Pruritus: an approach to diagnosis and management

Pruritus is a common presenting symptom in primary care medicine that can prove distressing to the patient and frustrating for the treating doctor. Here is a practical approach to the diagnosis of its causes and its management, including a discussion of some less familiar conditions in which pruritus is a feature.

IAN D. HAMANN
MB BS(Hons), DipRACOG, FACD

Dr Hamann is a Consultant Dermatologist in private practice in Chatswood, Sydney, Taree and Port Macquarie; Visiting Medical Officer, Westmead Hospital, Westmead; and Lecturer, University of NSW School of Rural Health, Port Macquarie Campus, NSW.

Pathophysiology

Pruritus originates in the skin from the release of chemical mediators, such as histamine, or from physical stimuli, such as wool fibres. It is thought to occur due to stimulation of an epidermal pruritus receptor unit, which has an uneven distribution and a density in areas where these units are common of about one receptor/mm^2. Transmission of pruritus involves neuropeptides and the primary afferent nociceptors A-delta and C fibres. These nerve fibres are sensitive to temperature, thus explaining the well recognised phenomenon of a lowered itch threshold when the skin temperature is raised.

It is now known that pruritus is an entirely separate sensory modality from pain; however, the neural pathways of both follow the same overall route.

Inflamed skin alters reactivity such that mechanical stimuli are interpreted centrally as itch. This is known as allokinesis. It is very important in patients with atopic dermatitis.

Pruritus is transmitted centrally by dedicated neurons, and processing appears to occur in the thalamus and cerebral cortex. Therefore, it may arise centrally as well as peripherally, producing neuropathic itch. Both central and peripheral processes may be important in producing itch in systemic disease, such as renal failure, and dermatological diseases, such as atopic dermatitis or psoriasis.

Psychological factors can be very important in neurogenic itch, and may modify patients' responses to all causes of pruritus. The degree of pruritus experienced by a patient may be out of proportion to the signs of clinical disease.

IN SUMMARY

- **It is important to distinguish pruritus with a rash from that without; pruritus without a rash suggests a systemic cause for the itch.**
- **If a systemic cause for pruritus is suspected, limited investigations are warranted.**
- **Attention to general skin care principles is essential for patients with pruritus.**
- **If possible, provide patients with written instructions of skin care and keep regimens reasonably simple.**
- **Topical corticosteroids are only helpful in treating the underlying disease in patients with inflammatory dermatoses.**
- **Oral treatments for pruritus, including antihistamines, tricyclic antidepressants, benzodiazepines and opioid receptor antagonists, may offer relief in specific circumstances.**
- **Pruritus is a feature of the following less familiar conditions: lichen simplex chronicus, prurigo nodularis, Grover's disease, brachioradial pruritus, notalgia paraesthetica and urticarial dermatosis.**

Table 1. Examples of common systemic causes of pruritus

Renal failure
Hepatic failure
Thyroid disease
Diabetes mellitus
Iron deficiency
Haematological malignancy
– Polycythaemia rubra vera
– Hodgkin's lymphoma
– Myelodysplasia
HIV infection

Diagnosis

Dermatologists like to distinguish pruritus with a rash from that without. This may sound straightforward but is not necessarily so in practice. Pruritus without a rash suggests a systemic cause for the itch (see Table 1). Table 2 gives an approach to determining the causes of pruritus according to the presence of a rash and the rash features. If a systemic cause for pruritus is suspected, limited investigation is indicated, as listed in Table 3.

It is important to examine carefully patients without a rash as they may have extensive excoriations, mimicking a dermatosis, but no other features of a skin disease. Similarly, patients with scabies may have very few clinical signs of the infestation, and if the history is highly suspicious, treatment may be advised as a diagnostic test. Other patients may show signs of generalised xerosis, which can occur with ageing of the skin but may also occur in patients with renal failure, thyroid disease, or malnutrition. Patients with urticaria may have clear skin on presentation but a careful history may reveal that there has been a pattern of evanescent itchy papules or wheals. The history can provide clues to the diagnosis of diseases as diverse as atopic dermatitis and drug eruptions.

Management principles

Unfortunately, no specific topical or systemic agent is available for the treatment of pruritus. Whenever possible, a specific cause should be sought and treated; however, often, multiple factors are involved, and attention to commonsense, general skin care principles is essential.

General skin care

Dry skin is itchy skin. Patients should be encouraged to avoid overheating, which is a problem especially for the elderly and those who are ill. Central heating and slow combustion fires dehumidify the atmosphere. Electric blankets and doonas may increase nocturnal itch. Long hot showers and baths should be avoided.

Water is a primary irritant for inflamed skin and worsens skin dehydration when it evaporates. However, its moisturising properties can be used if a bland moisturiser is applied after bathing to damp skin. In dry climates it is better to use thick creams supplied in tubs than thinner lotions supplied in pump packs.

Soft, synthetic fabrics are kinder to irritable skin than wool or rough natural fibres. Similarly, sand, carpets and upholstery will aggravate atopic dermatitis in small children.

If possible, provide patients with written instructions on skin care and keep regimens reasonably simple. Patients should cleanse with a neutral pH, soap-free wash, readily available from chemists and supermarkets. Alkaline detergent soaps effectively degrease the skin, potentially weakening the natural barrier to irritants and inflammatory mediators. If patients shower in the morning, they should be advised to apply moisturiser all over their damp skin. In the evening, a topical corticosteroid can be applied to any inflamed pruritic areas and a moisturiser applied over the top.

Topical corticosteroids are not a treatment for noninflamed skin, nor a substitute for a moisturiser. This is particularly relevant for elderly patients who have senescent itch and xerosis.

Medications should be considered as a primary or aggravating factor for pruritus – for example, lipid lowering agents and diuretics may exacerbate skin dehydration.

Topical corticosteroids

For patients with inflammatory dermatoses such as eczema, topical corticosteroids can be very helpful in treating the underlying disease, thereby reducing pruritus. I prefer ointment bases, which are more emollient than creams, although they can be more difficult to apply (warming the tube may help). Every clinician has his or her favourite corticosteroid preparation. My preference is for once daily applications of a moderately potent corticosteroid ointment such as mometasone furoate (Elocon, Novasone) or methylprednisolone aceponate (Advantan). Increased supplies of these ointments can be arranged through the PBS on authority.

Patients should be encouraged to use topical corticosteroids regularly until the skin inflammation has settled, then maintain the skin in that condition with a moisturiser.

An alternative to topical corticosteroids is use of one of the new topical calcineurin inhibitors, pimecrolimus (Elidel) and tacrolimus (Prograf). These medications do not cause the epidermal atrophy that can occur with corticosteroids, but they are relatively more expensive. A detailed discussion of these medications is beyond the scope of this article.

Other topical treatments

Other topical treatments are limited by marginal efficacy or local irritation.

- Doxepin 5% cream has H1 and H2 antihistamine properties and has shown efficacy in atopic dermatitis; however, about 25% of patients will experience drowsiness, limiting its usefulness.
- Capsaicin 0.025 to 0.075% cream depletes substance P from neurons

and is useful for some localised pruritic conditions. Local irritation is a limiting factor.

- Counterirritants such as menthol 0.5%, phenol 0.5% and camphor 0.5% provide a cooling sensation and can be made up in oily calamine. Their efficacy remains debatable.
- Crotamiton 10% cream or lotion has been used for many years for pruritus, but there are no published controlled trials of its efficacy in pruritus.
- The use of topical antihistamines other than doxepin and of local anaesthetic agents is actively discouraged because of the high incidence of irritancy or contact allergy, and questionable sustainable efficacy.

Oral treatments

Oral treatments for pruritus may offer some relief in certain circumstances – for example, antihistamines, but only when histamine is the principle pruritus mediator, as occurs in urticaria. Antihistamines *per se* are not helpful for neurogenic or local itch due to most other causes; however, the sedation provided by traditional antihistamines, as well as by tricyclic antidepressants, such as doxepin (Deptran, Sinequan), and benzodiazepines, may give patients some relief at night. Currently, there is interest in using opioid receptor antagonists such as naltrexone (ReVia) to inhibit pruritus centrally.

Examples of uncommon conditions in which pruritus is a symptom

Lichen simplex chronicus and prurigo nodularis

Lichen simplex chronicus and prurigo nodularis are distinct disorders occurring secondarily to scratching and rubbing of the skin. Why the skin reacts in this way is not known; however, the itch–scratch cycle is the main factor in perpetuating these dermatoses. Skin trauma worsens the skin thickening, makes the area itchier,

Table 2. A guide to causes of pruritus according to presence of rash and rash features

Generalised pruritus: no rash (can include xerosis, excoriations)
Systemic disease
Senile xerosis
Scabies
Urticaria (and variants)
Drug reactions
Illicit drug abuse (e.g. marijuana)

Generalised pruritus: rash
Senile xerosis
Scabies (polymorphic)
Drug reactions (variable)

Red, scaly rash (papules, patches, plaques)
Atopic dermatitis
Other forms of eczema (e.g. contact dermatitis, asteatotic eczema)
Psoriasis*
Tinea corporis
Lichen planus
Cutaneous T-cell lymphoma*

Red wheals, papules, plaques
Urticaria
Urticarial dermatitis
Mastocytosis

Maculopapular (morbilliform) rash
Viral infections
Drug reactions

Vesicles
Viral infections (e.g. varicella)
Drug reactions
Dermatitis herpetiformis

Blistering/erosions
Impetigo
Bullous pemphigoid (other immunobullous disorders*)

Pustules*
Psoriasis
Drug reactions
Folliculitis (caused by *Pseudomonas*; 'hot tub folliculitis')

Localised pruritus: rash
Atopic dermatitis
Other forms of eczema (e.g. contact dermatitis, asteatotic eczema)
Psoriasis*
Lichen planus
Infestation (e.g. scabies)
Insect bites

Photosensitive distribution
Drug reactions
Polymorphic light eruption
Cutaneous lupus erythematosus*

Located on limbs
Papular urticaria (e.g. insect bites)
Lichen simplex chronicus/prurigo nodularis
Folliculitis
Tinea
Brachioradial pruritus

Located on trunk
Pityriasis versicolor
Folliculitis (caused by *Pityrosporum*, corticosteroids)
Miliaria (prickly heat)
Grover's disease
Tinea
Notalgia paraesthetica

Vesicles/blistering/erosions
Contact dermatitis
Impetigo*

Occurring during pregnancy (can also be generalised)
All other causes possible
Polymorphic eruption of pregnancy
Prurigo of pregnancy

* Itch is a variable component.

continued

Table 3. Investigations for systemic causes of pruritus

Full blood count
Erythrocyte sedimentation rate
Renal and liver function tests
Total protein measurement
Thyroid function tests
Blood sugar measurement
Ferritin measurement
Electrophoresis or immunoelectrophoresis
IgE antibody measurement

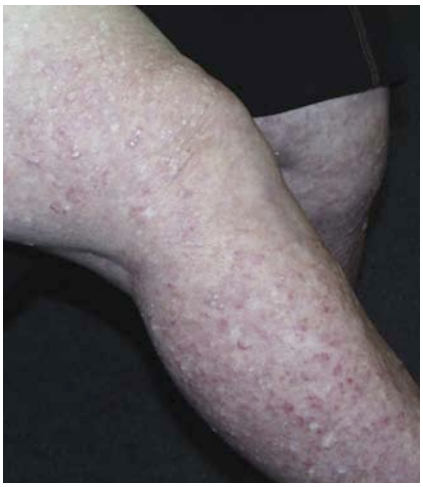


Figure 1. Prurigo nodularis and lichen simplex chronicus.

and may alter the morphology of the nociceptors producing the pruritus. Both conditions are relatively common and can coexist (Figure 1).

Lichen simplex chronicus is characterised by well circumscribed, lichenified, scaly, thickened plaques, which are often hyperpigmented. It is rare in children and most common in older adults. The sites most often affected are those that are easily reached, especially the nuchal area in women and perineum and scrotum in men. Other commonly affected areas are the wrists, extensor forearms and lower

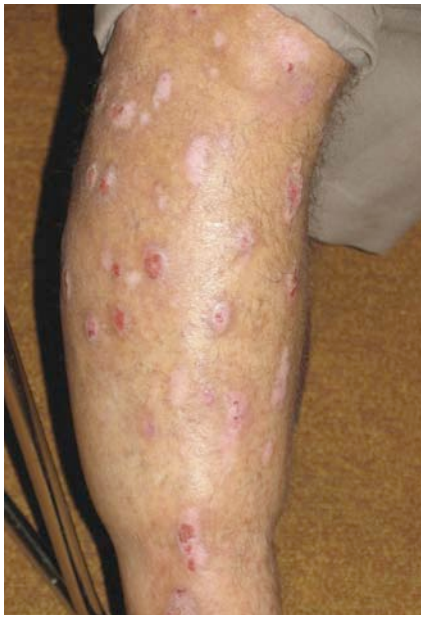


Figure 2. Prurigo nodularis.

legs. Occasionally extensive areas are affected.

Lichenification complicates persistent skin lesions of many types, and this should be considered in the differential diagnosis. Venous insufficiency of the legs, low grade contact dermatitis, asteatotic eczema and, occasionally, tinea must also be considered.

Prurigo nodularis is a chronic skin condition characterised by multiple papules and nodules with central scale or crust (Figure 2). It occurs in all age groups but is particularly common in middle-aged women. The dome shaped nodules are caused by the rubbing and scratching of susceptible skin. They occur most often on the extensor limbs, but are also common on the abdomen and sacral area. The face, palms, soles and mid upper back are spared. Prurigo nodularis may start with the scratching of insect bites.

In patients with either of these dermatoses, underlying causes for the pruritus need to be investigated. The most common causes are xerosis and atopy. In those with very widespread disease, a systemic cause should be considered.

Stress and psychosocial disorders are common factors in patients with these diseases. They worsen the pruritus and can give the scratching and/or rubbing component an obsessive, compulsive quality. Nocturnal sedation can be an important adjunctive treatment. Tricyclic antidepressants, such as doxepin, can be used for their sedative properties. Some patients benefit from SSRIs and/or counselling, and may need more formal psychiatric or psychological assessment.

As with other pruritic conditions, attention to good skin care is essential. Topical corticosteroids used initially should be potent preparations such as mometasone furoate, betamethasone dipropionate (Diprosone, Eleuphrat), or betamethasone valerate (Antroquoril, Betnovate, Celestone, Cortival). Recently, the ultrapotent topical corticosteroid, clobetasol has become available at compounding pharmacies, and has proved very useful. I would use wet dressings initially over the corticosteroid. Intralesional corticosteroids can be particularly effective for nodules and plaques. I use triamcinolone (Kenacort-A) in doses of 10 to 40 mg/mL (note that a maximum of 40 mg is recommended each treatment session).

Another treatment modality for the nodules and papules is cryotherapy, which may need to be administered for as long as 20 to 30 seconds for thick lesions. Palpation during the freeze gives a helpful guide.

The more severely affected patients may require narrow band UVB therapy, or immunosuppressive medication such as azathioprine, cyclosporin (Cicloral, Cysporin, Neoral, Sandimmun) or methotrexate (Ledertrexate, Methoblastin). Thalidomide has been used for patients with particularly recalcitrant prurigo with good success, but is limited by irreversible peripheral neuropathy (which is probably why it works). Severely affected patients are probably best referred to a dermatologist.

In Australia many patients with these

dermatoses have very sun damaged skin. Some of these patients may suffer from severe pruritus and treatment for those more severely affected may be complicated by the presence of significant skin cancer. It is sometimes difficult to differentiate skin cancer on the arms and legs, particularly *in situ* or well differentiated squamous cell carcinoma, from areas of prurigo nodularis.

Grover's disease (transient acantholytic dermatosis)

Grover's disease was first described in 1970, and in the Australian context is anything but transient. It is characterised by intensely pruritic, polymorphic papules, most often seen on the trunk of middle-aged and older Caucasian men (Figure 3a), although it also occurs in women. Sometimes papules will be found on the proximal extremities. Lesions may be vesicular and crusted (Figure 3b), bland or very inflammatory. They tend to fluctuate over the years and are exacerbated by heat, sweating, friction and sunlight. In some patients this condition is worse when their skin dries out in winter. Sun damage is a frequent cofactor.

The diagnosis is usually straightforward clinically but is confirmed by skin biopsy. As the histology can be variable, it is better to alert the pathologist to the possibility of this condition so that extra levels can be performed if needed.

Treatment can be frustrating. Good skin care with soap avoidance and moisturiser use helps, as does the use of moderate potency corticosteroids. Avoidance of occlusive clothing and overheating are important. Narrow band UVB therapy can be very helpful, despite sunlight being considered an exacerbating or contributing factor to the disease. Some patients will have a prolonged remission. The most severely affected patients may respond to oral retinoids such as acitretin (Neotigason).

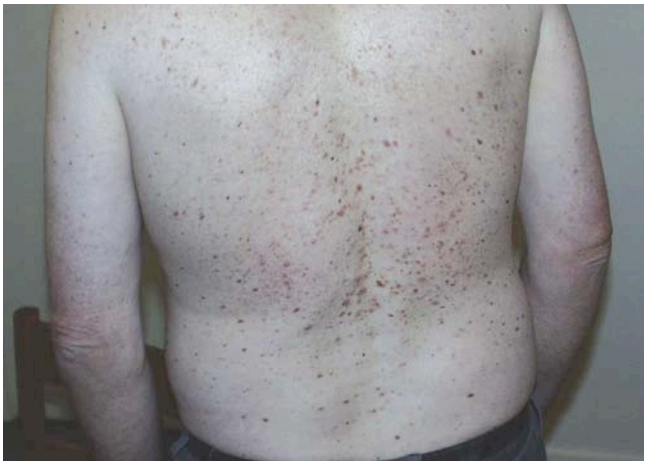
Brachioradial pruritus

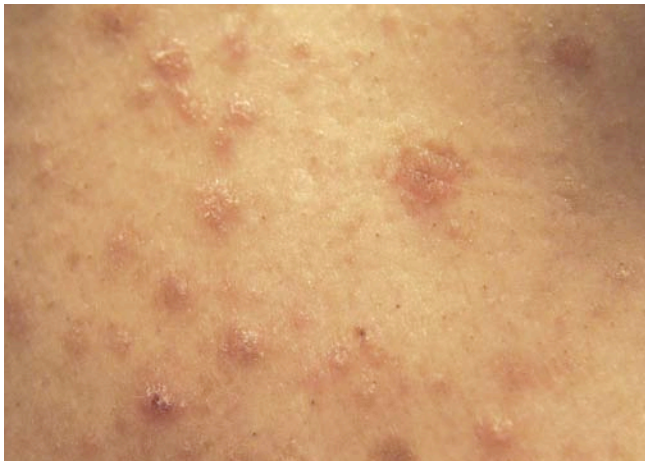
Brachioradial pruritus is an uncommon intermittent pruritus occurring above and/or below the elbow. The sufferer typically describes a severe itch, which can be burning in quality, is quite localised and may be more intense at night. There may be little to see clinically, although at times the skin may be excoriated and even eroded from scratching. Topical corticosteroids and moisturisers are of little or no benefit, but ice may provide some relief. The problem can be very severe and last for years. The clinical features are so consistent and distinctive that once recognised, the diagnosis is usually straightforward.

The exact aetiology of brachioradial pruritus remains debatable. Some patients are very sun sensitive and their skin may be very sun damaged. The condition may remit in the cooler months, and some dermatologists regard the condition as being due to cumulative solar damage. Others believe it is a form of radiculopathy with the localised pruritus corresponding to cervical dermatomes. It has been my experience that patients often have a history of neck pain, injury or other cervical pathology. An Australian study demonstrated good relief of symptoms with gentle cervical mobilisation, which has also been my experience. Other modalities that have helped include acupuncture, capsaicin (available from compounding chemists) and central medication with gabapentin.

Notalgia paraesthetica

Notalgia paraesthetica is another focal intense pruritus, which is localised to the medial scapular border. It is extremely common. Patients may have a hyperpigmented patch from rubbing, although often nothing is visible. Many patients will report that the itching sensation comes from deep within the body to the skin. It is thought to have a neuropathic or neurotoxic aetiology, but the exact cause is not known. Explanation to patients of the benign nature of the condition may





Figures 3a and b. a (left). Grover's disease on the trunk of a middle aged man. b (right). Typical vesicular and crusted lesions of Grover's disease.

suffice, but capsaicin is worth trying for those severely affected.

Other dysaethesias

Other dysaethesias often seen in patients referred to dermatologists include burning mouth syndrome, vulvodynia (chronic vulval pain), anodynia (chronic anal pain), burning scalp, penile pain and scrotodynia. Males with genital pain may also complain of a chronic red scrotum. These conditions are important causes of anxiety and suffering. They are too complex for discussion here, but in patients in whom there is no obvious pathology and chronic localised itch or pain it is worth considering a neurasthenic source for the symptoms.

Urticarial dermatitis

There is a group of poorly defined dermatoses characterised by chronic, often severe pruritus, occurring mainly on the trunk, with various clinical presentations, including papules, plaques and eczematous patches. In some patients, these dermatoses may evolve into late onset atopic dermatitis, or affected patients may be found to have contact dermatitis, a drug rash, or even cutaneous T-cell lymphoma. However, there remains a group of patients who do not fall into these categories and whose response to standard treatments for eczema, such as topical corticosteroids and moisturiser, is poor.

Kossard has coined the term urticarial dermatitis to categorise the dermatosis in one such group of patients. Urticarial dermatitis seems to have a consistent clinical course, rash morphology, treatment resistance pattern and histology. It usually affects middle aged to elderly men and women. The eruption consists of papules, patches and urticarial-like plaques, especially around the low back, hips and loins (Figure 4). The rash is longer lasting than that of urticaria, lasting weeks rather than hours, and responds poorly to antihistamines or topical corticosteroids. Oral corticosteroids in moderate dose (0.5 mg/kg) may produce relief, but this relief cannot be sustained with low doses. Other immunosuppressives have been used for the most severely affected patients. Narrow band UVB light administered three times a week has been the most effective remedy in my practice; however, it is not effective for all patients and is associated with some relapses.

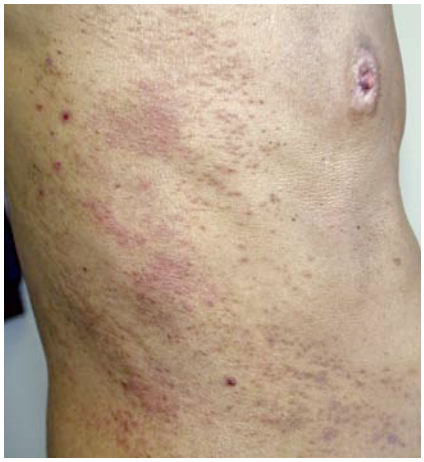


Figure 4. Urticarial dermatitis.

Conclusion

Pruritus is a common but complex management problem. Hopefully, this article has provided a practical approach both to the diagnosis of its causes, including some that are less well known, and to its treatment. MT

Further reading

1. Bolognia JL, Jorizzo JL, Rapini RP. Dermatology. New York: Elsevier; 2003.
2. Champion RH, Burton JL, Burns DA, Breathnach SM, editors. Rook/Wilkinson/Ebling textbook of dermatology. Oxford: Blackwell Science, 1998.
3. Tait CP, Grigg E, Quirk CJ. Brachioradial pruritus and cervical spine manipulation. Australas J Dermatol 1998; 39(3): 168-170.
4. Kossard S, Hamann I, Wilkinson B. Defining urticarial dermatitis: a subset of dermal hypersensitivity reaction pattern. Arch Dermatol 2006; 142: 29-34.

DECLARATION OF INTEREST: None.