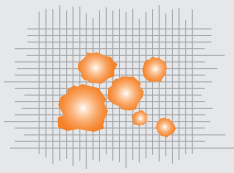

Skin infection? Avoid topical antibiotics

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KEY POINTS

- If a skin infection needs an antibiotic, then an oral antibiotic should be considered rather than a topical antibiotic.
- There is increasing bacterial resistance to fusidic acid and so we are losing the use of a valuable oral antibiotic.
- Bacterial resistance to mupirocin limits our ability to eradicate MRSA for people with recurrent staphylococcal skin infections.
- Most simple skin wounds heal without intervention, and minor skin infections are self-limiting: clean it, cover it, check it.

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Bacterial resistance—it is our problem

Imagine life without antibiotics. It would be similar to life prior to the development of sulfonamides in the 1930s and penicillin in the 1940s—people dying from wounds and 'simple' infections, limited surgical procedures, and an inability to use most chemotherapy for cancer. Yet after only 70 to 80 years, common but deadly bacteria such as *Streptococcal pneumoniae*, *Staphylococcus aureus* and *Escherichia coli* are fighting back, and our armament of antibiotics is severely depleted, with few new antibiotics in the pipeline.

This has raised the issue of antibiotic stewardship, with the appropriate use of antibiotics being the responsibility of all of us. The overuse, through unnecessary use, of antibiotics has resulted in bacterial resistance to antibiotics developing at a faster pace than we can develop new agents.

One area to consider for rationalising antibiotic use is the use of topical antibiotics for skin infections. The incidence rates of skin infections have doubled since 1990 in New Zealand,[1] including a doubling of the hospitalisation rates to around 4.5% of hospitalisations in 2004 to 2008.[2] Promotion of good skin health activities and routine management of the usual self-limiting skin infections and abrasions is important ('clean it, cover it, check it'), as is managing skin infections of those people at risk of more severe consequences and hospitalisation.

Skin infection—think oral antibiotic

Being a world leader in the development of resistance to mupirocin through overuse in the 1990s is not an enviable position,[3] yet New Zealand still has one of the highest uses of topical antibiotics in the world and a rapidly growing bacterial resistance to fusidic acid.[4]

We generally think of topical medicines as being safer than oral medicines and so, perhaps, have a lower threshold for prescribing them, but using fusidic acid topically and generating bacterial resistance means that we lose a valuable oral antibiotic. Overusing mupirocin means that we lose an antibiotic that is effective against MRSA, which we require for people with recurrent *S. aureus* infections that need decolonisation treatment.

Minor cuts and abrasions heal well without intervention, other than: clean it, cover it, check it. Minor skin infections are usually self-limiting and, although there is a lack of evidence for topical antiseptics for treating, as opposed to preventing, infections,[5] the use of these agents (chlorhexidine, hydrogen peroxide cream, povidone iodine) would be preferable to prescribing a 'just in case' topical antibiotic.

When a skin infection such as infected eczema or impetigo requires an antibiotic, then an oral antibiotic should be used. Traditionally, very small, localised areas of infected eczema or impetigo have been considered suitable for a topical antibiotic.[6] However, increasing problems and admissions with skin infections, plus growing bacterial resistance to fusidic acid in New Zealand,[4] suggests reducing our threshold for using oral antibiotics[1] and keeping our topical antibiotics to use when they are really needed, such as for MRSA eradication regimens.[7] This may also reduce the risk of patients using the 'left over' topical antibiotics inappropriately (Note: patients do not need topical antibiotics in their first aid kit).

NUGGETS *of* KNOWLEDGE provides succinct summaries of pharmaceutical evidence about treatment of common conditions presenting in primary care and possible adverse drug reactions.

Table 1. Potential interactions with macrolides

Interacting medicine(s)	Effect	Mechanism	Comment
Statins	Increased statin concentrations	Inhibition of CYP3A4 to increase serum concentration of the statin	Pravastatin is cleared renally and so unlikely to interact
Warfarin[11]	Increased risk of bleeding	Debated—potential CYP3A4 mechanism, plus an effect on gut flora and Vitamin K	Monitor INR every two days; may be a delayed effect
Dabigatran/rivaroxaban[12]	Increased risk of bleeding	Inhibition of p-glycoprotein increases bioavailability of dabigatran/rivaroxaban	Currently an ill-defined, potential interaction but caution recommended
Digoxin[13,14]	Increased digoxin concentrations	Inhibition of p-glycoprotein increases bioavailability of digoxin	
Colchicine[15]	Increased colchicine toxicity	Inhibition of p-glycoprotein increases bioavailability of colchicine	

Which oral antibiotic for skin infections?

Prescribe seven days of flucloxacillin, or a macrolide or cephalexin for those with a hypersensitivity to penicillins (see the March 2013 *Nuggets of Knowledge* column[8]). Depending on local prevalence and sensitivities of methicillin-resistant *S. aureus* (MRSA), if MRSA is causative, use co-trimoxazole, clindamycin or doxycycline.

Do not use amoxicillin/clavulanic acid, unless for a human or animal bite.[6] Using a broad-spectrum antibiotic increases exposure to a wider range of bacteria species, and therefore increases resistance of bacteria that are not causing the infection being treated. Subsequent survival leaves us with resistant bacteria.

Amoxicillin/clavulanic acid also has a high rate of adverse effects, with the number needed to treat to cause diarrhoea being only 10 and the number needed to treat to cause candidiasis being 27 (with or without the clavulanic acid).[9]

Oral antibiotic cautions: reminders

The following content is not a complete list of cautions, but highlights current issues of concern.

Macrolides: interactions

Table 1 summarises important interactions with macrolides. The mechanism of the potential interactions include:

- Inhibition of cytochrome P450 3A4 (CYP3A4) with a potential increase in serum concentrations of medicines metabolised by this enzyme system
- Inhibition of p-glycoprotein, a 'protective' transporter protein. Inhibition of this transporter protein results in increased serum concentrations of some medicines[10]
- An additive effect when used with medicines that may increase QT interval.

While there is debate about the extent of drug-drug interactions with the different macrolides, all should be considered to have the potential to interact and care taken with any combination.

Clindamycin: adverse effects

Clostridium difficile should be considered for any person taking an antibiotic, particularly a broad-spectrum antibiotic,[16] and developing diarrhoea, but clindamycin appears to be particularly problematic.[17]

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Calcium intake and reducing blood pressure

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THE PROBLEM: Hypertension is a known public health problem that affects both the economically developed and developing world. It affects somewhere between 25 and 33% of the adult population.[1] Hypertension is one of the leading factors attributing to global mortality, and is the third highest risk factor for the global burden of disease.[2] The National High Blood Pressure Education Program in the US suggests that population strategies that aim to achieve a downward shift of the blood pressure distribution in the general population is an effective method to relieve some of this disease burden.[3] One potential population-based method could be dietary supplementation.

CLINICAL BOTTOM LINE: This systematic review shows that an increase in calcium intake will slightly reduce both systolic and diastolic blood pressure.[4] The effect was shown in a dose-response relationship, as well as being confirmed in multiple groups. Although the effect was small, it is based on high-quality evidence and, at the very least, the authors suggest that it should be an objective to make sure there is adequate calcium intake in the population. No adverse events were reported, but this would be an essential factor for any future research to monitor.

Calcium supplementation: effect on systolic and diastolic blood pressure[4]

	Success	Evidence	Harms
Systolic blood pressure (SBP)	Calcium significantly lowered SBP with a difference between the placebo group and the calcium supplementation group of -1.43 mm Hg (-2.15 to -0.72) This effect showed a dose-response treatment effect and was largest in those taking >1500 mg/day and in those studies with patients with a mean age of <35 years of age	This was based on high-quality evidence from 16 individual studies containing 3048 participants in total	There were no reported adverse events
Diastolic blood pressure (DBP)	Calcium supplementation also significantly lowered DBP with a difference between the placebo group and the calcium supplementation group of -0.98 mm Hg (-1.46 to -0.50) This effect showed a dose-response treatment effect and was largest in those taking >1500 mg/day, in men, and in those studies with patients with a mean age of <35 years of age.	This was based on high-quality evidence from 15 studies containing 2947 participants in total	

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