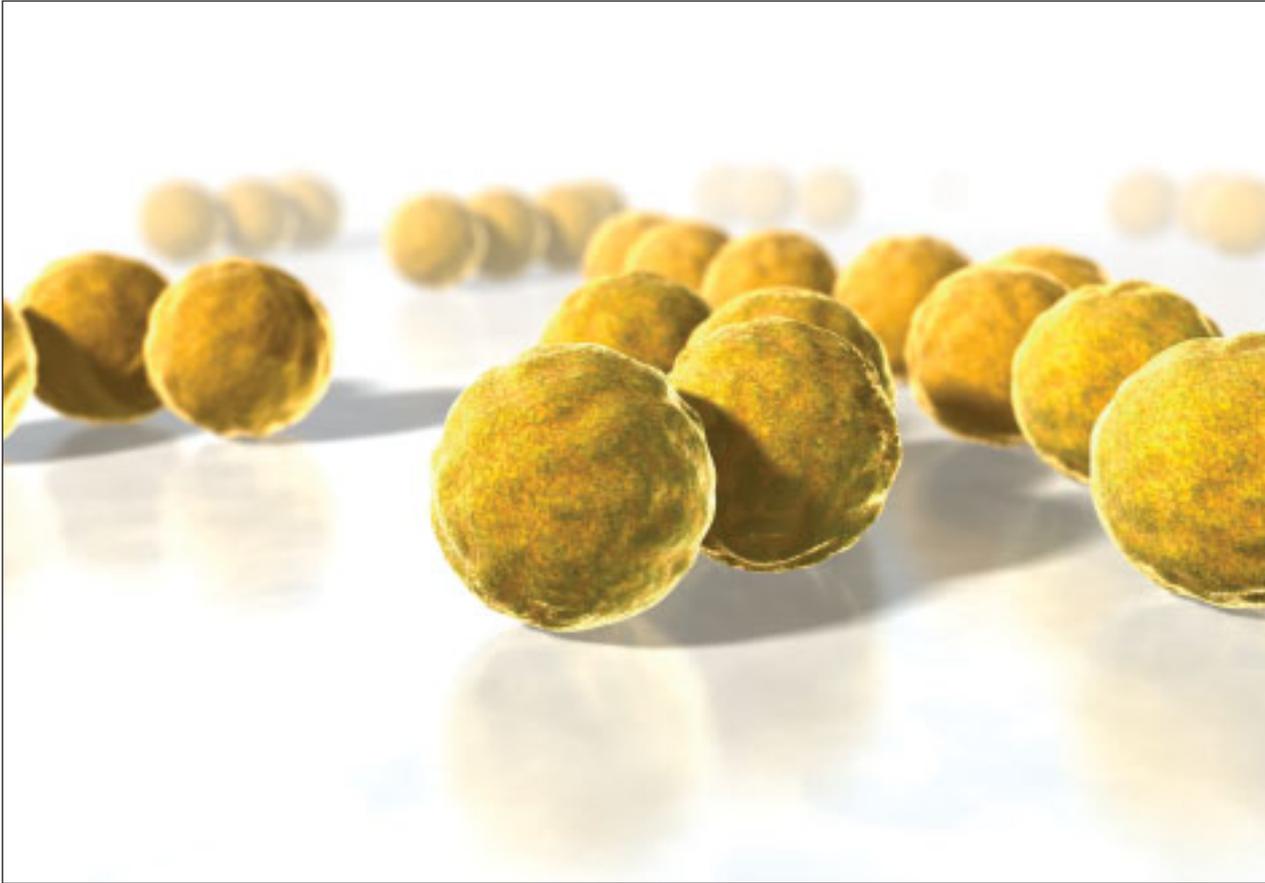


Primary care management of bacterial skin infections

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Bacterial skin infections are commonly seen in primary care and can usually be successfully managed with topical or systemic antibiotics. Our Drug Review discusses their recommended treatment, followed by sources of further information and the Datafile.

Although the skin is populated with very large numbers of bacteria that may be resident or transiently carried, it forms a very effective barrier against invasion. It is tough, constantly desquamating and self-renewing, dry and acidic in pH, all of which contribute to its defence. In order for bacterial infection to

develop, the defensive mechanisms of the skin must be overcome. The commonest conditions predisposing to bacterial skin infections (BSIs) involve breaches to the integrity of the skin barrier. Trauma such as lacerations, abrasions, excoriation, inflammatory skin conditions and ulceration associated with vascular disease may all render the skin vulnerable. The primary bacterial infections of skin most commonly encountered in clinical practice are due to either *Staphylococcus aureus* or *Streptococcus pyogenes* or both organisms together.

Common primary infections

BSIs may be classified according to the level of involvement of skin and associated structures, such as hair follicles, and by whether or not there is extension of

Infection	Bacterium
<i>Impetigo</i>	<i>Staph. aureus</i> alone <i>Staph. aureus</i> with <i>Strep. pyogenes</i> <i>Strep. pyogenes</i> alone
<i>Folliculitis</i>	<i>Staph. aureus</i>
<i>Furuncles (boils)</i> <i>and carbuncles</i>	<i>Staph. aureus</i>
<i>Erysipelas</i>	<i>Strep. pyogenes</i> occasionally Group C or G beta-haemolytic streptococci
<i>Cellulitis</i>	<i>Strep. pyogenes</i> <i>Staph. aureus</i> <i>Strep. pyogenes</i> plus <i>Staph. aureus</i> Group B, C or G beta-haemolytic streptococci

Table 1. Pathogens most frequently implicated in common primary infections

infection into the lymphatics and subcutaneous tissue.¹ Pathogens most frequently implicated in commonly encountered primary BSIs are outlined in Table 1.

Impetigo (see Figure 1)

Impetigo is a superficial, intraepidermal BSI. The infection and associated skin lesions are confined to the epidermis and do not ulcerate and, therefore, heal

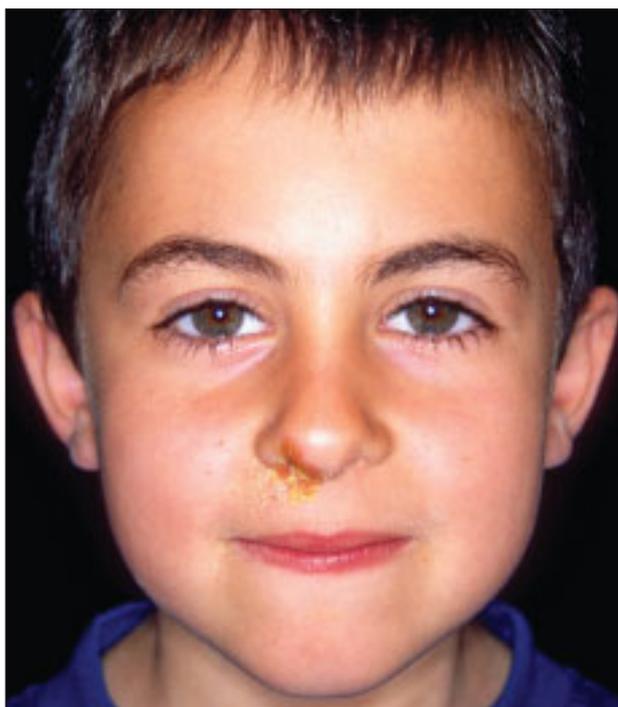


Figure 1. Impetigo, more frequent in children than adults, is treated with topical preparations if mild and localised

without scarring. Clinically there are two recognised forms of impetigo: bullous, which is due to certain strains of *Staph. aureus* that produce an exfoliative toxin,² and non-bullous, which is most commonly caused by *Staph. aureus* but may be caused by *Strep. pyogenes* alone or in combination with *Staph. aureus*.^{3,4} The nonbullous form is most common, accounting for almost 75 per cent of cases.

Impetigo occurs more frequently in children than in adults, and is most common during hot and humid summer weather. The most common sites of lesions in nonbullous impetigo are exposed areas of skin, such as on the face or extremities, and there is frequently a predisposing breach in skin integrity with a cut or area of excoriation. Impetigo develops as superficial vesicles and pustules that then rupture, with the purulent discharge forming a thick adherent crust ‘stuck on’ to the underlying erythematous area.

Management requires antibacterial therapy that may be administered either topically or systemically, depending on the extent and severity of the infection. Where impetigo is mild and the lesions localised, topical antibacterial therapy is appropriate. Efficacy of topical antibiotic therapy is increased if crusting areas are removed before application by soaking in soapy water.

Fusidic acid (Fucidin) is the first-line recommended topical agent, with mupirocin (Bactroban) as an alternative if fusidic acid is not tolerated or has been ineffective. As mupirocin is an essential therapy for the treatment of methicillin-resistant *Staph. aureus* (MRSA), the Health Protection Agency recommends that, where possible, use of mupirocin should be reserved for the treatment of MRSA. Due to concerns about increasing antimicrobial resistance, it has been recommended that topical antibiotic therapy should be used judiciously. It is best reserved for cases where infection is very mild and limited to very localised lesions.^{5,6,7}

If lesions are widespread or the infection is more severe, then systemic antibacterial therapy is indicated. First-line recommended oral antibiotic therapy is flu-cloxacillin with erythromycin as an alternative if the patient has a history of penicillin allergy.^{7,8,9}

Ecthyma resembles impetigo but extends deeper to the dermis. This BSI is more commonly encountered in debilitated and older patients and most frequently occurs on the lower extremities. Lesions appear as shallow skin ulcers covered by thick, adherent crusts and heal to leave scarring. Treatment with the same systemic antibacterial therapy as for impetigo is indicated.



Figure 2. Superficial folliculitis may respond to a local antiseptic, but resistant cases may require treatment with topical fusidic acid or, if severe, systemic therapy

Folliculitis (see Figure 2)

Bacterial infection occurring within hair follicles results in folliculitis. *Staph. aureus* is the usual cause, most frequently seen in the beard region, axillae or buttocks. Occasionally, folliculitis may follow pseudomonal infection associated with inadequately chlorinated water in whirlpools or hot tubs, with lesions classically occurring on the trunk.

Superficial staphylococcal folliculitis may respond well to simple local antiseptic measures, but recalcitrant cases may require topical antibacterial therapy with an antistaphylococcal antibiotic, such as fusidic acid.

If the folliculitis is widespread or severe, then systemic therapy with an oral antistaphylococcal agent such as flucloxacillin or erythromycin may be warranted.

Furuncles and carbuncles (see Figure 3)

Follicular infection with *Staph. aureus* may extend to a deeper level than in superficial folliculitis, resulting in furuncles (boils) or carbuncles. A furuncle is a deep inflammatory nodule developing from a preceding folliculitis, which begins as a firm, tender, erythematous nodule that becomes fluctuant and painful and commonly ruptures spontaneously with drainage of pus and resolution. If a number of adjacent furuncles coalesce, a more extensive lesion known as a carbuncle is formed. Multiple abscesses may develop within the large carbuncle that discharge pus to the surface along hair follicles. Furuncles are more commonly seen on the face, axillae and buttocks, whereas carbuncles are more commonly found on the nape of the neck, back or thighs.



Figure 3. Furuncle treatment is focussed on drainage of pus; large nodules may also require incision and antibiotics

Management of furuncles and carbuncles is aimed at drainage of pus. Many furuncles and some small carbuncles may drain spontaneously or following application of moist heat, which accelerates localisation and drainage. Larger nodules will usually require incision and drainage, together with treatment with an antistaphylococcal antibiotic such as flucloxacillin or erythromycin.¹⁰

Cellulitis and erysipelas

Cellulitis and erysipelas are acute, spreading BSIs in which the skin is red, hot and swollen. Cellulitis (see Figure 4) involves the subcutaneous tissues. Erysipelas (see Figure 5) is a clinically distinctive form of cellulitis, which is usually more superficial but with lymphatic involvement. Classical erysipelas

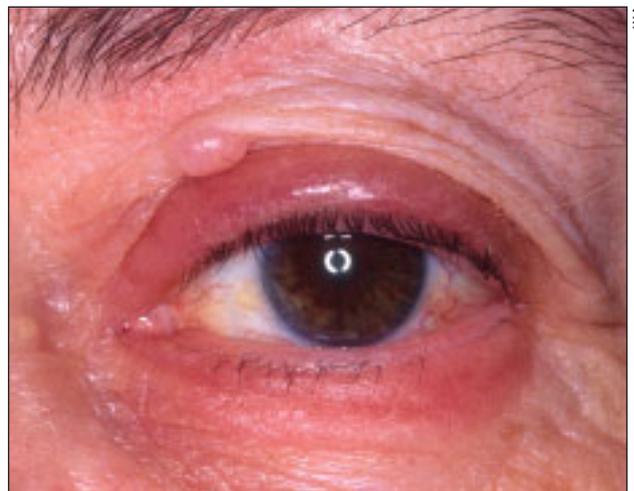


Figure 4. Co-amoxiclav is recommended for facial cellulitis to cover pathogens from the mouth and sinuses



Figure 5. Erysipelas is treated with amoxicillin (500mg every eight hours) or erythromycin (500mg every six hours) is clinically differentiated from cellulitis by the appearance of a well-defined and raised border, which sharply demarcates it from adjacent non-infected skin. In contrast, the advancing margins of cellulitis are less well demarcated and flat. In practice, it may be difficult to distinguish the two conditions.

Erysipelas was classically described as occurring most commonly on the face, where it was frequently bilateral, but more recent reports indicate that it now most frequently involves the legs and feet.¹¹ Erysipelas

is caused by *Strep. pyogenes* in most instances, with the remaining minority due to other streptococci, such as Group C or G beta-haemolytic streptococci. Erysipelas is treated with a penicillin or alternatively erythromycin.

Cellulitis is more commonly seen on the lower limbs, frequently involving the calf. In many cases there is an obvious antecedent skin lesion, such as a traumatic wound or ulcer, or other area of damaged skin, such as interdigital athlete's foot, which provide a portal for bacterial entry. The vast majority of cases are caused by *Strep. pyogenes*, *Staph. aureus*, or both organisms together. While *Strep. pyogenes* is the most commonly implicated streptococcus in cellulitis, Group B, C or G beta-haemolytic streptococci are sometimes the cause.

Cellulitis is treated with antibiotics that are active against *Staph. aureus* and *Strep. pyogenes*. In sufficient dosage, flucloxacillin may cover both organisms. Most UK authorities now recommend flucloxacillin alone as first-line therapy provided the patient is afebrile and healthy other than the cellulitis.^{7,12,13} Facial cellulitis is an exception, where co-amoxiclav is recommended for first-line therapy to cover organisms from the mouth and sinuses.

Treatment

Topical antibiotics

Fusidic acid is active against most Gram-positive bacteria, but is particularly active against staphylococci. However, recently there have been a number of reports in the UK of increasing resistance to fusidic acid among *Staph. aureus* isolates from patients in the community, directly in line with topical fusidic acid usage.^{5,6} This has resulted in recommendations for reserving its use for mild and very localised skin infections. Fusidic acid is used topically on skin as a 2 per cent preparation and is generally without significant side-effects, although rarely hypersensitivity reactions may occur.

Mupirocin, a fermentation product of *Pseudomonas fluorescens*, has a broad spectrum of activity and is highly active against both staphylococci and streptococci. Emergence of resistant isolates of *Staph. aureus* has been observed following prolonged use for dermatological conditions, so topical treatment courses should not exceed 10 days.

Mupirocin is available as a 2 per cent topical preparation and is generally well tolerated, although it may sting. The ointment base contains polyethylene glycol, which if absorbed from damaged skin may be nephrotoxic, and the manufacturer advises caution in renal impairment.

Skin infection	Antibiotic agent	Oral dose
<i>Impetigo</i>	flucloxacillin or erythromycin	500mg every 6 hours
<i>Folliculitis, widespread/severe</i>	flucloxacillin or erythromycin	500mg every 6 hours
<i>Large furuncles (boils) and carbuncles</i>	flucloxacillin or erythromycin (plus incision and drainage if indicated)	500mg every 6 hours
<i>Erysipelas</i>	amoxicillin or erythromycin	500mg every 8 hours 500mg every 6 hours
<i>Cellulitis nonfacial facial</i>	flucloxacillin co-amoxiclav	500mg every 6 hours 500/125mg every 8 hours

Table 2. Oral antibiotic management for common bacterial skin conditions

Antibiotic	Mode of action	Spectrum of activity	Side-effects	Drug interactions
<i>Penicillins</i> , eg phenoxymethylpenicillin, amoxicillin, flucloxacillin, co-amoxiclav	interfere with bacterial cell wall synthesis	phenoxymethylpenicillin, amoxicillin and co-amoxiclav are active against streptococci; flucloxacillin and co-amoxiclav are active against staphylococci	hypersensitivity reactions, diarrhoea, hepatitis, cholestatic jaundice	anticoagulants, methotrexate, oral contraceptive pill, probenecid
<i>Macrolides</i> , eg erythromycin, clarithromycin	inhibit bacterial protein synthesis, bacteriostatic	<i>Staph. aureus</i> and streptococci	nausea, vomiting, diarrhoea	inhibit liver enzymes affecting metabolism of anticoagulants, carbamazepine, digoxin
<i>Cephalosporins</i> , eg cefalexin and cefradine	interfere with bacterial cell wall synthesis	<i>Staph. aureus</i> and streptococci	hypersensitivity reactions, diarrhoea	anticoagulants, probenecid

Table 3. Properties of oral antibiotics used in bacterial skin infections

Oral antibiotics

Amoxicillin As with other beta-lactam antibiotics, amoxicillin exerts its antibacterial effect by interfering with bacterial cell wall synthesis, targeting cell wall-synthesising enzymes, known as penicillin-binding proteins. The relatively low toxicity of penicillins is attributed to the absence of penicillin-binding proteins in mammalian cells. Amoxicillin is highly active against streptococci, including *Strep. pyogenes*, but most *Staph. aureus* are resistant due to production of a penicillin-inactivating enzyme. The pharmacokinetic profile of amoxicillin, in particular its reliable oral absorption, makes it a suitable oral penicillin against streptococcal skin infections and, in combination with an antistaphylococcal agent, for treatment of mixed infections.

Potential side-effects of amoxicillin include nausea, vomiting and diarrhoea, as well as adverse reactions resulting from hypersensitivity. The most common manifestation of hypersensitivity is skin rash, which is estimated to occur in 1-7 per cent of cases.

Flucloxacillin is a semi-synthetic penicillin that is stable to the penicillin-degrading enzyme produced by *Staph. aureus*. The spectrum of its activity is primarily Gram-positive, being active against staphylococci and beta-haemolytic streptococci, although it is less active against the latter than penicillin. Flucloxacillin is well absorbed and the principal side-effects are those of the penicillin group as described for amoxicillin above.

Methicillin- and flucloxacillin-resistant *Staph. aureus* isolates are increasing throughout the UK. Infections with these resistant isolates are still primarily encountered in patients with a prior history of

hospitalisation, other significant healthcare institution exposure or repeated courses of prior antibiotic therapy. The number of reports of infections in patients without such risk factors is also increasing, however.

Erythromycin belongs to the macrolide class of antibiotics unrelated to penicillins. It is active against staphylococci and streptococci, which makes it a useful agent for use in the treatment of BSIs in patients allergic to penicillins. Resistance, particularly among *Strep. pyogenes* isolates, is increasing worldwide, and threatening its use in this setting.

The side-effects most commonly encountered following erythromycin administration are gastrointestinal, including nausea, vomiting and diarrhoea, or skin reactions including urticaria and rash.

Cefradine and *cefalexin* are group 2 cephalosporins that are active against staphylococci and streptococci. Both are well absorbed after oral administration. They may be used as alternatives to penicillins in the treatment of staphylococcal and streptococcal skin infections in patients allergic to penicillin. This is provided there has not been a severe reaction or anaphylaxis to penicillin: it is estimated that between 3 and 9 per cent of patients allergic to penicillin are cross-allergic to cephalosporins. Other principal side-effects are gastrointestinal, including diarrhoea, nausea, vomiting and abdominal discomfort.

Summary

BSIs are among the most frequently seen infectious conditions in the community and account for a sig-

nificant proportion of patient presentations in primary care. The commonest primary BSIs are impetigo, folliculitis, furuncles and carbuncles, erysipelas and cellulitis. The majority of these infections are due to *Staph. aureus*, *Strep. pyogenes*, or both organisms together. In most cases primary infections are mild to moderate in severity and may be managed with either topical or oral antibiotic therapy.

In general, to avoid increasing emergence of resistant isolates in the community, topical antibiotic therapy should be used judiciously and reserved for mild and very localised BSIs. Oral antibiotics, principally beta-lactams and macrolides, are generally of low toxicity and well tolerated. Continued surveillance of resistance patterns among bacterial skin pathogens is needed, together with monitoring for clinical failures associated with such resistance. Unless resistance to these older agents reaches a critical level and is associated with more widespread clinical failures, they remain the most appropriate antibiotics for treating primary BSIs in the community.

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Resources

Useful addresses

British Association of Dermatologists, 4 Fitzroy Square, London W1T 5HQ. Tel: 020 7383 0266, fax: 020 7388 5263. Website: www.bad.org.uk.

Skin Care Campaign, Hill House, Highgate Hill, London N19 5NA. Tel: 020 7281 3553, fax: 020 7281 6395. Website: www.skincarecampaign.org.

Skinship (UK). Mr Ashley Medicks, Plascow Cottage, Kirkgunzeon, Dumfries DG2 8JT. Helpline: 01387 760567. Welcomes calls from anyone with any kind of skin problem.

Further reading

Cellulitis and subcutaneous tissue infections. Swartz MN. In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and practice of infectious diseases*. 5th ed. Philadelphia, London; Churchill Livingstone, 2000;1037-57.

Management of infection. Guidance for primary care for consultation and local adaptation. www.hpa.org.uk/infections/topics_az/primary_care_guidance/menu.htm.

PRODIGY guidance. Management of cellulitis and erysipelas (November 2005) and impetigo (May 2006). Website: www.prodigy.nhs.uk.

CREST guidelines on the management of cellulitis in adults. Clinical Resource Efficiency Support Team (CREST). 2005. Website: www.crestni.org.uk.

Patient Information

www.patient.co.uk has information leaflets on boils, carbuncles and furunculosis, cellulitis, folliculitis and impetigo.

www.dermatology.co.uk – useful website.