribe antibiotics is that they are concerned they may put their patients at risk from the complications of acute sore throat — ie complicating otitis media, rheumatic fever, glomerulonephritis or

**Table 2. Natural history of respiratory tract infections**

- Acute otitis media: 4 days
- Acute sore throat/acute pharyngitis/acute tonsillitis: 1 week
- Common cold: 1½ weeks
- Acute rhinosinusitis: 2½ weeks
- Acute cough/acute bronchitis: 3 weeks

From: NICE CG69 July 2008<sup>2</sup>

quinsy. Although some evidence may suggest that the incidence of complications is reduced by antibiotics the overall rates of complication are low.<sup>8</sup> If the use of antibiotics are compared to placebo then:

- 71 patients would need to be treated to prevent one patient from suffering from otitis media
- 50 patients would need to be treated to prevent one case of quinsy.

The incidence of rheumatic fever has fallen over time in the UK and so there is no support from the literature for the use of antibiotics to prevent it. The same principles apply to the prevention of glomerulonephritis. Most of the studies were performed on military personnel after the second world war. Clearly, this does not translate to the patient populations encountered in general practice. On balance the absolute risk of complications is small. If this is balanced against the development of antibiotic resistance and the experience of adverse events from treatment then it would appear appropriate to reserve antibiotics for use if complications occur.

So when should antibiotics be used? The Centor criteria<sup>9</sup> (see Table 3) list clinical signs that are indicative of Group A beta-haemolytic streptococcus (GABHS) which is the most common cause of bacterial infection. If a patient has three or four of these signs then they have a 40–60% chance of having GABHS. The criteria can act as a tool to use when considering the management of a sore throat.

The most appropriate treatment of sore throat is simple analgesia and paracetamol

is the drug of choice. Non-steroidal anti-inflammatory drugs could be used although they offer no real advantage and have associated risks such as gastrointestinal bleeding, nausea, vomiting, abdominal pain and diarrhoea. There is minimal literature to suggest that combination analgesics have an advantage over paracetamol. Weak opiates are also associated with side-effects like constipation, nausea and disorientation.

### Acute otitis media

Here we make a distinction between acute otitis media and the chronic otitis media with effusion (commonly known as glue ear) because the management is different. Acute otitis media is a common condition and 8 out of 10 children recover without antibiotics. Even if antibiotics are used it makes little real difference to the rates of recovery and can cause side-effects like diarrhoea. Many cases of otitis media are viral and illness resolves in around four days in 80% of patients without antibiotics. Often, worried parents can have an expectation of antibiotics for ear ache. Studies have shown that delayed antibiotics could be an option if there is no improvement after three days. The results of these studies are comparable with those on sore throat and demonstrate low uptake of prescriptions. Prescribing antibiotics could be considered for children aged less than two years with bilateral acute otitis media, ear discharge or perforation.

How should acute otitis media be managed? Decongestants, antihistamines and mucolytics have been used for symptom

control. There is a lack of evidence for their benefit and so these agents cannot be recommended. Simple analgesia is the most appropriate treatment for the management of pain and raised temperature.

### Acute sinusitis

Sinusitis is a common diagnosis in general practice and it causes significant morbidity, which is associated with time off work. This is a main reason why a GP may prescribe antibiotics. Sinusitis is generally caused by viral upper RTIs and only 2% of cases are associated with bacteria. Even when sinusitis is caused by bacteria it will resolve without antibiotics. Furthermore, the signs and symptoms of viral and bacterial sinusitis are indistinguishable from each other. About 70% of sinusitis cases resolve in 7–10 days without antibiotics. How should sinusitis be treated? One review reports that there is some evidence to support the use of antibiotics, with a small difference in cure rate compared with placebo.<sup>10</sup> Therefore, antibiotics could be reserved for situations when the symptoms are severe or prolonged (more than 5 days). The mainstay of treatment for sinusitis is simple analgesia. There is little evidence to support the use of antihistamines, intranasal steroids, nasal douches or decongestants.

### Acute bronchitis

Acute bronchitis is commonly caused by a viral infection and sometimes bacterial by infection. However, it will resolve without antibiotic treatment regardless of the cause. It is important to distinguish between community acquired pneumonia and acute bronchitis as outlined in Table 4. Routine antibiotic treatment is unnecessary for previously well patients with acute bronchitis regardless of cough duration. Coloured sputum arises from either viral

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or bacterial infection; bright green sputum might simply be related to allergic conditions and is not an indication for antibiotic treatment unless the patient has COPD.

### Urinary tract infections

Urinary tract infections (UTIs) are common and account for 1–3% of all GP consultations each year. Uncomplicated UTI often resolves in a few days without treatment and is rarely associated with serious consequences. Routine use of urine culture is unnecessary. Instead, diagnosis should be guided by symptoms, urine appearance and dipstick urine tests. Antibiotic treatment may be indicated if the patient has more than three typical symptoms of UTI (dysuria, urgency, frequency, polyuria, suprapubic tenderness, haematuria). Empirical treatment with a course of trimethoprim for three days would be appropriate. If a patient has two or less symptoms then simple analgesia will help to relieve pain. There is little evidence to support symptomatic treatments like increasing fluid intake or alkalinising the urine. Investigation and treatment will increase side-effects and also medicalise the condition. Asymptomatic bacteruria in the elderly is very common and is not related to increased morbidity or mortality. In catheterised patients it is inappropriate to test and then treat patients unless they

#### Table 3. CENTOR criteria

- History of fever
- Absence of cough
- Swollen tender anterior cervical lymph nodes
- Tonsillar exudates

The Centor criteria are 4 symptoms, which if present, indicate that a patient has a streptococcus rather than a viral infection. If a patient has 3 out of the 4 symptoms then there is a 50% chance of a throat infection.

From: *Centor RM et al (1981)*<sup>9</sup>

#### Table 4. Severe features that are associated with worse outcomes in lower RTI, which may mean that antibiotic treatment is required

- Raised respiratory rate (>30 breaths/min)
- Low blood pressure (systolic <90mmHg and/or diastolic <60mmHg)
- Confusion of recent onset
- Co-existing disease (e.g. cardiac failure, cerebrovascular, neoplastic, renal or liver disease)
- High or low temperature (<35°C or >40°C)
- Tachycardia (>125 beats/min)

## Infection management

are pyrexial, have a raised white cell count and are unwell. Some patients experience recurrent UTI and need prophylactic drugs to prevent recurrence. Nitrofurantoin and trimethoprim are the agents of choice rather than cephalosporins.

### Cellulitis

Cellulitis is an acute bacterial infection of the dermis and subcutaneous tissue. The grades of severity are categorised from class I to IV. Only people with class I symptoms should be managed in primary care and this includes patients who have no signs of systemic toxicity, have no uncontrolled co-morbidities and can be managed with oral antibiotics. Before commencing antibiotics it is important to draw around the margins of infection with a permanent marker for future comparison. A seven-day course is given in the first instance. The usual antibiotic of choice is flucloxacillin 500mg four times per day or erythromycin 500mg four times per day for people with penicillin allergy. Patients with leg ulcers are an important consideration because bacteria will always be present. Antibiotics do not improve healing and should not be used. Culture swabs and antibiotics are only indicated if there is evidence of clinical infection — increased pain, pyrexia and >2cm surrounding erythema. One important area to address is the practice of the local district nurse teams who may be sending swabs away for culture inappropriately. A common understanding of when they should be sent is an important aim.

### Conjunctivitis

Infective conjunctivitis is an inflammation of the conjunctiva (the thin protective membrane that covers the surface of the eye and inside the surface of the eyelids) caused by a bacteria or virus. It is difficult to distinguish between viral and bacterial conjunctivitis. However, bacterial conjunctivitis is more common when the eyes are glued by discharge, there is an absence of itching and there is no history of previous episodes. If a viral infection is suspected then a delayed approach to prescribing could be considered. If antibiotics are to be used then chloramphenicol is the therapy of choice.

However, most bacterial infections are self-limiting with 64% resolving when patients have taken a placebo. Infective conjunctivitis is contagious so, in our practice, we would usually give advice on measures to reduce the spread of infection. This is reinforced with a patient information leaflet produced by the practice.

### *Clostridium difficile*

*Clostridium difficile* is a bacterium that is present naturally in the gut of around 3% of adults and 66% of children. It does not cause problems in healthy people but when some antibiotics are used to treat other infections they can interfere with the balance of the 'good' gut bacteria. *C. difficile* can then multiply and cause symptoms such as diarrhoea or fever. Once the bacteria begin to multiply toxins are produced. Spores are produced to enable the bacteria to multiply. The spores are excreted in the diarrhoea of the infected person. They can contaminate their surroundings, such as toilets, bed-clothes, skin and clothing. Spores can also be spread through the air. They are only removed by thorough cleaning. This means that infection control is essential if the spread of the infection to other individuals is to be minimised. *C. difficile* occurs most commonly in patients who are aged more than 65 years, have serious underlying disease or are immunocompromised. Most patients will have mild disease, which will probably respond to discontinuation of the antibiotic alone. A recent paper has challenged the belief that infection with *C. difficile* occurred exclusively after antibiotic exposure.<sup>11</sup> Dial and colleagues investigated community patients who had been admitted to hospital with community acquired *C. difficile*. Interestingly, just more than 50% of patients had not been exposed to antibiotics in the preceding 45 days. This led the authors to suggest that there may be a significant confounding of the association between antibiotics and *C. difficile* infection with hospital admission. Clearly, more work needs to be done to fully understand the pattern of spread of *C. difficile* in the community. However, it is important to send off samples and the latest work would suggest that doing so without an antibiotic antecedent may be useful.

### Conclusion

The appropriate use of antibiotics in the management of infections has become a pressing public health concern given the growing resistance and lack of new drugs in development. GPs face many challenges when assessing treatment options for infections. Patients often come with the expectation that antibiotics are necessary and changing this view is not easy. In this article we have outlined considerations in the decision to prescribe for common infections in primary care. In the next article we will look at how to implement change in prescribing antibiotics. ✚

This article is based on guidelines from the Scottish Intercollegiate Guidelines Network, National Prescribing Centre, National Institute for Clinical Excellence, Clinical knowledge summaries and Health Protection Agency.

### Declarations of interest

The authors have no interests to declare.

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