

Skin infections

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ABSTRACT A huge number of infections affect the skin either directly, as the primary site of infection, or indirectly, by virtue of causing an exanthem or other secondary eruption, such as erythema multiforme or vasculitis. Space does not permit significant discussion of such indirect associations so most of this review concentrates on direct skin infection and is highly selective. The emphasis is on disorders that are common but that may have significant health implications, and on some rarer but readily diagnosable disorders. Thus, the topics chosen for review are streptococcal cellulitis of the leg, staphylococcal scalded skin syndrome, herpes simplex and varicella zoster infections, and a potpourri of tropical skin infections that may present in returning travellers.

KEYWORDS Skin infections, staphylococci, streptococci, tropical infections, varicella zoster

LIST OF ABBREVIATIONS Acute generalised exanthematous pustulosis (AGEP), antistreptolysin O (ASO), C-reactive protein (CRP), enzyme-linked immunosorbent assay (ELISA), erythrocyte sedimentation rate (ESR), herpes simplex virus (HSV), polymerase chain reaction (PCR), staphylococcal scalded skin syndrome (SSSS), toxic epidermal necrolysis (TEN), varicella zoster virus (VZV)

DECLARATION OF INTERESTS No conflict of interests declared.

STREPTOCOCCAL CELLULITIS (ERYSIPELAS) OF THE LEG

This is the most common severe skin infection in the UK, accounting for 2–3% of medical admissions.

Cause

Usually a streptococcal infection; staphylococci can cause a similar picture. If there is a preceding ulcer or wound, other causes of infection should be considered.

Clinical

Foot oedema and malaise, fever or rigors precede proximally spreading redness, tenderness and swelling. Common differential diagnoses are:

- Deep venous thrombosis – no fever/malaise.
- Wound/ulcer infection – history of preceding lesion, inflammation usually localised.
- Eczemas (venous, asteatotic, contact) – have scaling and itch.
- Lymphoedema – often confused with cellulitis as it causes redness and swelling, and predisposes to cellulitis. Usually symmetrical (by contrast, symmetrical cellulitis is intrinsically highly improbable) (see Figure 1).
- Compartment syndrome – usually anterior tibial, marked tenderness.
- Necrotising fasciitis – characterised by ‘crescendo’ pain, clinical necrosis (cold dusky areas/severe blistering within cellulitis), malaise, hypotension; investigations as below.

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FIGURE 1 Severe cellulitis with blistering and a background of chronic lymphoedema.

Diagnosis

Direct proof from bacteriology swabs is unusual, as the skin is usually intact, but swabs should be sent from any ulcer slough, blister fluid or macerated toe webs; scrapings from toe webs may help to identify tinea pedis as the cause of maceration. An elevated ASO titre is retrospective proof of streptococcal infection.

Investigations that suggest necrotising fasciitis and streptococcal toxic shock syndrome include elevated transaminases and creatinine, marked leukocytosis, coagulopathy, positive blood cultures (uncommonly positive in uncomplicated cellulitis), hyponatraemia, hyperglycaemia, and elevated inflammatory markers (ESR, CRP).

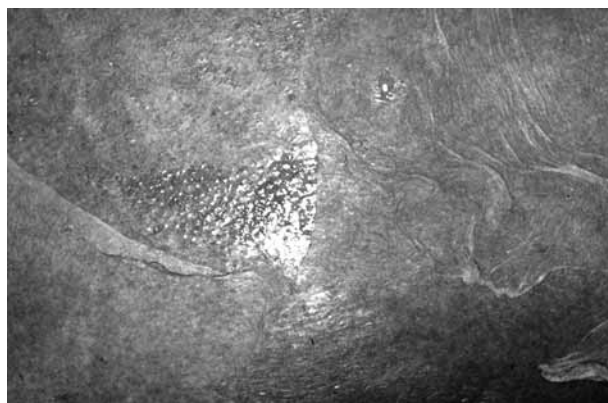


FIGURE 2 Staphylococcal scalded skin syndrome: sheets of fragile blistering with a raw-looking appearance to the underlying skin.

Treatment

Treatment is usually with intravenous flucloxacillin 500 mg four times a day and benzylpenicillin 2.4 g four times a day, although there is evidence that flucloxacillin alone may be adequate. In severe or unresponsive infections, clindamycin should be used as high bacterial loads reach a 'stationary phase', during which they are less susceptible to penicillin and also produce penicillin-binding proteins. Outpatient once-daily ceftriaxone has been studied and is effective if the patient is well enough and has adequate support to permit home treatment. Linezolid is sometimes used; pristnamycin is popular in some countries. A change to oral therapy is usually made when the patient has been afebrile for at least 24 hours and there are signs of improvement (receding erythema, decreased swelling or tenderness, etc.).

Recognition of necrotising fasciitis is important because the management is surgical debridement rather than systemic antibiotics alone.

STAPHYLOCOCCAL SCALDED SKIN SYNDROME

This is a rare but potentially fatal condition when it occurs in adults.

Cause

The underlying cause is a focus of staphylococcal infection, often of the nasopharynx or focally in the skin. The organism is usually a phage type II *S. aureus* (type 71 or 55); the widespread skin changes are due to proteolysis by staphylococcal exfoliative (epidermolytic) toxins A or B, and are not themselves infected. The target that is cleaved by the toxin is desmoglein-1, a molecule involved in cell-cell adhesion; recent studies have demonstrated that this is the same molecule in which function is impaired by IgG autoantibodies in pemphigus foliaceus, a variant of pemphigus in which there is a superficial split in the subcorneal area of the epidermis.

The toxin is renally excreted, so most cases occur in the context of renal immaturity (young children) or chronic renal failure, sometimes in patients with impaired immune function, but rarely in previously healthy adults.

Clinical

Initial changes are fever, with burn-like redness and tenderness of the facial skin, and flexures. This erythema may become generalised (sparing palmoplantar skin and mucosae), with peeling of large sheets of skin (see Figure 2). Lateral pressure on the skin causes shearing, the Nikolsky sign.

Diagnosis

Despite sharing the same target molecule for damage as that in pemphigus (toxic damage in SSSS, immunological in pemphigus), the latter disorder is not usually considered in differential diagnosis as it has slower evolution, lacks the preceding fever and typically affects the oral mucosa some months before skin involvement. The main differential diagnosis is from TEN, which is usually drug-induced; if necessary, the two can be distinguished histologically by the level of the epidermal split (superficial subcorneal in SSSS; deeper at the dermoepidermal junction in TEN). Rarer immunobullous disorders may need to be considered, especially in patients with malignancy (e.g. *epidermolysis bullosa acquisita* or paraneoplastic pemphigus).

Treatment

Treatment is intensive supportive care, with careful attention to fluid balance, as well as intravenous administration of a penicillinase-resistant penicillin (e.g. flucloxacillin 500 mg, four times a day) or cephalosporin.

HERPES SIMPLEX VIRUS

Cause

These are herpes simplex viruses type 1 (any site) or 2 (mainly genital). This discussion relates mainly to HSV-1.

Clinical

Most recurrent infections consist of localised small blisters on an erythematous background, preceded by a tingling or burning sensation. Primary infections are usually more severe and may take several weeks to heal; HSV at uncommon body sites such as the thigh or trunk may cause diagnostic problems.

The most important HSV-related issues for generalists, as all cases may need aggressive therapy, are:

- Herpes simplex virus infection in immunosuppressed individuals – lesions may be multiple, disseminated,

large and ulcerated or may form chronic verrucous or pustular plaques. Additionally, aciclovir resistance in such patients is of the order of 5–10%, compared with less than 0.5% in immunocompetent subjects.

- *Eczema herpeticum*, a disseminated infection (particularly affecting the head and upper trunk, but potentially widespread) in individuals with atopic dermatitis at any age (skin immune function to deal with HSV is abnormal).
- Systemic/internal infection such as encephalitis or pneumonia.
- Neonatal HSV, which may be focal (often at scalp electrode sites) or disseminated.

Diagnosis

Diagnosis is usually clinical for recurrent disease of the vermillion of the lips or of the genitalia. However, primary infection at other sites – disseminated or otherwise atypical forms, especially in immunosuppressed subjects – requires virological confirmation. Swabs may be taken for culture, ELISA or (more recently) PCR analysis of type-specific glycoproteins (gG-1 of HSV-1 and gG-2 of HSV-2).

Treatment

Topical therapy for milder HSV infection is usually with aciclovir or penciclovir. Systemic treatment options for HSV include aciclovir (oral and intravenous), famciclovir (genital HSV; oral) and valaciclovir (oral). If resistance appears likely, alternative systemic agents are foscarnet and cidofovir. Topical resiquimod is under evaluation – it is not antiviral per se, but modifies the immune response to herpes virus infections. Vaccines are also being developed.

VARICELLA AND HERPES ZOSTER

Cause

Varicella zoster virus.

Clinical

Both the primary viraemic illness (varicella) and the reactivation of latent virus (herpes zoster) can be associated with serious systemic infection as well as causing significant rash. Diagnosis is not always easy.

Problem areas include:

- Fever preceding varicella in children is usually mild or absent, but may be significant and last over 24 hours before any skin eruption in adults.
- Other acute-onset vesicopustular eruptions with systemic malaise may mimic varicella. These include generalised pustular psoriasis and AGEP (a pattern of drug eruption), as well as other infections such as rickettsial pox (common in some parts of the US),

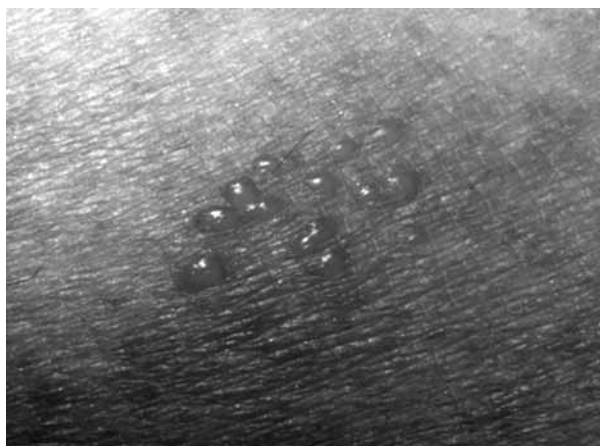


FIGURE 3 Herpes zoster. This was an isolated lesion which might have been diagnosed as herpes simplex, but the blisters were slightly more variable in size and less clustered than would be typical for HSV, and there was dermatomal pain.

scabies with streptococcal secondary infection, and exanthems such as erythema multiforme or the rash of Epstein-Barr virus infection.

- Initial lesions of zoster may be just one or a few red plaques – if solitary, with vesicles, herpes simplex may be suspected (dermatomal pain is a clue for VZV) (see Figure 3).
- In immunosuppressed individuals, VZV may present as disseminated vesicles (with or without dermatomal involvement), or as zoster affecting multiple adjacent dermatomes.
- Zoster may occur in unusual forms (e.g. without rash; motor rather than sensory symptoms) or in severe forms (meningoencephalitis, pneumonia, hepatitis, Ramsay-Hunt syndrome, severe ocular involvement and others).

Complications of varicella include:

- **Secondary infection.** A major cause of morbidity in the tropics if rarely important in the UK, although varicella is one of the more important predisposing causes of necrotising fasciitis in children.
- **Encephalitis.** Rare, and complete recovery is usual.
- **Pneumonitis.** Most frequent in adults, especially in smokers.

Complications of herpes zoster include:

- **Necrotic skin lesions.** These may take months to heal in some instances.
- **Urinary retention.** In zoster affecting the anogenital area.
- **Severe pain.** This may persist after the eruption has settled (post-herpetic neuralgia). The duration and severity are greatest in the elderly, in whom facial zoster is more common, and in patients immunosuppressed by disease (HIV, lymphoma) or medication.
- **Post-herpetic itch,** rather than pain, is a less well-recognised entity but occurs in up to 50% of patients

following zoster, especially facial. Topical lidocaine, capsaicin or doxepin may be useful, as may oral tricyclics or gabapentin.

- **Varicella-like lesions** (and complications). Usually in immunosuppressed individuals, but disseminated lesions may occur in immunocompetent (although usually elderly) subjects.

Diagnosis

This is usually clinical for either varicella or herpes zoster. Viral culture, direct serology, immunofluorescence or PCR may be necessary in some cases.

Treatment

Treatment of chickenpox is usually symptomatic in children with mild and uncomplicated disease. Systemic aciclovir is indicated in the following:

- infants
- severe infection at any age
- immunosuppression
- subjects with severe cardiorespiratory disease
- patients with a chronic skin disorder

Aciclovir, famciclovir and valaciclovir are all licensed for treatment of herpes zoster. In immunocompromised subjects or those with internal organ involvement or disseminated infection, intravenous aciclovir is required.

Varicella zoster immune globulin should be administered to individuals who fulfil all of the following three criteria:

- exposure to severe chickenpox or herpes zoster
- high risk of severe varicella (e.g. immunosuppressed or pregnancy)
- no protective antibodies

Varicella vaccination is licensed for any seronegative individual over one year of age, but in the UK routine use in children is not recommended unless a child is exposed to severe infection. Vaccination is indicated for seronegative healthcare workers exposed to varicella zoster. The vaccine is contraindicated in pregnancy, and pregnancy should be avoided for three months after vaccination.

TROPICAL INFECTIONS OF THE SKIN

There are many direct skin infections as well as exanthems due to tropical diseases. The four most common direct skin infections are discussed below.

Larva migrans

Larva migrans is typically caused by the dog and cat hookworm *Ancylostoma braziliensis*, acquired from sand or

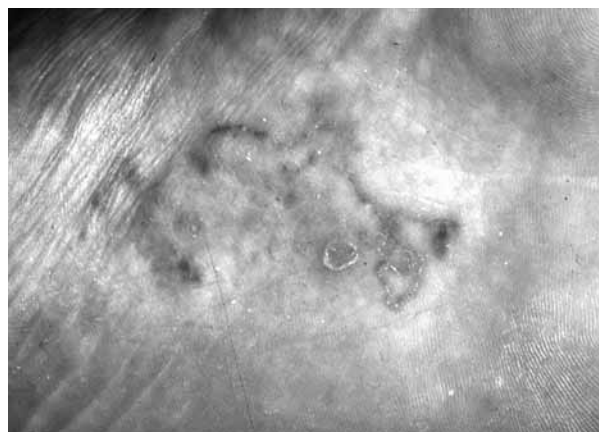


FIGURE 4 *Larva migrans* due to cat/dog hookworm, causing a serpiginous eruption on the ankle.

soil. An itchy serpiginous track appears at the site (see Figure 4), most commonly the foot or buttock. In severe cases the tracks merge as an irregular inflammatory plaque.

Diagnosis is usually clinical. Biopsy is rarely necessary, but if performed it must be about 0.5–1 cm ahead of the visible track, as this is where the parasite is situated.

Treatment options include oral albendazole or topical tiabendazole. The parasite typically dies after about two weeks regardless, as humans are an accidental host.

Myiasis

This is a term applied to various infections by fly larvae. The most common type in travellers is cutaneous infection by botfly larvae, mainly *Dermatobia hominis*.

A furuncle-like or abscess-like lesion develops, with a central punctum (or several puncta in the furunculoid pattern). Pyogenic infection is the usual differential diagnosis, but these lesions are sterile as the larvae produce bactericidal chemicals.

Diagnosis is usually clinical. Larvae can be stored in alcohol if species identification is important.

Removal of larvae can sometimes be achieved with simple downwards pressure, or by injecting lidocaine to paralyse the larvae. Occlusion of the punctum with various greasy agents means that larvae will eventually emerge to avoid asphyxiation, and can then be grasped with forceps; however, this may require many hours of observation. Topical albendazole has recently been described as highly effective, but a veterinary preparation unlicensed in humans was used.

Tungiasis

This is infection of the skin, usually of the foot (often in the toe webs or under the nail), by the female sand flea,

Tunga penetrans. The flea may be visible as a dark 1-mm dot. It causes an enlarging inflammatory nodule, which can be treated by curettage or excision.

Leishmaniasis

Leishmaniasis is a protozoal disease. The most common type seen in UK travellers is the localised cutaneous form due to *Leishmania tropica*, known as oriental sore and acquired from sandfly bites. Lesions of *L. major* are more numerous and wetter.

Lesions are usually single but may be multiple, usually on the face; initial papules evolve into larger plaques, nodules or ulcers. They can be very difficult to distinguish from chronic or infected insect bite reactions.

Diagnosis is by biopsy or smears, which demonstrate the amastigotes within a granulomatous infiltrate.

Lesions of the localised form will gradually regress even if untreated, but are destructive. Cryotherapy can be used but most commonly systemic or intralesional antimony (usually as sodium stibogluconate) is used. Oral fluconazole or systemic or topical paromycin are also effective.

FURTHER READING

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- <http://www.prodigy.nhs.uk/search/0/cellulitis>
PRODIGY is an organisation that produces Clinical Knowledge Summaries as part of the National Library for Health. As well as background information and management issues, these guidelines have quick reference guides and patient information leaflets.

KEYPOINTS

- In cellulitis, warning features of necrotising fasciitis include ‘crescendo’ pain, clinical necrosis, hypotension, elevated transaminases and creatinine, leukocytosis, coagulopathy, positive blood cultures, hyponatraemia, hyperglycaemia and elevated inflammatory markers.
- Herpes simplex is normally highly sensitive to aciclovir treatment, but be aware that resistance to aciclovir in immunosuppressed subjects is of the order of 5–10%.
- Vesicopustular eruptions with fever and malaise, which are in the differential diagnosis of varicella, include generalised pustular psoriasis, drug-induced acute generalised exanthematous pustulosis and other infections such as rickettsial pox or Epstein-Barr virus infection.
- Urinary retention must always be considered in patients with herpes zoster affecting the anogenital area.
- The most common tropical infection of the skin is *larva migrans*, which is usually clinically characteristic and easily treated.

Myre Sim Grants

Applications are invited from **Fellows and Collegiate Members of the Royal College of Physicians of Edinburgh** or **medical graduates of Edinburgh University** for grants to assist eligible individuals to further their professional competence and research activities.

Any activity that assists a viable research project will be considered, including payments for secretarial, library or computer facilities or nursing, laboratory or student assistance. A grant may also be given to assist with travel expenses to attend scientific meetings, courses of postgraduate education, visits to special clinics and other educational activities.

Awards will be up to a maximum of £2,000 and are not intended to be salary supporting. Preference will be given to those who have not had the advantage of an academic or research post in the past five years.

A short paper reporting on the research or activity undertaken will be required.



Further details and application forms are available from:

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