Topical antibiotics: very few indications for use
Topical antibiotics in general have been excessively used in New Zealand in recent years. The increasing prevalence of resistance to fusidic acid in Staphylococcus aureus means that treatment will often be ineffective. Topical antibiotics may be considered for patients with localised areas of impetigo. Antibiotic treatment, whether given topically or orally, is rarely indicated for the treatment of patients with furuncles (boils) or carbuncles (multiple headed lesions). Oral antibiotics, but not topical antibiotics are indicated for wound infections, cellulitis or other deeper skin infections. It is important to reconsider the use of topical antibiotics in skin infections and reduce inappropriate prescribing.

The role of topical antibiotics in the treatment of minor skin infections

1. Not all patients with a skin infection require an antibiotic (Table 1)
2. If an antibiotic is required, topical antibiotics are only appropriate for patients with minor, localised areas of impetigo

Most minor skin infections are self-limiting and resolve without the use of an antibiotic (with standard skin hygiene advice). The decision to treat will be determined by several factors, including the extent and severity of infection, the patient's co-morbidities and socioeconomic status (e.g. living environment).

Despite increasing bacterial resistance to fusidic acid, it remains a valid treatment option for patients with localised areas of impetigo caused by Staphylococcus aureus, Streptococcus pyogenes or other related streptococci. Oral antibiotics are appropriate for patients with more extensive areas of infection or systemic symptoms. Fusidic acid may also be considered for treating patients with small, localised areas of infected eczema, however, oral antibiotics are more likely to be required as infected eczema is often extensive.

Topical mupirocin should be reserved for treating patients with localised mild skin infections (impetigo or infected eczema), that are resistant to fusidic acid and have sensitivity to mupirocin.

Antibiotic management of impetigo

Topical treatment with fusidic acid may be considered for a patient with no more than three areas of impetigo or an area of infection of less than 5 cm². Response to treatment should be regularly assessed, and a switch to oral antibiotics considered if the infection is not resolving or is worsening. A swab for culture and sensitivity will help to guide treatment in this case.

Table 1: General guidance for use of antibiotics for skin infections most commonly seen in general practice

<table>
<thead>
<tr>
<th>Antibiotics (topical or oral) rarely required</th>
<th>Topical antibiotics may be considered</th>
<th>Oral antibiotics (not topical) usually indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furuncles (boils)</td>
<td>Impetigo (small, localised patches)</td>
<td>Infected wounds, including bites</td>
</tr>
<tr>
<td>Carbuncles (multiple headed lesions)</td>
<td>Occasionally considered for infected eczema (small, localised patches, not improving with standard care)</td>
<td>Cellulitis</td>
</tr>
<tr>
<td>N.B. In most cases these can be treated with incision and drainage</td>
<td></td>
<td>Widespread impetigo or infected eczema</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mastitis</td>
</tr>
</tbody>
</table>
The history of fusidic acid use in New Zealand

Fusidic acid is a relatively narrow-spectrum antibiotic, active against Gram-positive bacteria, such as *Staphylococcus* and *Streptococcus spp*. It is most commonly used in topical form. Fusidic acid belongs to the fusidane class (a fungal derivative), with a chemical structure similar to corticosteroids, although it does not have anti-inflammatory properties.8

Fusidic acid has been available for many years in New Zealand, however, use has increased significantly over the past decade. This occurred after restrictions were placed on another topical antibiotic, mupirocin, which has similar activity to fusidic acid. Mupirocin was available as an “over-the-counter” medicine from 1991, however, its status reverted to a prescription only medicine in 2000. This was due to concerns over increasing bacterial resistance, particularly in methicillin-resistant *Staphylococcus aureus* (MRSA). This resulted in a significant reduction in dispensing of mupirocin, but at the same time, dispensing of fusidic acid increased as topical antibiotics continued to be widely prescribed.9

The total number of community-dispensed prescriptions of topical fusidic increased from approximately 146 000 in 2008 to approximately 220 000 in 2013 (Figure 1).10 The incidence of *S. aureus* skin infections in New Zealand has increased by approximately 5% each year over the last decade,11 which may account for some of the additional use of topical antibiotics.

This change in prescribing also had an effect on bacterial resistance to both fusidic acid and mupirocin. The prevalence of resistance in *S. aureus* to mupirocin, which was 28% in 1999 (based on a national survey of isolates from community and hospital laboratories),12 had fallen to 11% in 2013 (based on a survey of isolates from an Auckland community laboratory).9 In contrast, the increased level of prescribing of fusidic acid over recent years resulted in a rapid rise in the prevalence of resistance, from 17% in 1999,12 to 29% in 2013.9

Latest antibiotic resistance surveillance data from ESR (from both community and hospital laboratories) show that in 2012, 15% of all sampled *S. aureus* isolates were resistant to fusidic acid, compared to 8% resistant to mupirocin.13 Of those isolates which were methicillin-resistant (i.e. MRSA), 37% were resistant to fusidic acid and 10% resistant to mupirocin.13

It appears that the increased and widespread use of fusidic acid has rapidly resulted in it becoming a much less effective antibiotic treatment for the skin infections it is indicated for, i.e. localised areas of impetigo.
Advise the patient/carer to remove crusted areas on lesions, with warm water and a soft, clean cloth. Apply fusidic acid 2% ointment or cream to lesions three times daily, for seven days. Oral antibiotics are more appropriate than topical treatment for patients with widespread lesions or if systemic symptoms are present. The recommended oral antibiotic treatment is fusidic acid:

- **Child** – 12.5 mg/kg/dose, four times daily, for five to seven days
- **Adult** – 500 mg, four times daily, for five to seven days

If compliance is an issue, an alternative regimen is fusidic acid 10 – 25 mg/kg/dose, three times daily (maximum 500 mg per dose) for five to seven days. To optimise absorption, oral fusidic acid is ideally taken on an empty stomach.

Cephalexin has been recommended as an option for children who find fusidic acid syrup unpalatable, however, consideration should be given to the disadvantages of using an unnecessarily broad spectrum antibiotic and the effect on the spread of antimicrobial resistance (see: "Antibiotic resistance in New Zealand, Page 24"). Erythromycin is an alternative for patients with penicillin allergy. If MRSA is found to be present, the recommended treatment is oral co-trimoxazole (see: New Zealand Formulary or the bpac® antibiotic guide for recommended doses of these medicines).

In children with impetigo, the affected area should be kept covered and the child excluded from day-care or school until 24 hours after antibiotic treatment has been initiated.

Information and resources for families about impetigo are available from: www.kidshealth.org.nz/impetigo-school-sores

**Antibiotic management of infected eczema**

A topical antibiotic may be considered for patients with a small area of infected eczema (a single patch < 5 cm²), that is not resolving with usual eczema management (including antiseptic baths). Advise the patient/carer to apply fusidic acid 2% ointment or cream to the infected area three times daily, for seven days. A combination fusidic acid/corticosteroid product is also an option (see opposite).

Oral antibiotics are appropriate when the infection is more widespread (i.e. > 5 cm²), if there is more than one area of infection or if systemic symptoms occur. The same oral antibiotic regimen as recommended for impetigo can be used.

Where possible, topical emollients and medicines should be provided in a tube or pump dispenser to reduce the risk of contamination. Emollients in a tub should be scooped out for application to skin using a spoon or ice-cream stick. After an infection patients/careers should be advised to discard and renew topical medicines in tubs, as they may have become contaminated.

Recurrently infected eczema is usually due to under-treatment of the eczema. Factors such as adherence should be addressed, and a referral made to dermatology if eczema persists despite primary care intervention.

**Combination topical antibiotic + corticosteroid**

Several topical combination antimicrobial/corticosteroid products are available in New Zealand. Fusidic acid is combined with betamethasone in Fucicort (partly subsidised). Pimafucort contains hydrocortisone, natamycin and neomycin (fully subsidised).

These products are best reserved for treating small areas of localised infection in patients with an underlying inflammatory skin condition that will respond to a corticosteroid. For example, Fucicort may be considered for a patient with a small area of eczema (in which a corticosteroid is part of the treatment regimen) with a secondary bacterial infection (for which fusidic acid may be appropriate). Pimafucort may, for example, be considered for the treatment of a patient with superficial skin lesions that will respond to corticosteroids, complicated by a secondary candidal infection.

It is recommended that these combination products are used regularly, for a short time period, e.g. twice daily, for seven days.

Fucicort and Pimafucort are not appropriate for the treatment of acne vulgaris. **Topical antibiotics** (e.g. clindamycin, erythromycin) are no longer funded for the treatment of acne but may be used for patients with mild inflammatory acne which does not respond to topical retinoids or where topical retinoids are not tolerated.
The emergence of MRSA

Penicillin was first used to treat *S. aureus* infections, but now approximately 90% of isolates in New Zealand are resistant. Methicillin (a semi-synthetic penicillin) and other closely related antibiotics, such as flucloxacinil, dicloxacinil and cloxacinil, were then used to treat *S. aureus* infections, but this led to the “super bug” methicillin-resistant *S. aureus* (MRSA) which became endemic in many hospitals in New Zealand in the 1990s. Measures were implemented to control MRSA, and levels in New Zealand hospitals are now lower than in many other countries, such as the United States. In 2013, the national rate of MRSA in New Zealand was 23.9 cases per 100 000 people, however, there are significant geographical variations in incidence. The DHB regions with the highest MRSA incidence rates per 100 000 people in 2013 were Northland (60.5), Counties Manukau (54.9) and Tairawhit (53.5).

Preventing recurrent skin infections

*S. aureus* skin infections in New Zealand have increased significantly over the past decade. More people are being hospitalised with skin infections, and there is an increase in the number of infections being reported in the community. The incidence rate of patients hospitalised with *S. aureus* skin infections in the Auckland DHB region increased from 81 cases per 100 000 people in 2000 to 140 cases per 100 000 people in 2011, which represents an increase of approximately 5% per year. Māori and Pacific peoples, adults aged over 75 years, children aged under five years and people living in more deprived areas have been found to have a higher incidence of hospitalisation for *S. aureus* infection. Factors contributing to the high rates of *S. aureus* infections in New Zealand are thought to include delayed access to health care, increasing overcrowding in households and declining socioeconomic circumstances in some population groups.

With the high rates of *S. aureus* skin infections in New Zealand and the increasing emergence of resistant strains, it is important that measures are put in place to reduce the risk of recurrent infections, especially among households. This primarily involves educating patients and their families about infection control measures and the principles of good hygiene. A formal decolonisation regimen, using topical antibiotic and antiseptic techniques, is not necessary for all patients, but may be appropriate for those with recurrent staphylococcal abscesses.

General messages for preventing skin infections

General lifestyle and hygiene measures can be discussed with families to reduce the likelihood of skin infections.

These include:

- Use an emollient to treat dry skin
- Ensure that skin conditions such as dermatitis or eczema are optimally managed
- If skin is dry or damaged, avoid soaps which can irritate the skin, and prolonged exposure to hot water
- Where possible, store and use skin products from pump or pour bottles, rather than jars
- Keep fingernails and toenails trimmed and clean
- Do not share personal hygiene items such as hairbrushes, razors, facecloths and towels, and regularly clean these items
- Wash and dry hands after using the toilet and before eating
- Wash clothes, towels and sheets regularly; if a family member has a skin infection, ideally use hot water and dry items in a hot clothes dryer (although acknowledging that this is often not affordable for families). A hot iron can be used after clothes are dry.
- Regularly wash toys using a mild disinfectant – hard toys can be washed in a dishwasher, soak soft toys prior to washing; there is no evidence that freezing soft toys reduces bacterial contamination.
- If a skin injury occurs, clean and cover it to help prevent infection and regularly change the dressing.
- Avoid scratching skin lesions.
- Avoid sharing bath/cleaning water when a member of the family has a skin infection.
- Avoid swimming in unclean/untreated water if an open wound is present.


**Decolonisation of S. aureus in patients with recurrent abscesses**

Patients presenting in primary care with recurrent staphylococcal abscesses (furuncles or carbuncles) are likely to be carrying a high bacterial load of *S. aureus* (some with MRSA), which is causing multiple re-infections when skin becomes damaged, e.g. through scratching or injury. The most common site of staphylococcal colonisation is inside the nostrils. Other frequently colonised sites include the groin, perineum, axillae and pharynx. There is conflicting evidence as to whether undergoing staphylococcal decolonisation results in fewer skin infections (see: “Evidence of effectiveness of decolonisation measures”, over page). However, if a patient with recurrent staphylococcal abscesses (or their parents/carers) is likely to be compliant with a decolonisation regimen, it is reasonable to try this. Treatment to eliminate *S. aureus* colonisation in the most affected member of the household is usually all that is required to prevent recurrences in all household members.

Decolonisation should only begin after acute infection has been treated and has resolved.

The first step is to take a nasal swab to determine whether the patient has *S. aureus* nasal colonisation and if so, whether the *S. aureus* colonising the patient is sensitive to fusidic acid or mupirocin:

- If *S. aureus* is present and the isolate is sensitive to fusidic acid the patient should be treated with fusidic acid 2% cream or ointment, applied inside each nostril (with a cotton bud or finger), twice daily, for five days.
- If *S. aureus* is present and the isolate is resistant to fusidic acid, but sensitive to mupirocin, the same treatment regimen should be undertaken, but with mupirocin 2% ointment.
- If *S. aureus* is not present or if the isolate is resistant to both fusidic acid and mupirocin, topical treatment is not indicated. Systemic antibiotics may be required in some patients with particularly resistant strains of *S. aureus*; discuss this with an infectious diseases specialist.

**Bleach baths or antiseptic washes should also be used**

To help reduce the bacterial load, patients undergoing *S. aureus* decolonisation should also be advised to shower or bathe for one week using an antiseptic.

For a bleach bath, add 1 mL of plain unscented 5% bleach per 1 L of bathwater (or 2 mL of 2.2% bleach per 1 L of water). Products that contain added detergent (e.g. Janola) are not recommended. N.B. A regular-sized bath filled to a depth of 10 cm contains approximately 80 L of water and a baby's bath holds approximately 15 L of water.

After immersing in the bath water for 10 – 15 minutes, rinse with fresh water. The bleach bath should be repeated two to three times within the week.


Alternatively, patients may shower daily for one week, using triclosan 1% or chlorhexidine 4% wash. The wash can be applied with a clean cloth, particularly focusing on the axillae, groin and perineum. Although difficult in a showering situation, the antiseptic should ideally be left on the skin for at least five minutes before being rinsed off. Hair can be washed with the antiseptic also.

Bleach baths or antiseptic washing can be carried out intermittently after the initial decolonisation period, to help prevent recurrence of infection. This can also be recommended for patients with recurrent skin infections who have not undergone formal decolonisation.
**Mouth gargle**
As *S. aureus* can also colonise the pharynx, an antiseptic throat gargle (e.g. chlorhexidine 0.2% solution, three times daily) is also recommended for the duration of formal decolonisation treatment.17

**Linen and clothing can also be decolonised**
To support the decolonisation regimen, potentially contaminated clothing, towels, facecloths, sheets and other linen in the household should be washed then dried on a hot cycle in a clothes dryer, or dried then ironed. Clothing and linen that is white or colourfast can be washed with diluted household bleach. Washing is recommended twice within the one week decolonisation period.17

**Evidence of effectiveness of decolonisation measures**
There is mixed evidence of the effectiveness of formal decolonisation regimens in reducing recurrent infections in patients with persistent carriage of *S. aureus*. A 2003 Cochrane review of six randomised controlled trials did not find evidence to support decolonisation of patients with MRSA, with either topical or systemic methods.20 However, further trials have subsequently been published, some with more positive results.

A recent United States-based study randomised patients with *S. aureus* colonisation to receive hygiene education only, education + 2% mupirocin ointment applied inside the nostrils, twice daily for five days; education + mupirocin + chlorhexidine 4% body wash daily; or education + mupirocin + bleach bath daily.21 After one month, the rate of *S. aureus* nasal colonisation in patients who received mupirocin (27%), mupirocin + chlorhexidine (26%) and mupirocin + bleach (17%) was approximately half that in patients who received education alone (46%).21 However, after four months, only the group who received mupirocin + bleach had significantly lower rates of *S. aureus* nasal colonisation (15%) compared to those who received education alone (50%). The group who received mupirocin + chlorhexidine had a significantly lower rate of recurrent skin infections after one month (11%) compared to the group who received education alone (26%). However, there was no effect on the rate of skin infections at either four or six months after the intervention.21

The eradication of *S. aureus* was thought to be more successful in the group who used mupirocin + bleach compared to other groups, because soaking in the bleach bath allowed fuller body exposure to the antiseptic and a longer period of contact, therefore increasing the antimicrobial effect of the intervention.21

As the effect of the initial interventions was not sustained over time it may suggest that decolonisation regimens should be repeated regularly to successfully eradicate *S. aureus*. However, there is currently no evidence to support the efficacy of this approach.

N.B. Mupirocin was used in this study, but is only recommended in New Zealand if colonisation with *S. aureus* that is resistant to fusidic acid and sensitive to mupirocin has been confirmed.

Ideally, the household should also replace toothbrushes, razors, roll-on deodorants and skin products. Hair brushes, combs, nail files, nail clippers can be washed in hot water or a dishwasher.17

Surfaces that are touched frequently, such as door handles, toilet seats and taps, should be wiped daily, using a disinfectant, e.g. alcohol wipes, bleach.17

Soft furnishings that cannot easily be cleaned, e.g. couches and arm chairs, can be covered in a sheet or blanket that is regularly washed.
The role of topical antiseptics in treating skin infections

Antiseptics slow or stop the growth of micro-organisms on external surfaces of the body, i.e. the skin and mucus membranes, and help to prevent infections. Antiseptics have broad-spectrum bactericidal activity and can also act against fungi, viruses and protozoa. There has been recent interest in the use of antiseptics for treating skin infections, to help to reduce the use of topical antibiotics. Antiseptics contribute to bacterial resistance to some degree, but not to the extent that antibiotics do. This is because antiseptics generally eliminate or inhibit all bacteria, whereas antibiotics act only on susceptible bacteria.

There is currently a lack of evidence to support the use of topical antiseptics in the treatment of minor skin infections. However, they do have a role in preventing infection in wounds. Like topical antibiotics, antiseptics only work on external surfaces of the body and do not have any effect on systemic infections.

In general, antiseptics may be used for:

- Cleaning cuts, abrasions and other minor injuries to help prevent infection from occurring
- Hand washing to prevent cross-contamination
- Prior to surgical procedures to reduce resident skin flora
- In the prevention of recurrent skin infections to reduce bacterial load on the skin

N.B. Antiseptic solutions can cause irritation or contact dermatitis in some people, and some products may stain the skin.

Most antiseptics reduce bacterial load: the clinical significance of this is uncertain

Much of the evidence about antiseptics is in regards to their use in dressings for preventing infection in open wounds rather than as a treatment for minor skin infection. Many antiseptics do reduce bacterial load in a wound, but the clinical significance of this is uncertain. Bacterial load is also not the only predictor of infection – other predictors include the presence of foreign bodies in the wound, the patient’s comorbidities and the virulence of the bacteria present. There is evidence that some antiseptics can be toxic to human cells important in the healing process, e.g. fibroblasts, keratinocytes and leukocytes, however, this is usually only when antiseptics are used at high concentrations.

Povidone iodine is one of the more frequently used antiseptics. It has been shown to reduce the bacterial load in wounds and not to impede healing, however, there is no evidence that it increases the rate of wound healing.

Hydrogen peroxide does not negatively affect wound healing, but it is thought to be ineffective at reducing bacterial count. It may be useful as a chemical debriding agent.

Chlorhexidine does not adversely affect wound healing, and is likely to be useful as a rinse, but it is uncertain how effective it is in preventing infection in open wounds.

Antiseptics are not usually associated with bacterial resistance

Although there have been isolated reports of bacterial resistance to povidone iodine, the consensus is that iodine-resistant strains of micro-organisms have not yet emerged, after over 150 years of use of iodine-containing antiseptics. There have been no reports of bacterial resistance to hydrogen peroxide. Some bacterial resistance has been reported to quaternary ammonium antiseptics (Pseudomonas aeruginosa), chlorhexidine (staphylococci) and triclosan (P. aeruginosa).

Refer to the New Zealand formulary for available antiseptics and subsidy details

Take home messages

- Antibiotics are not required for all skin infections; only use them when they are clinically indicated
- Use topical antibiotics for small areas of localised impetigo and oral antibiotics for more extensive infections
- If a topical antibiotic is the most appropriate treatment option, use fusidic acid as first-line treatment, but be alert to the relatively high prevalence of resistance in S. aureus. Reserve the use of mupirocin for the treatment of infections that are resistant to fusidic acid and susceptible to mupirocin.
- In patients with recurrent skin abscesses, investigate for carriage of S. aureus and decolonise if present
- Prevention is better than cure, so educate patients about the importance of good hygiene and keeping their skin healthy
Antibiotic use and resistance rates in New Zealand

New Zealand has one of the highest levels of antibiotic use in the world. Microbial resistance is directly related to the amount of an antimicrobial medicine that an organism is exposed to. Therefore the high rate of consumption of antibiotics in New Zealand means that we also have increasing rates of antibiotic resistance.

Antibiotic use is standardised in studies by reporting results as defined daily doses (DDD). The DDD is the amount of medicine that is internationally agreed as the standard daily dose when treating an otherwise healthy adult, e.g. the DDD of oral amoxicillin is 1 g.

In a recent New Zealand study it was calculated that the annual per capita consumption of antibiotics in New Zealand in 2012 was approximately 25 DDDs/1000 people/day (i.e. an average over the year of 25 daily treatment doses of an antibiotic, per 1000 people in New Zealand, per day). Compared to European countries, the volume of antibiotic consumption in New Zealand was higher than in the United Kingdom, Spain, the Netherlands, Scandinavia, the Czech Republic, Austria and Germany, and only lower than in Greece, Belgium, France and Italy.

Use of broad-spectrum antibiotics is a contributing factor to antibiotic resistance and narrow-spectrum antibiotics should be used where possible. In 2012, narrow-spectrum penicillins represented only 21% of the total number of DDDs of various penicillins consumed by patients in the community in New Zealand.

There are still relatively effective treatments for most antibiotic-resistant bacteria seen in New Zealand, although these treatments are not necessarily cost effective, and can be associated with significant adverse effects. However, some strains of treatment-resistant Escherichia coli and Klebsiella pneumoniae are now beginning to be seen in New Zealand.

If these resistant strains become prevalent, this will have serious consequences for the provision of surgical treatments, such as implantation of prostheses or organ transplant, where the risk of fatal infection and increased morbidity from failed procedures would be high.

So what can we do?

The use of all antibiotics, including topical antibiotics, is contributing to the increasing rates of antimicrobial resistance in New Zealand and the rest of the world. Some things that health care professionals can do to help preserve usefulness of antibiotics include:

- Do not prescribe an antibiotic when it is not required, e.g. for a viral upper respiratory tract infection, sinusitis, self-limiting cases of otitis media and conjunctivitis (which is often viral), boils (unless co-morbidities) and most diarrhoeal illnesses
- Use an antibiotic appropriate for the infection, and where possible avoid broad spectrum antibiotics, e.g. prescribe flucloxacinil for a S. aureus infection instead of cephalaxin or amoxicillin clavulanate
- Prescribe antibiotic treatment for the recommended duration and advise patients to complete the full course; avoid prolonged or repeated courses without a strong clinical justification
- Prioritise consideration of antibiotic resistance, over palatability and convenience for the patient, when deciding which antibiotic to prescribe

Patient education is also important in reducing the inappropriate use of antibiotics. This includes:

- Inform the patient about the problems associated with the increasing rates of antimicrobial resistance
- Ensure the patient understands what the antibiotic is being prescribed for, what dose to take and how often
- Educate the patient about the importance of completing the full course of antibiotic treatment
- Encourage the patient to appropriately dispose of any antibiotic that may be left over after completion (e.g. unused topical antibiotic) or cessation of treatment (e.g. antibiotic changed due to susceptibility), and not to use it for a subsequent infection
- Ensure the patient is aware that the antibiotic being prescribed is for them only and should not be used by family members or friends
- Educate the patient that the antibiotic should only be used for the condition it was prescribed for and should not be used for other conditions, e.g. topical antibiotics should not be applied to minor cuts and abrasions
References


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