

References

1. Arroll B, Goodyear-Smith F, Thomas DR, et al. Delayed antibiotic prescriptions: what are the experiences and attitudes of physicians and patients? *J Fam Pract* 2002;51:954–9.
 2. Spurling GKP, Del Mar CB, Dooley L, et al. Delayed antibiotics for respiratory infections. *Cochrane Database Syst Rev* 2013;4:CD004417.
 3. Little P, Moore M, Kelly J, et al. Delayed antibiotic prescribing strategies for respiratory tract infections in primary care: pragmatic, factorial, randomised controlled trial. *BMJ* 2014;348:g1606.
 4. Arroll B, Kenealy T, Kerse N. Do delayed prescriptions reduce the use of antibiotics for the common cold? A single-blind controlled trial. *J Fam Pract* 2002;51(4):324–8.
 5. Little P, Rumsby K, Kelly J, et al. Information leaflet and antibiotic prescribing strategies for acute lower respiratory tract infection. A randomised controlled trial. *JAMA* 2005;293:3029–35.
 6. Little P, Stuart B, Hobbs FDR, et al. Antibiotic prescription strategies for acute sore throat: a prospective observational cohort study. *Lancet Infect Dis* 2014;14:213–9.
 7. Coenen S, Francis N, Kelly M, et al. Are patient views about antibiotics related to clinician perceptions, management and outcome? A multi-country study in outpatients with acute cough. *PLoS ONE* 2013;8:e76691.
 8. Welschen I, Kuyvenhoven M, Hoes A, et al. Antibiotics for acute respiratory tract symptoms: patients' expectations, GPs' management and patient satisfaction. *Fam Pract* 2004;21:234–7.
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Should I prescribe a topical antiseptic cream instead of a topical antibiotic for minor skin infections?

Increasing rates of resistance to topical antibiotics continues to change the use of these medicines in primary care. Topical antiseptics have been suggested as an alternative, but at present, there is little evidence to support their effectiveness in the treatment of minor skin infections.

Topical antibiotics are associated with high rates of antibiotic resistance

In October, 2014 we published an article outlining appropriate use of topical antibiotics in response to concerns over increasing rates of bacterial resistance, in particular to fusidic acid (See: "Topical antibiotics: very few indications for use", BPJ 64). In early 2015 we updated our advice on the management of eczema in children (See: "Treating childhood eczema: a topical solution for a topical problem", BPJ 67). It has become increasingly apparent in the intervening months that recommendations regarding the role of topical antibiotics, such as fusidic acid, in superficial skin infections have narrowed

further. Expert opinion now suggests that topical fusidic acid should no longer be considered for use in the treatment of children with infected eczema. The preference is for oral antibiotic treatment, chosen based on local resistance patterns, and with appropriate coverage for *Staphylococcus aureus* and *Streptococcus pyogenes* (Group A β haemolytic streptococcus). Fusidic acid may remain an effective treatment option for children with three or less localised areas of impetigo,¹ however, in many cases, as with infected eczema, an oral antibiotic is likely to be more appropriate. Topical mupirocin should only be considered instead of fusidic acid if the infection is known to be resistant to fusidic acid and sensitive to mupirocin. Topical antibiotics (chosen according to culture results) do continue to have a role in the management of patients with recurrent skin infections who require *S. aureus* nasal decolonisation. The role of combination antimicrobial/corticosteroid products, such as hydrocortisone, natamycin and neomycin cream and ointment (Pimafucort) and betamethasone and fusidic acid cream (Fucicort), is unclear due to a lack of quality research and concerns about increasing resistance rates. Currently it is suggested that they are only used short term for the treatment of small areas of localised skin infection (including fungal infection) in patients with underlying inflammatory skin conditions.²

 In the majority of healthy patients, minor skin infections do not require antibiotic treatment at all. Other skin infections, such as furuncles and carbuncles, are usually more appropriately managed by incision and drainage.

Are topical antiseptics an acceptable alternative?

Topical antiseptic agents have been used for centuries in the management of wounds but their role and their effectiveness

has been debated in the literature.^{3,4} Most antiseptic agents are intended for use on intact skin, e.g. for hand hygiene or for skin preparation prior to a surgical procedure. Their use in these situations is widely accepted.³ The role of antiseptic agents for the prevention of infection and as antimicrobial agents in established infections remains more controversial.^{3,5}

The use of topical antiseptics to treat patients with minor skin infections has been proposed as a potential solution to the problem of increasing resistance to topical antibiotics.^{3,4} However, because of a lack of randomised controlled trial data, most reviews and meta-analyses conclude only that further research is required.^{3,4,6} In addition, much of the evidence surrounding the use of topical antiseptics relates to the prevention of infection in wound management rather than as treatment for established skin infections.⁷

Antiseptic agents have a broad-spectrum of antimicrobial activity and exert their effects on cellular metabolism through a variety of mechanisms, which means that they are associated with lower levels of resistance.^{3,8} Antibiotics in contrast exert a selective pressure, acting on susceptible bacteria but resulting in the survival of other strains of bacteria and leading to an increased risk of resistance developing.

Antiseptic agents act to reduce bacterial load, but the clinical significance of this in the management of wounds and the treatment of skin infections is not always clear.⁵ Most open skin wounds and other lesions eventually become colonised with bacteria but this does not always result in infection or impaired healing.^{5,9} Wound healing can be affected by a number of factors including the bacterial species, bacterial load and the patient's co-morbidities and immune status.⁹ Current evidence suggests that topical antiseptic agents may have a role in wound management where there is significant bacterial colonisation that can affect healing.^{5,10} In this situation, topical antiseptics may help to reduce the bio-burden and allow effective natural healing to occur.⁹

Do topical antiseptics have any adverse effects?

Topical antiseptics can cause both irritant and allergic reactions, e.g. an allergic contact dermatitis with iodine and rarely anaphylaxis with chlorhexidine.¹¹ The risks of a reaction are likely to be increased if the antiseptic agent is used in too high a concentration or in a person with eczematous skin.¹² However, when used appropriately they are regarded as having a lower allergenic potential than antibiotics. There is evidence that some antiseptic agents can be toxic towards human cells that have an important role in the healing process, e.g. fibroblasts, keratinocytes and leukocytes, however, the majority of these

"Antiseptic" terminology

A **disinfectant** is a substance used to kill or inhibit microorganisms on inanimate surfaces, e.g. benches and dressing trolleys. The concentration of the antiseptic agent is usually higher than in those products used on the skin.^{9,11}

An **antiseptic** is a substance used to kill or inhibit microorganisms on intact skin, e.g. iodine, or within a wound, e.g. hydrogen peroxide. Topical antiseptics, however, may also be referred to as **skin disinfectants**, particularly in the United States.^{9,11}

studies have relied on *in-vitro* models and the concentrations of antiseptics used were much higher than those that are in antiseptic agents intended for use on the skin.^{3,9}

What products are available?

A number of antiseptic products are available in New Zealand for a variety of uses, depending largely on their concentration and properties (see "Antiseptic terminology").¹¹ Chlorhexidine and povidone-iodine are the most commonly used topical antiseptic agents for intact skin, e.g. for hand hygiene, surgical scrub or skin preparation prior to invasive surgical procedures. Hydrogen peroxide has a variety of uses depending on the concentration of the product (see: "Hydrogen peroxide antiseptic cream").¹¹ At low concentrations (1–5%) it can be used as an antiseptic, most often in wounds rather than on intact skin, and as a topical treatment for acne.¹³

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

So, should a topical antiseptic cream be used for minor skin infections?

It is important to note that most healthy patients with minor skin infections do not require treatment with either a topical antiseptic or a topical antibiotic. The use of topical antiseptic agents over topical antibiotics could help reduce antibiotic use if evidence emerges to suggest there are comparable outcomes. However, at present there is a shortage of quality evidence demonstrating any clear benefit for their use in minor skin infections. With the growing concern over rates of antibiotic resistance, it is hoped that future studies will clarify the role of topical antiseptic agents, but at present, their place in the treatment of minor skin infection remains uncertain.

Hydrogen peroxide antiseptic cream

Products containing hydrogen peroxide 1% are commonly marketed to both clinicians and the public in New Zealand. Currently, two brands of topical hydrogen peroxide 1% cream are available; one is fully subsidised (Crystaderm) and the other is available over-the-counter (Crystacide).² Manufacturer's information states that these products are indicated for acne and for the treatment and prevention of superficial skin infections in wounds, impetigo, insect bites, minor burns and body piercings.^{14, 15, 16}

Topical hydrogen peroxide has been compared to fusidic acid for the treatment of impetigo in a single randomised controlled trial, published in 1994.¹⁷ In this study, 256 participants with non-bullous impetigo were randomised to be treated with either topical fusidic acid or hydrogen peroxide. After three weeks of treatment, it was found that fusidic acid resulted in a cure rate of 82% and topical hydrogen peroxide produced a cure rate of 72%.¹⁷ The difference between the products was not statistically significant and therefore this study has been used to promote the effectiveness of the topical antiseptic agent.¹⁵ However, the trial was judged by a 2012 Cochrane review to have inadequate blinding.⁶ The conclusion of the Cochrane review was that there was insufficient evidence to recommend the use of topical antiseptics in the treatment of impetigo and this has been reiterated in more recent review articles.^{6, 18} It should be noted that although topical antibiotics continue to be recommended in much of the current literature for patients with limited areas of impetigo^{6, 18}, as discussed above, recent expert opinion in New Zealand now suggests this is not best practice.

Hydrogen peroxide cream 1% has been compared to topical benzoyl peroxide gel in an industry-sponsored study for use in people with mild to moderate acne and was shown to provide similar effectiveness with a lower rate of skin erythema.¹⁹ A topical hydrogen peroxide 1% cream was funded on the National Pharmaceutical Schedule in 2006 to provide an alternative topical agent to be used in the treatment of acne.

References

1. Starship Children's Health. Cellulitis/Skin infections. Available from: www.starship.org.nz (Accessed Jun, 2015).
2. New Zealand Formulary (NZF). NZF v34. 2015. Available from: www.nzf.org.nz (Accessed Jun, 2015).
3. Drosou A. Antiseptics on wounds: an area of controversy. *Medscape Wounds* 2003;15. Available from: www.medscape.com/viewarticle/456300_1 (Accessed Jun, 2015).
4. Leaper D. Topical antiseptics in wound care: time for reflection. *Int Wound J* 2011;8(6):547–9.
5. Gottrup F, Apelqvist J, Bjansholz T, et al. EWMA Document: Antimicrobials and non-healing wounds-evidence, controversies and suggestions. *J Wound Care* 2013;22:S1–92.
6. Koning S, van der Sande R, Verhagen A, et al. Interventions for impetigo. *Cochrane Database Syst Rev* 2012;1:CD003261.
7. Cooke J. When antibiotics can be avoided in skin inflammation and bacterial colonization: a review of topical treatments. *Curr Opin Infect Dis* 2014;27:125–9.
8. Leaper DJ, Schultz G, Carville K, et al. Extending the TIME concept: what have we learned in the past 10 years? *Int Wound J* 2012;9 Suppl 2:1–19.
9. Wounds UK. Best Practice Statement: The use of topical antimicrobial agents in wound management (3rd Edition). 2013. Available from: www.wounds-uk.com/pdf/content_9969.pdf (Accessed Jun, 2015).
10. Kahn MN, Naqvi AH. Antiseptics, iodine, povidone iodine and traumatic wound closing. *J Tissue Viability*;16(4):6–10.
11. DermNet NZ. Antiseptics. DermNet NZ, 2015. Available from: <http://dermnetnz.org/treatments/antiseptics.html> (Accessed Jun, 2015).
12. Lachapelle J-M. A comparison of the irritant and allergenic properties of antiseptics. *Eur J Dermatol*;24:3–9.
13. DermNet NZ. Hydrogen peroxide. DermNet NZ, 2015. Available from: <http://dermnetnz.org/treatments/hydrogen-peroxide.html> (Accessed Jun, 2015).
14. AFT Pharmaceuticals Ltd. Crystaderm. Available from: www.aftpharm.com/nz-products/crustaderm (Accessed Jun, 2015).
15. AFT Pharmaceuticals Ltd. A new parallel in fighting skin infection. 2006. Available from: www.aftpharm.com/nz/brochures/Crustacide%20brochure.pdf (Accessed Jun, 2015).
16. AFT Pharmaceuticals Ltd. Crystacide. 2009. Available from: www.medsafe.govt.nz/consumers/cmi/c/crustacide.pdf (Accessed Jun, 2015).
17. Christensen OB, Anehus S. Hydrogen peroxide cream: an alternative to topical antibiotics in the treatment of impetigo contagiosa. *Acta Derm Venereol* 1994;74:460–2.
18. Hartman-Adams H, Banvard C, Juckett G. Impetigo: Diagnosis and treatment. *Am Fam Physician* 2014;90:229–35.
19. Milani M, Bigardi A, Zavattarelli M. Efficacy and safety of stabilised hydrogen peroxide cream (Crystacide) in mild-to-moderate acne vulgaris: a randomised, controlled trial versus benzoyl peroxide gel. *Curr Med Res Opin*;19:135–8.

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