Introduction

If the use of antibacterials for infections for which they are not needed is not reduced urgently then we will see many deaths from infections of resistant bacteria. This is because resistance to antibacterials is now emerging at a faster rate than replacement antibacterials can be developed. The resistance issue has moved from theoretical warnings about the future to an urgent priority for action now! 1,2,3,4,5,6,7

A Canadian coalition, including eight leading health, medical, patient and pharmacy organisations, has recently endorsed an action plan to reduce community antimicrobial use by 25% over three years.1

The new UK Campaign on Antibiotic Treatment (CAT) recommendations for GPs are ideas that are well established in New Zealand and are worth repeating:

• No prescribing of antibiotics for simple coughs and colds.
• No prescribing of antibiotics for viral sore throats.
• Limit prescribing for uncomplicated cystitis to 3 days in women who are otherwise fit.
• Limit prescribing for antibiotics over the telephone to exceptional cases.2

Below is an analysis of advertisements for antibacterials published in NZ Doctor or NZ GP during 1998. We call attention to the appeals that we believe are being used in those advertisements. We believe some of these appeals are justified and some are not. Please decide for yourself whether or not you should be influenced by them. Advertising appeals are often ambiguous and thus open to different interpretations.

Consequently for each advertisement we have tried to clarify the appeals by writing “possible interpretations” that promote increased use of the drug. Each of our “possible interpretations” is only one of many possibilities for each appeal. We do not claim that our “possible interpretations” are necessarily what was intended by the advertiser. However, in our opinion, they would be reasonable interpretations for readers to make if they were relying on the advertisement because of lack of time to seek other sources of information.

“Possible interpretations” which, in our opinion, are:
• unjustified are indicated with: ✗
• justified are indicated with: ✓
• borderline are indicated with: ?

Advertisement 1: Augmentin (amoxycillin/clavulanate, SKB)

Headlines: “with Augmentin it’s your choice”

Images: Cartoons about doctors

Appeals: Doctors’ desires to be free from restrictions and able to make our own choices. Also uses the attraction of humour.

Possible interpretations:
1. ✗ Augmentin is the best choice for unspecified indications. (Advertisements often are designed to get the reader to “fill in” the details. In this case the reader may interpret the claim as referring to “many common bacterial infections” or “all the indications listed in the data sheet” or “the infections the reader is currently treating with Augmentin,” etc.)

2. ✗ Augmentin has no important adverse effects worth mentioning.

How good is the evidence?
1. SKB has not mentioned any specific indications. SKB has not provided any evidence to support the use of Augmentin
in general practice. In fact, in this advertisement, SKB has not provided any helpful information at all!

Amoxycillin/clavulinate (as with some other antimicrobials) may be effective in the Petri dish but not so good for our patients. Our job is to treat patients, not Petri dishes. For example, Bailey (1996) wrote that for UTIs, “This drug is over-rated and in our hands has proven extremely disappointing when used for pathogens that are listed from the laboratory as being resistant to amoxycillin, but sensitive to Augmentin. The response rate to this drug combination is low, the relapse rate high (as it is with all of the other beta-lactam antibiotics) and the side effect profile unacceptable.”

Amoxycillin/clavulinate is not recommended by the Australian Antibiotic Guidelines as first line initial therapy for the most common infections seen in general practice: bronchitis, otitis media, pharyngitis, sinusitis, or urinary tract infections. However, it is recommended for less common infections. These include mild post-operative pneumonia and for moderate bites and clenched fist injuries following a single dose of procaine penicillin. Amoxycillin/clavulinate is recommended in combination with doxycycline for sexually acquired acute epididymo-orchitis and for mild to moderate non-sexually acquired pelvic inflammatory disease. Amoxycillin/clavulinate is an alternative to metronidazole with cephalexin for mild diverticulitis and mild to moderate diabetic foot infections.

2. The most important adverse effects are diarrhoea, especially in children (more frequently than with most alternatives), and hepatotoxicity, especially in the elderly (which is rare but can be serious although seldom fatal).

**Possible interpretations:**
1. **✗** “Bacterial bronchitis” should be treated with amoxycillin/clavulinate or with cefaclor and the latter is cheaper.
2. **✗** Cefaclor is highly effective (potent) for “bacterial bronchitis”.
3. **✗** Cefaclor has no important adverse effects.
4. **✗** The price of Ceflor is now very low.

**How good is the evidence?**
1. This claim works in the context of the widespread belief that bacteria are an important cause of bronchitis and so bronchitis should be treated with antibacterials. However, according to the Australian Antibiotic Guidelines, “in an immunocompetent adult or child, acute bronchitis is most often viral and does not require antibiotic therapy.” (original emphasis). “Randomised controlled trials show that antibiotic therapy provides no overall benefit to the patient and may cause harm” even when acute bronchitis is caused by bacteria. In chronic bronchitis at least half of patients are persistently colonised with S. pneumoniae, H. influenza or M. catarrhalis. Antibiotics are not useful for chronic bronchitis unless there is an acute exacerbation with “increased cough and dyspnoea together with increased sputum volume and/or purulence.” (original emphasis). The recommended initial therapy for such exacerbations is amoxycillin or doxycycline unless the patient is allergic to those drugs.

The advertisement supports the false assumption that “bacterial bronchitis” should usually be treated with an antibacterial. It also uses the wrong comparator because cefaclor should be compared with amoxycillin and doxycycline rather than amoxycillin/clavulanate.

2. No antibacterial is highly effective for bronchitis. The aim of therapy for exacerbations of chronic bronchitis is not to eradicate the colonising organisms, but merely to reduce the volume and purulence of the sputum.

3. Cefaclor may cause a serum sickness-like syndrome (skin eruptions, lymphadenopathy and arthralgia/arthritis), especially in young children. This effect is very rare, but more common with cefaclor than alternative antibiotics.

4. If sales of Ceflor were not profitable then Lilly would not be willing or able to pay for promotion so Lilly’s complaint about low prices deserves scepticism. Amoxycillin and doxycycline are currently cheaper in New Zealand.
### Advertisement 3: Diclocil ((dicloxacillin, BMS)

**Headlines:** “The new narrow spectrum penicillin for skin and soft tissue infections whatever the body part.”

**Key copy:** “The reported incidence of liver toxicity with Diclocil is less than half that reported with flucloxacillin. So now when you’re faced with infections caused by Staphylococcus aureus, there is only one name you should think of frankly.”

**Images:** Frankenstein with a clean fresh uninflamed laceration of the face.

#### Second opinion

**Appeals:** The desire for simplicity. One size fits all. Also uses fear of failure and complications.

**Possible interpretations:**
1. It is appropriate to use dicloxacillin as prophylaxis for clean fresh wounds. (The headline says infections, but the image adds the concept of prophylaxis and images can be a powerful way to communicate.)
2. Diclocixil is appropriate for all skin and soft tissue infections.
3. Dicloxacillin is dramatically safer than flucloxacillin.
4. Dicloxacillin is appropriate for all infections that might be caused by S. aureus.

**How good is the evidence?**
1. “Antibiotics are not routinely required in all wounds. Careful cleaning and debridement of wounds is important in preventing infection, and immobilisation and elevation are also helpful.”
2. Dicloxacillin is not recommended for bites and clenched fist injuries or diabetic foot infections.
3. BMS’s claim is based on a study which calculated that there were 1.63 reports of liver damage possibly or probably caused by dicloxacillin per million defined daily doses (DDD) vs 2.9 reports per million DDD for flucloxacillin in Sweden. The relative risk reduction used by BMS is the ratio between those two rates. Promotion often uses relative risk reduction (RRR) because it can make differences appear more dramatic than they really are. The RRR of “less than half” sounds more dramatic than the absolute risk reduction suggested by the same numbers: 1.27 cases per million DDD. However, we do not know how many cases of liver damage occurred with either drug, but were not reported. The real absolute risk reduction may be more than 1.27 cases per million DDD, but we do not know how much more. The safety difference between dicloxacillin and flucloxacillin may not be as dramatic or as certain as suggested by the advertisement. However dicloxacillin is probably safer than flucloxacillin.
4. Dicloxacillin is not appropriate for patients who are allergic to penicillins.

### Advertisement 4: Helicosec (omeprazole, amoxycillin, metronidazole, Astra)

**Headlines:** “Introducing Helicosec OAM. All in one pack, and one purpose for all. Happy endings to H. pylori infections.”

**Key copy:** “Losec-based 7 day triple therapies are now recommended as first choice regimens for Helicobacter pylori eradication, because they are “associated with higher efficacy, fewer side effects and better patient compliance” than standard triple therapy. …One convenient pack contains all three products”

**Images:** The three musketeers.

#### Second opinion

**Appeals:** Novelty. (Words like “new” and “introducing” have been used in advertising to increase sales for centuries. As advertising guru, Claude Hopkins, wrote back in 1923: “…curiosity is one of the strongest of human incentives. We employ it whenever we can.”) In this advertisement, Astra also appeals to the desire for convenience and uses fear of failure and complications.

**Possible interpretations:**
1. Losec (omeprazole) based triple therapy as used in Helicosec is recommended in the reference quoted by Astra.
2. Helicosec is the most effective way to treat H. pylori.
3. Helicosec is the simplest, most convenient way to treat H. pylori.
4. Eradication is recommended for all cases of H. pylori infection.

**How good is the evidence?**
1. Astra has used a selective quotation of half a sentence from the expert opinion consensus guidelines produced by the European Helicobacter Pylori Study Group (EHPSG). The recommendation actually referred to “proton pump inhibitors” in general, not “Losec” specifically. However, the EHPSG does claim that there have been more studies of omeprazole-based triple therapy than of lansoprazole or pantoprazole-based therapy. EHPSG recommends using proton pump inhibitors in standard doses twice a day but Helicosec uses omeprazole 40mg mane only. The EHPSG report does not disclose the funding source and provides little information on the procedures used to reach the consensus.
2. Helicosec (omeprazole 40mg mane, amoxicillin 500mg tds, metronidazole 400mg tds) may lead to an 80-85% eradication rate. Omeprazole 20mg bd, clarithromycin 500mg bd and amoxycillin 1g bd may lead to a 90-95% eradication rate. However, eradication rates depend on the prevalence of metronidazole and clarithromycin resistance. A 1996 study in New Zealand found 31% of H. pylori were metronidazole resistant. So far resistance to clarithromycin is much less common, presumably because it is less often used.

3. Twice a day dosing schedules such as the one mentioned above would be more convenient than the three doses a day schedule used in Helicosec. However, Helicosec is more convenient than previous regimens. As yet, cost competitive clarithromycin-based triple therapy packs are not being provided by the pharmaceutical industry for the people of New Zealand.

4. Prevalence rates for H. pylori in different communities in New Zealand vary from 5% to 70%. Only about 20% of H.pylori carriers have a gastric or duodenal ulcer. Eradication of H. pylori is recommended for proven infections with duodenal ulcer, gastric ulcer, MALT lymphoma (very rare) or gastritis with severe atrophy and metaplasia. It is not recommended for non-ulcer dyspepsia nor for carriers with no GI disease.

Advertisment 5: Noroxin (norfloxacin, MSD)

Headlines: “She won’t want to see you again.”
Key copy: “First time relief for her simple UTI.”
Images: A young woman doubled up in very severe pain.

Second opinion

Appeals: Sympathy by dramatising the severity of the illness. (Simple UTIs can be very painful and cause significant restriction of activity for a few days, but in general practice are rarely as severe as depicted in the advertisement. Dramatisation of the severity of the illness is generally used to justify use of more expensive or more dangerous therapy. Norfloxacin may not be more dangerous, but is more expensive.)

Possible interpretations:
1. Norfloxacin is the best therapy for simple UTIs because it is always effective (including always preventing recurrences) and never causes adverse effects so the patient never has to come back to the doctor.

How good is the evidence?
1. MSD cites four references. Only one of these compares norfloxacin with alternative therapy. That study (which was performed by MSD staff) compared norfloxacin with trimethoprim-sulphamethoxazole. This is the wrong comparator because both PreMeC and the Medlab Guide advise against using it for UTIs. The effect of therapy on symptoms (such as pain) was not reported. There was no significant difference in the incidence of early or late “reinfection”. Reinfection was detected after norfloxacin in six of 190 patients. The study report contains contradictory statements about the number of patients in the norfloxacin group who experienced adverse events. Norfloxacin is not recommended for pregnant women or children.

For empiric therapy of low risk UTIs, PreMeC recommends trimethoprim 600mg stat or 300mg daily for 3 days as the therapy of choice. Norfloxacin is the second choice for stat therapy and the third choice after nitrofurantoin 50mg tds for three-day therapy. “Norfloxacin should be reserved for resistant infections because widespread use as a first line agent will encourage the emergence of resistant organisms.”

Conclusions

If the use of antibacterials for infections for which they are not needed is not reduced urgently then we will see many deaths from infections of resistant bacteria. The advertisements analysed in this edition do not help us to advise our patients in accord with the best available recommendations.

End of the trial of Healthy Scepticism

This is the last of three editions of Healthy Scepticism funded by PHARMAC under an agreement to trial the concept. Whether Healthy Scepticism will cease, continue unchanged or continue with changes, will depend on your feedback. This edition is being finalised just prior to a tour of New Zealand by Healthy Scepticism’s primary author, Dr Peter Mansfield, during 22 -26 February 1999 to discuss misleading pharmaceutical promotion and to hear your views. For further information, please contact your local IPA, PreMeC or PHARMAC. If you were unable to meet Peter and wish to comment then please use the reply card.

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