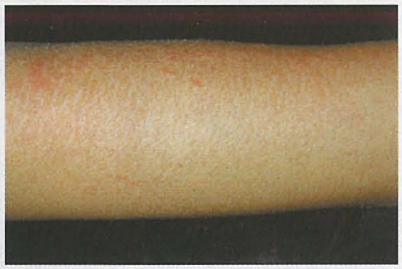
The skin and internal disease

The importance of looking beyond the skin

by **Michael Boffa** *MD FRCP(Edin) FRCP(Glasg) FAAD CCST(Derm)(UK) MSc(Lond)*
Consultant Dermatologist

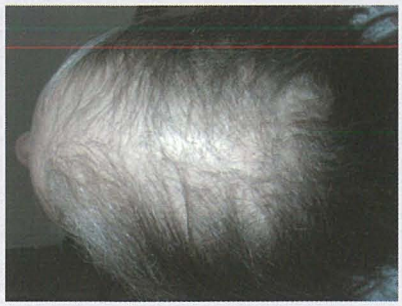
The skin is the largest organ in the human body. It has important 'local' roles such as protecting internal structures from potentially harmful factors in the environment but in addition is very much an integral part of the body and has a complex structure endowed with a rich blood supply and elaborate immune system. It is therefore not surprising that the skin and its appendages can be affected by a wide range of diseases of other organ systems. Correct diagnosis of cutaneous manifestations may be of immense help in the diagnosis of underlying medical conditions. This article will focus on a selection of skin problems and discuss their associations with internal disease and also briefly review skin manifestations of certain disease states. Topics likely to be relevant to a general medical audience are emphasised.



Xerosis

Generalised pruritus

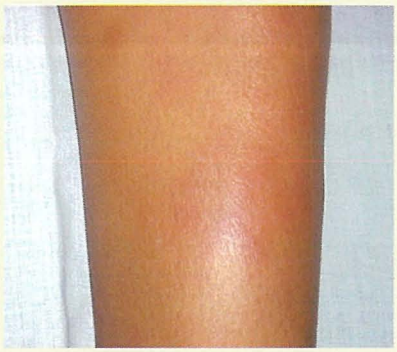
In most cases pruritus is due to obvious skin conditions such as eczema, xerosis (dry skin), urticaria, lichen planus, scabies, pediculoses and psoriasis. Less common cutaneous causes of pruritus include dermatitis herpetiformis, bullous pemphigoid, pemphigus foliaceous and mycosis fungoides. Occasionally, pruritus may be caused by an underlying medical problem and in some cases itching may be the presenting complaint and an important clue in its diagnosis. Patients with unexplained pruritus should get a thorough history and examination and basic blood investigations (full blood count, ferritin, creatinine, liver and thyroid function tests) to detect possible underlying medical conditions.



Diffuse hair loss

Diffuse hair loss

Diffuse alopecia affects hairs throughout the scalp in a more or less uniform pattern without visible inflammation or scarring. Causes of diffuse alopecia include drugs (eg. coumarins and heparin), telogen effluvium (as seen after childbirth, major surgery and illnesses, psychological stress and crash dieting) and anagen effluvium (as seen following cancer chemotherapy). Iron deficiency is an important and common cause of diffuse hair loss in menstruating women who habitually eat little red meat. Diffuse alopecia may occur in several endocrine syndromes including hypo- and hyper-thyroidism, hypopituitarism and hypoparathyroidism. Useful investigations in patients with diffuse hair loss therefore include full blood count, ferritin and thyroid function tests. Chronic, progressive, diffuse, 'androgenetic' hair loss in women starting in their 20s and 30s is common and is usually due to an inherited trait. Serious underlying hormonal abnormalities are rare but should be considered especially in patients with menstrual irregularities and hirsutism with or without signs of virilisation.



Erythema nodosum

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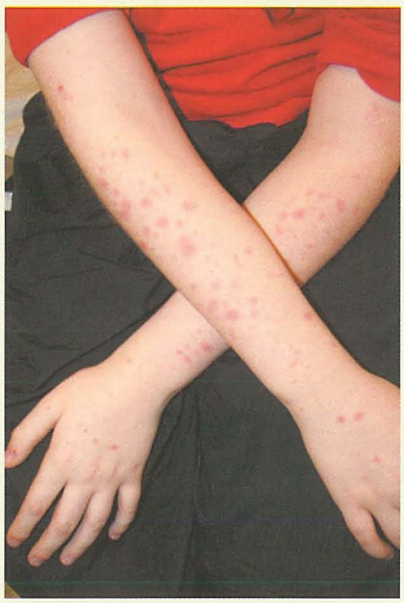
Erythema nodosum is a reactive inflammation of the subcutaneous tissue that typically presents with ill-defined, tender, erythematous plaques or nodules symmetrically distributed over the shins. The condition may be triggered by a variety of factors including infections (eg. streptococci, *mycobacterium tuberculosis*, yersinia, chlamydiae and viruses), sarcoidosis, drugs (especially oral contraceptives and sulphonamides), inflammatory bowel disease and, rarely, malignant disease. Investigations required depend on the clinical setting but in most cases include full blood count, throat swab, antistreptolysin O titre and chest X-ray.



Erythema multiforme

Erythema multiforme

Erythema multiforme is characterised, as the name implies, by varying clinical manifestations ranging from symmetrically distributed erythematous maculopapules with central ischaemia ('target lesions') on the acral regions, elbows and knees to severe disease with mucous membrane involvement (Stevens-Johnson syndrome). Causes include infection (eg. *Herpes Simplex*, mycoplasma, hepatitis B, infectious mononucleosis and other organisms), drugs (eg. sulphonamides, non-

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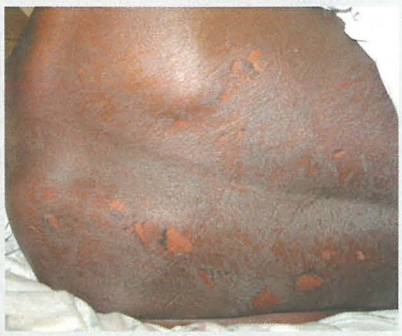
steroidal anti-inflammatory drugs, antiepileptics, oral contraceptives and others), connective tissue diseases, pregnancy and internal malignancy. In toxic epidermal necrolysis, Stevens-Johnson-like mucous membrane disease is accompanied by progressive, generalised loss of skin; the condition is life-threatening and usually caused by a drug reaction.



Toxic Epidermal Necrolysis

Diabetes mellitus

Patients with diabetes are prone to various skin problems. The commonest is probably cutaneous candidiasis, particularly of the genitals (where it may be the presenting feature of diabetes), intertriginous areas, mouth and nail folds. Good diabetic control is essential for managing cutaneous candidiasis. Furuncles and other *Staphylococcus Aureus* infections are also more common in diabetics. Specific cutaneous complications of diabetes include diabetic dermopathy (dull-red papules on the shins evolving into atrophic brownish scars) due to microangiopathy and possibly neuropathy, necrobiosis lipoidica (degenerative disease of collagen causing erythematous, atrophic, yellowish plaques on the anterior surfaces of the lower legs; this disease is very resistant to treatment) and insulin reactions and lipodystrophy (rare with modern insulins). Diabetic neuropathy may present with decreased sweating of the lower extremities, erythema, atrophy and oedema associated with numbness, tingling and burning. Diabetic neuropathy may lead to catastrophic trophic ulceration over pressure sites and deserves the utmost attention. Skin conditions that are commoner in diabetics include disseminated granuloma annulare, vitiligo, eruptive xanthomas, scleroedema and reactive perforating collagenoses. Contrary to popular belief, diabetes *per se* does not cause generalised pruritus however anogenital candidiasis associated with poor diabetic control may, of course, cause troublesome localised itching.

Liver disease

Hepatobiliary diseases are often associated with abnormalities of the skin, nails and hair. Pruritus is the commonest cutaneous symptom in liver disease and may precede the appearance of jaundice. In obstructive liver disease itch is thought to be due to the presence of bile salts in the skin but other liver metabolites may be involved. Other cutaneous signs of chronic liver disease include telangiecteses (due to hyperoestrogenaemia), hyperpigmentation, xanthomatosis (typically in primary biliary cirrhosis), diffuse alopecia (may be due to zinc deficiency) and nail changes including clubbing. Pellagra, seen mainly in alcoholics, is due to dietary deficiency of niacin; it typically presents with dermatitis and pigmentation in photoexposed areas, sometimes associated with diarrhoea and mental disturbances and responds rapidly to oral vitamin replacement.

Renal disease

Pruritus is a common and distressing complication of chronic renal failure and is seen in the majority of patients on haemodialysis. It may be persistent, extensive and intractable but in others may be transitory and localised. The pathophysiology is debated but may include secondary hyperparathyroidism, aluminium overload during dialysis and skin dryness. Treatment is difficult. Emollients may be helpful for patients with dry skin and some may benefit from ultraviolet B phototherapy.

Internal malignancy

The skin may be associated with internal malignancy in a number of ways. Skin changes may be a marker for an inherited condition associated with malignancy (eg. Peutz Jeghers syndrome – periorificial lentigines associated with intestinal polyposis), occur as a result of treatment of internal malignancy or represent direct tumour extension or metastases to the skin. Paraneoplastic syndromes are diseases that appear before or concurrently with an internal malignancy and result from production of biologically active hormones, growth factors or antigen-antibody interactions induced by the tumour. Examples include dermatomyositis, acanthosis nigricans, acquired ichthyosis, acquired hypertrichosis and erythema gyratum repens. Such syndromes may be associated with cancer of a wide range of internal organs including lung, breast, female and male genital tracts, stomach, kidney, colon and rectum and lymphoid tissue. The skin changes may be the initial clue to the presence of an underlying neoplasm and it is therefore vital that such changes are recognised and investigated properly.

Figure 1

Systemic conditions associated with generalised pruritus

Chronic renal failure

Biliary disease
- Primary biliary cirrhosis
- Drugs
- Extrahepatic biliary obstruction
- Intrahepatic biliary obstruction of pregnancy

Hyper & hypothyroidism

Malignancies
- Lymphoma (especially Hodgkin's lymphoma)
- Leukaemia
- Multiple myeloma
- Other malignancies

Haematological disorders
- Iron deficiency
- Myeloproliferative disease especially polycythaemia rubra vera