Review Article

ECZEMA: THE SPECTRUM OF CLINICAL PRESENTATIONS

Rannakoe J Lehloenya
Division of Dermatology, Department of Medicine, University of Cape Town
Combined Drug Allergy Clinic, Groote Schuur Hospital, Cape Town
Email | rannakoe.lehloenya@uct.ac.za

INTRODUCTION

In 1982, A Bernard Ackerman, considered by many to be the founding father of dermatopathology, published a plea to expunge the word 'eczema' from the lexicon of dermatology and dermatopathology. His reasoning was that the term has never been defined in a repeatable way and despite innumerable attempts at a definition, the word 'eczema' still lacks specific meaning.[1–3] The definition of eczema that is most acceptable to dermatologists is that it is a non-infectious papular or papulo-vesicular eruption characterised histologically by spongiosis (intercellular oedema within the epidermis). However, there are other dermatoses such as pityriasis rosea that fit this definition but are not considered eczematous. In the same breath, the prototype eczematous condition, atopic eczema, often does not exhibit spongiosis.[1] Despite Ackerman's attempts as well as those of many others, the terms 'eczema' and 'dermatitis' are used interchangeably both in clinical medicine and dermatopathology.[4] In this review, we use the term 'eczema' as a synonym for both terms.

The challenge in case definition, suggests that what is commonly referred to as eczema is a group of heterogeneous conditions that have a spectrum of overlapping clinical and histological features that do not always all manifest in one phenotype. This is possibly the reason why many non-dermatologists sometimes find it difficult to diagnose eczema. Even the most experienced dermatologists frequently rely on a correlation of clinical features and histology to make the diagnosis of eczema. Until we can determine the pathogenesis, develop diagnostic tests and protocols to differentiate the individual conditions broadly referred to as eczema, clinicians will have continue managing this constellation of disorders under this broad term.

Pattern recognition is an integral part of diagnosing any skin disease. To recognise these patterns, primary, secondary and tertiary features of the eruption need to be identified and described. Primary morphology refers to the single unit or lesion of the eruption, for example a patch, a plaque, a nodule, a blister, etc. Secondary morphology refers to how these single units relate to each other, for example: Are they grouped, like vesicles in herpes simplex, are they annular papules as seen in granuloma annulare or are they linear blisters as in herpes zoster? Tertiary morphology refers to the distribution of the lesions in the context of the whole body, for example grouped vesicles on the lower lip or dermatomal in herpes simplex and herpes zoster respectively, erythematous patches and plaques that are accentuated in the cubital and popliteal fossae in childhood atopic eczema. These, together with the history and the context help reach the diagnosis. It is also important to remember that a clinician usually encounters the eruption at one point in time and needs to make an inference on how the lesions appeared previously and how they will evolve. Using this approach, this article will describe briefly and pictorially the spectrum and evolution of conditions that are referred to as eczema. We will also briefly highlight important management considerations for each phenotype of eczema.

ATOPIC ECZEMA

Atopic eczema is a clinically defined chronic, relapsing, pruritic, inflammatory skin disease that clusters in families with atopic diseases (atopic eczema, bronchial asthma and/or allergic rhinoconjunctivitis). Prevalence of atopic eczema ranges from 2% in young adults and up to 20% in children. Atopic eczema is a result of a complex interaction of genetic and environmental factors. Barrier defect of the skin, characterised by increased transdermal water loss, is central to the pathogenesis. The skin in atopic eczema is more susceptible to irritation by soaps and other contact irritants, coarse fibres in clothes, high ambient temperature and weather changes among others. The morphology and distribution pattern of atopic eczema lesions varies, not only between individuals, but also with age and anatomical location. In infancy, the cheeks are usually the first to manifest a dry, scaly, erythematous rash that over time becomes generalised. In severe cases, the rash is wet and weepy, often sparing the central face (see Figure 1). Excoriations are a common feature at this age. As the children start to become mobile and up to preschool years, the lesions tend to become localised to extensor surfaces of joints and genitalia, lichenified and the excoriations deeper (see Figure 2). In later preschool years and school-going age, the lesions tend to be more accentuated in the flexor surfaces, particularly elbows and knees. Other body folds, for example eyelids, earlobes and the neck can also be affected (see Figure 3). In adulthood, the clinical presentation is more variable. The childhood pattern may be maintained or the lesions may localise to flexures, eyelids, nipples, lips and hands (see Figure 4). The adulthood lesions tend to be dry and lichenified.[5] People with atopic eczema are more susceptible to bacterial, viral and fungal infections, some of which play a role in triggering and maintaining the chronic inflammation (see Figure 5).[6,7]

The natural history of atopic eczema in an individual cannot be predicted. Atopic eczema persists in less than 5% of 20 years olds who had the disease as children. However, predisposition to contact eczema and skin sensitivity persists lifelong.[5] Management of atopic eczema requires a multi-pronged approach to control the triggers and drivers of the disease as well as targeted treatment. The management strategies include avoidance of allergens, irritants, long hot baths, dry environmental conditions and coarse fibres in clothes. Emollients, wet wraps, topical steroids, topical calcineurin inhibitors, sedating antihistamines, antibiotics, phototherapy and systemic immunomodulators are used, depending on the severity of the disease.[4]

Figure 1: Weepy eczema on the cheeks of atopic children. (Note the sparing of the central face.)

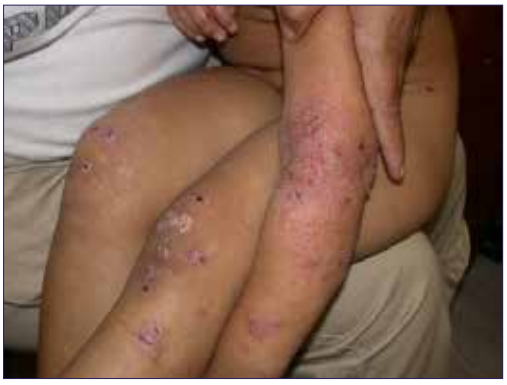


Figure 2: Eczema in an older child showing flexural accentuation as well as deep excoriations.

PITYRIASIS ALBA

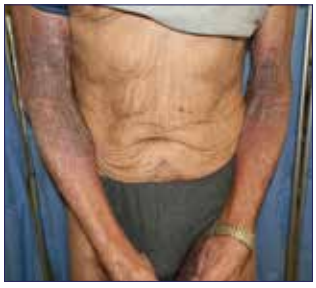
This is considered to be a low-grade form of eczema that predominantly affects children and adolescents. Pityriasis alba is characterised by round, scaly, hypopigmented patches that are usually found on the face. The lesions go through stages of being palpably scaly and erythematous; hypopigmented plaques with fine scale; hypopigmented macules; and then resolution. Itch is not a major feature of the condition. The pigmentary changes are more prominent in dark skin (see Figure 6). Emollients, mild topical corticosteroids and calcineurin inhibitors are effective treatments.[8]

SEBORRHEIC ECZEMA

Seborrheic eczema is a common, chronic and relapsing dermatosis that affects areas of the body that have large sebaceous glands with or without associated terminal hairs. These include the scalp, nasolabial folds, ears, eyebrows, the beard area, presternum, axillae and groin. Pseudonyms

Figure 3: Involvement of flexures in atopic eczema A) ear lobes, B) eyes, C) angle of the mouth, D) popliteal fossa, E) gluteal fold.

Figure 4 (right): Eczema in the cubital fossae of an adult.



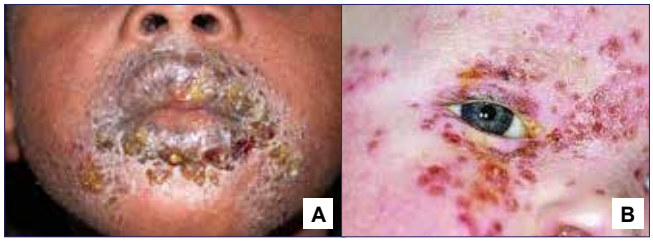


Figure 5: Secondarily infected atopic eczema, A) impetigo B) eczema herpeticum due to herpes simplex.

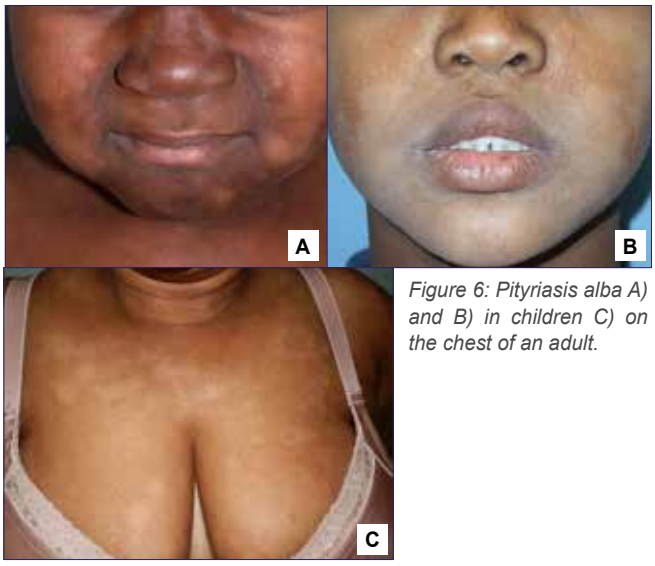


Figure 6: Pityriasis alba A) and B) in children C) on the chest of an adult.

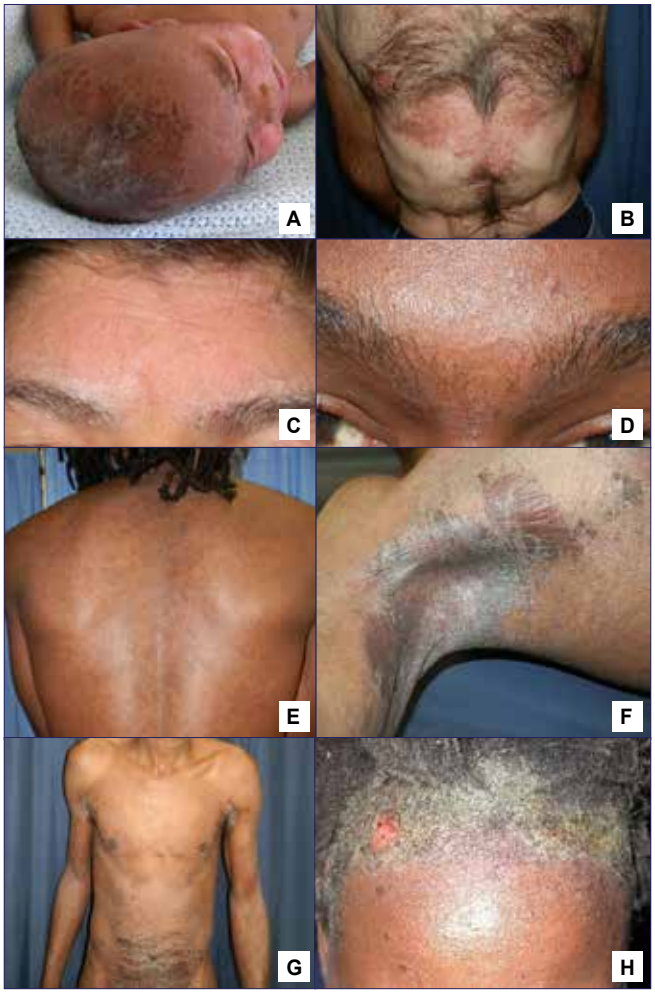


Figure 7: Seborrheic eczema; A) cradle cap in a baby, B) on the chest of an adult, d) on the scalp and eyebrows of two adults, D) & E) petaloid variant on the eyebrows and the back of an adult, F) & G) severe weepy variant in an HIV-infected adult, H) scalp involvement in HIV

of seborrheic eczema include sebopsoriasis, seborrheic dermatitis, dandruff and pityriasis capitis again reflecting a wide clinical spectrum and uncertain pathogenesis. The incidence of seborrheic eczema peaks in the first 3–6 months of life, puberty and after the age of 50. Androgens, *Malassezia furfur* (a fungus) infection, neurologic and psychiatric disease, and altered immunity (as seen in HIV and organ transplant) are thought to play a pathogenic role.[9] An autosomal recessive inherited seborrheic eczema has been identified in mice, although a similar pattern is yet to be identified in humans.[10] The morphology of seborrheic eczema ranges from that of acute eczema, psoriasis-like, petaloid (petal-like), greasy or dry flaky scale. In moist areas the lesions becomes wet and weepy. Erythema in pigmented skin is less visible and post-inflammatory hyperpigmentation is common (see Figure 7).[11] In HIV-infected patients the incidence can be as high as 80%, being reported as the second most frequent cutaneous finding is some series. In this setting, it is more severe, usually starting in the typical areas then becoming more widespread.[11] Treatment is directed at treating known causes and triggers, clearing signs and symptoms of the disease and maintaining remission with long-term therapy. Based on this, the most common treatments are topical antifungal and anti-inflammatory agents. Other therapeutic modalities used include coal tar, keratolytics such as salicylic acid and lithium gluconate/succinate.[12]

NUMMULAR ECZEMA

Also referred to discoid eczema, nummular eczema is a relapsing, itchy condition characterised by round, well demarcated 'coin-like' lesions. Two forms of the condition are recognised: exudative acute nummular eczema which presents with weepy blisters and plaques; whereas dry nummular eczema, the subacute or chronic variant is characterised by dry plaques that sometimes have an annular configuration (see Figure 8). In darker skin it is often associated hyperpigmentation. Nummular eczema is most prevalent on the lower legs, although arms and trunk can be affected. Although the exact pathogenesis is not

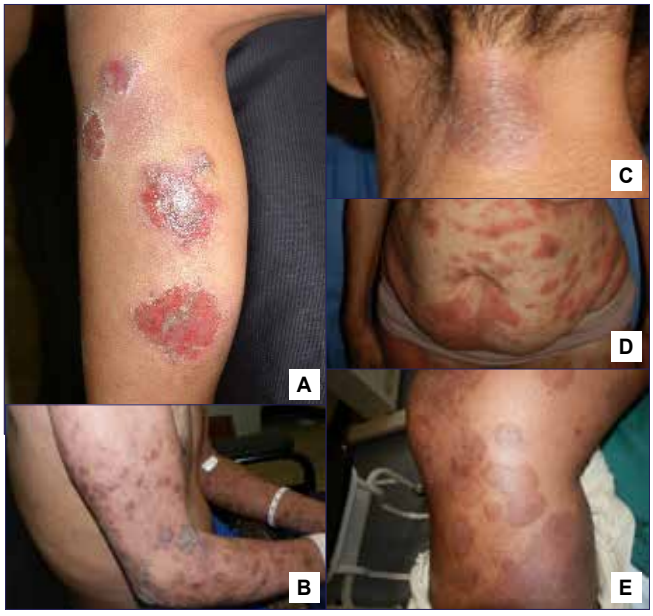


Figure 8: Nummular eczema variants. Note E) the annular variant that is often confused with tinea corporis.

clear, background of atopy, previous contact eczema and stasis eczema have a strong association with nummular eczema. Allergens, bacterial infection, drugs, xerosis and varicose veins are among known precipitants. Nummular eczema is fairly resistant to treatment but responds to emollients and potent topical steroids, sometimes under occlusion. In resistant cases, phototherapy and oral immunomodulators are used.

STASIS ECZEMA

This is also referred to as gravitational or venous eczema. It is characterised by oedema of the lower legs that is associated with itchy erythematous plaques. The plaques can be weepy, crusted or scaly. Over time, they become confluent, circumferential, hyperpigmented and may ulcerate (see Figure 9). Hyperpigmentation is a result of haemosiderin deposition from extravasated red blood cells. In advanced stages of stasis eczema, there is fibrosis of the lower legs resulting in narrowing and the 'inverted wine bottle' appearance and ulceration.[13] Stasis eczema can also be seen following breast surgery and lymph-node dissection.[14] Apart from topical corticosteroids and emollients, lifelong compression stockings are the mainstay of treating stasis eczema.[13]

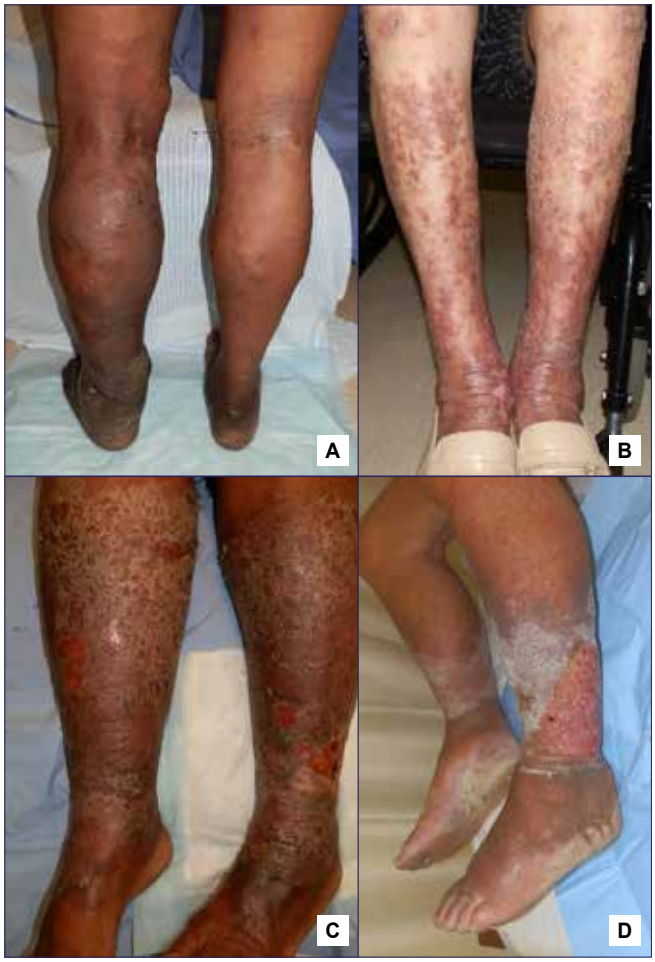


Figure 9: Stasis eczema. A) on the background of varicose veins. The left leg had a previous fracture, B) acute weepy variant, C) early ulceration, D) dry scale with ulceration.

ERYTHRODERMIC ECZEMA

Erythroderma is defined as an erythematous eruption affecting more than 90% of the body surface area as a result of any inflammatory condition. Erythroderma refers more to the extent of erythema rather than the cause. Chronic erythroderma results in excessive scale, referred to as exfoliative dermatitis (see Figure 10). Erythroderma should be differentiated from flushing, which has no associated scale. Causes of erythroderma include eczema, psoriasis, drug reactions, pityriasis rubra pilaris, cutaneous T-cell lymphoma, congenital ichthyosis disorders and internal malignancies. Complications of erythroderma include impaired temperature control, fluid loss, secondary infection and hypoalbuminaemia. Children are more susceptible to hypothermia. Management includes treating the underlying disorder, managing complications, emollients and topical steroids.[15]

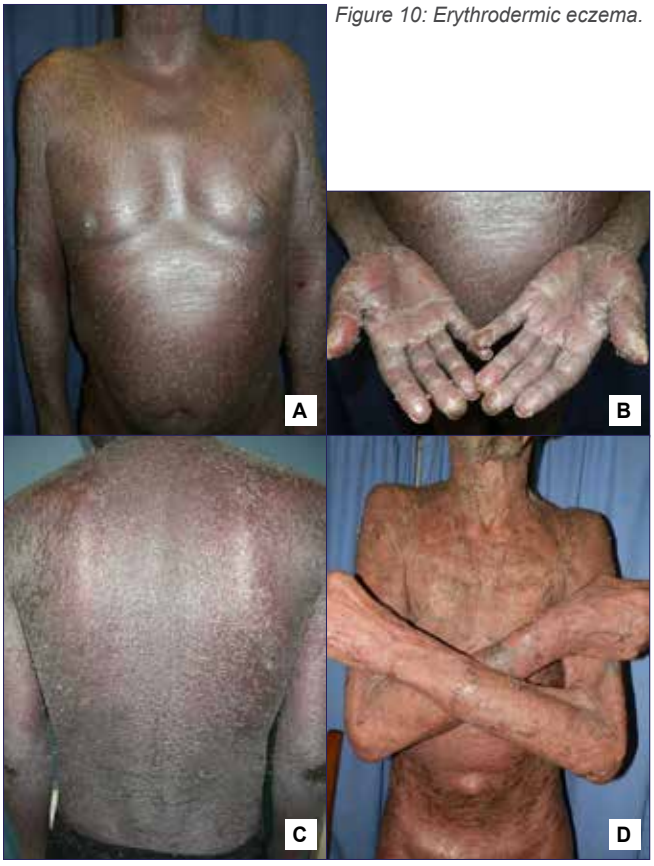


Figure 10: Erythrodermic eczema.

DYSHIDROTIC ECZEMA

Dyshidrotic eczema, also known as pompholyx, is a chronic relapsing disease characterised by itchy vesicles and blisters on the palms and soles. On resolution and, if untreated, it results in thick scale and deep painful fissuring of the hands and feet (see Figure 11). The disease does not affect sweat glands and the term 'dyshidrosis' is a misnomer. Dyshidrotic eczema has been associated with atopy, allergic contact eczema, irritants, hyperhidrosis and fungal infection.[16] Management is challenging and includes identification and avoidance of triggers.

Topical therapies include corticosteroids, calcineurin inhibitors, bexarotene and phototherapy. Systemic agents that have been tried in severe recalcitrant cases include corticosteroids, azathioprine, methotrexate, mycophenolate mofetil and retinoids. Botulinum toxin has been successfully used in a small series of patients.[16]

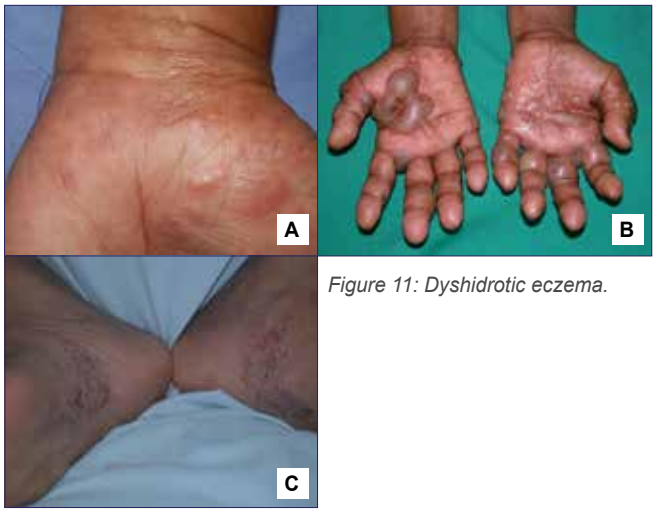


Figure 11: Dyshidrotic eczema.

NIPPLE ECZEMA

Nipple eczema can be a manifestation of atopic eczema or exist in isolation. The clinical presentation is variable and ranges from erythema, scale, blisters, scale crust, fissures, erosions and lichenified plaques (see Figure 12). Nipple eczema is usually bilateral but can be unilateral, particularly when it is not associated with atopy. Although most commonly seen in young women, nipple eczema has also been reported in males.[17] The pathogenesis of nipple eczema has not been clearly defined, but it has been shown to have a strong relationship with atopy and allergic-contact eczema.[17,18] Paget's disease is the major differential diagnosis of nipple eczema, although the latter has an insidious onset and is almost always unilateral.[19] In breastfeeding women, allergic or irritant contact eczema and superimposed candidiasis have to be considered in the differential diagnosis. Eczema on the nipple is treated like eczema in other parts of the body.

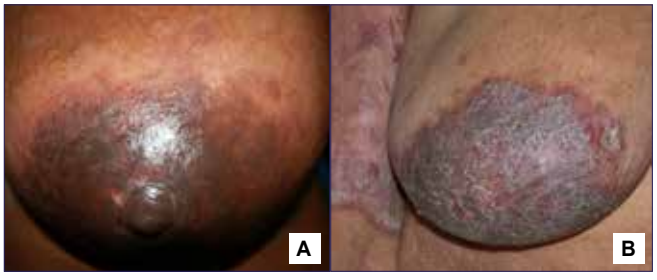


Figure 12: Nipple eczema.

NODULAR PRURIGO

Nodular prurigo is a manifestation of severe prolonged scratching due to multiple underlying conditions. Nodular prurigo has the strongest association with atopic eczema which is reported in 80% of cases. Other associated disorders include liver failure, chronic renal failure, nerve compression and HIV-associated papular urticaria. The lesions present as symmetrical firm nodules with a warty or eroded surface. In darker skin they are often hyperpigmented (see Figure 13). Nodular prurigo is resistant to treatment and standard treatment modalities include potent topical and intralesional corticosteroids, calcineurin inhibitors and phototherapy. Cryotherapy, capsaicin, systemic immunomodulators, gabapentin, thalidomide and tricyclic antidepressants have also been tried.[20]

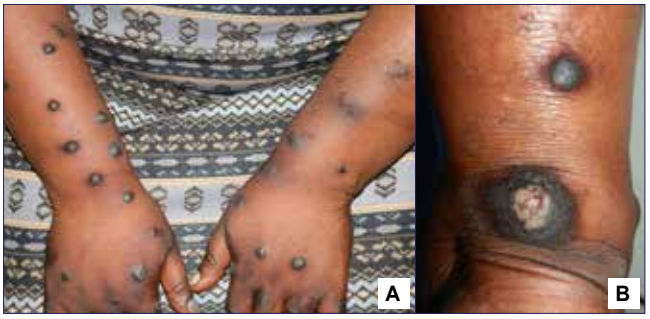


Figure 13: Nodular prurigo showing verrucous warty nodules in B.

LICHEN SIMPLEX CHRONICUS

Lichen simplex chronicus also referred to as lichenification, is a result of chronic scratching from any cause, eczema included. It characterised by exaggerated skin markings, leathery induration, pigmentary changes and scale (see Figure 3D and Figure 14). Broken hairs and scratch marks may be a feature. Back of the scalp and neck, wrists and forearms, lower legs and genitalia are the most commonly affected areas. Apart from identifying and eliminating the underlying cause, topical corticosteroids, emollients, topical calcineurin inhibitors, intra-lesional corticosteroids and phototherapy are the major treatment modalities of lichenification.[21]

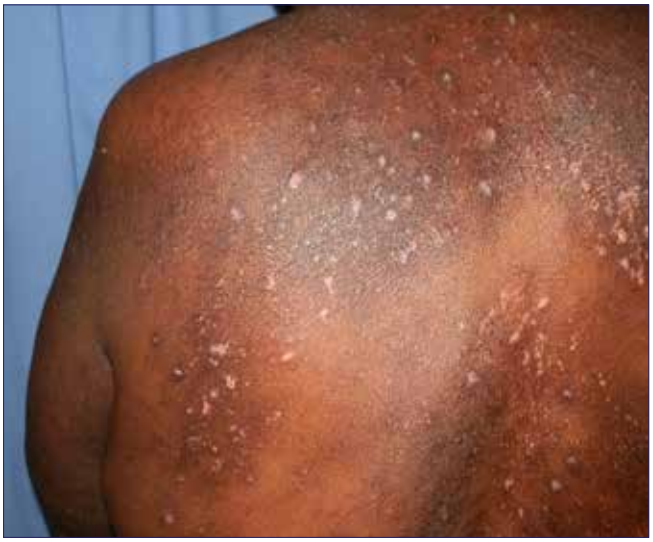


Figure 14: Lichen simplex chronicus.

ASTEATOTIC ECZEMA

Asteatotic eczema, also known as eczema craquele because of its 'cracked appearance', is a common disorder in the elderly characterised by a crazy paving appearance of the skin associated with pruritus. It is most common on the lower legs, but it may occur elsewhere including upper limbs and trunk (see Figure 15). The exact pathogenesis is not clear but it is thought to be a result of desiccation of the stratum corneum resulting in cracked skin. The cracks expose free nerve endings on the skin, triggering itch. Soaps, detergents, excessively hot baths and dry environments aggravate asteatotic eczema. The conditions can be associated with old age, malnutrition, hypothyroidism, inherited and acquired forms of ichthyosis, internal malignancies and drugs (e.g. retinoids). Emollients and mild topical corticosteroids are the mainstay of asteatotic eczema treatment. Avoidance of triggers and exacerbating factors improves treatment outcomes. Although infrequent, it is important to rule out underlying disease.[22,23]

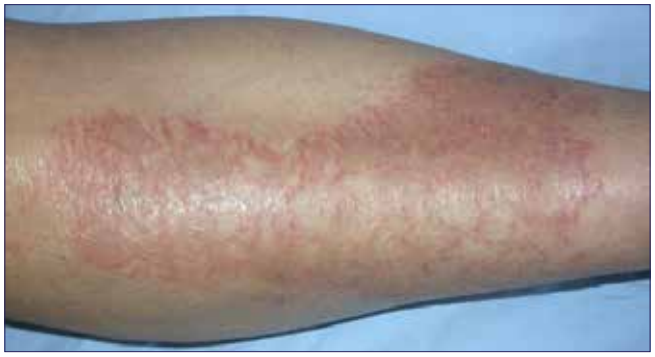


Figure 15: Asteatotic eczema.

CONTACT ECZEMA

Contact eczema refers to a group of disorders in which the skin reacts to a direct contact with the causative agent. Contact eczema is classified into allergic, irritant, photo and systemic forms based on the underlying mechanism and clinical appearance. There is often overlap between the different forms.

ALLERGIC-CONTACT ECZEMA

In allergic-contact eczema, the material coming into contact with the skin is an allergen that induces a delayed type hypersensitivity reaction only in susceptible people. Impaired barrier function of the skin as seen in ulcers and atopy predisposes to allergic-contact eczema. The reaction usually mirrors the area of contact although it may extend beyond the margins (see Figure 16). Although common in the general population, allergic-contact eczema tends to cluster in certain occupational groups such as hairdressers, cleaners and florists. Common causes include nickel, acrylates in glue, fragrances, rubber, hair dye, preservatives, topical antibiotics and topical steroids. A good history and pattern recognition are critical in the diagnosis of this and other forms of contact eczema. Patch tests are used to confirm the allergen.

IRRITANT-CONTACT ECZEMA

Irritant-contact eczema occurs when exposure to chemicals (body fluids, water, detergents) and physical agents (friction, heat, cold) damage the skin resulting in impaired barrier function and subsequent inflammatory response. The speed of onset and severity depend on the anatomical location, strength and quantity of irritant, as well as frequency and duration of exposure. Unlike in allergic-contact eczema, anyone with adequate exposure to the irritant can develop irritant-contact eczema. The rash is usually confined to the area of contact with the irritant (see Figure 17). Common examples of irritant-contact eczema include napkin eczema, drool eczema and chemical burns. There are no tests that can confirm irritant-contact eczema.

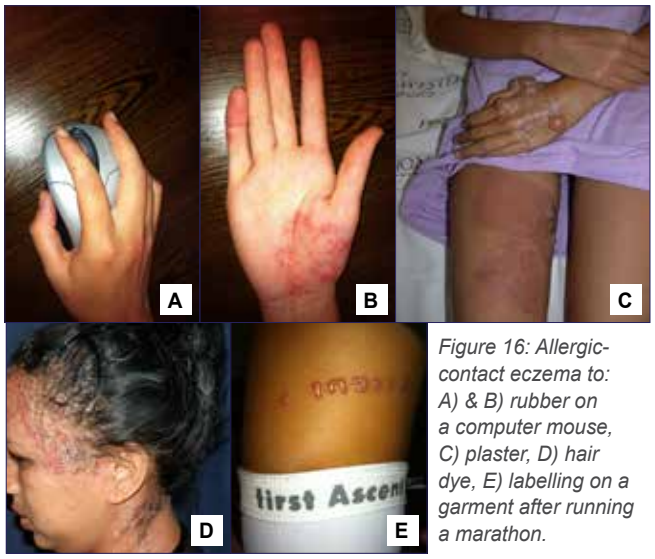


Figure 16: Allergic-contact eczema to: A) & B) rubber on a computer mouse, C) plaster, D) hair dye, E) labelling on a garment after running a marathon.

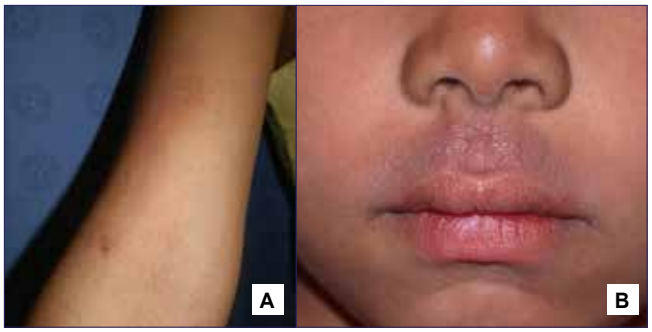


Figure 17: Irritant-contact eczema to A) a liquid B) chronic lip sucking.

PHOTOCONTACT ECZEMA

Photocontact eczema refers to an eczematous reaction that develops when a chemical applied to the skin interacts with ultraviolet (UV) radiation. The reaction can either be photoallergic or phototoxic. Photoallergic reaction is a delayed type hypersensitivity reaction to the UV-activated chemical, whereas phototoxicity results from direct tissue damage by the UV-activated chemical. Phototoxicity resembles severe sunburn, whereas photoallergy presents as an eczematous eruption in sun-exposed areas.[24]

SYSTEMIC-CONTACT ECZEMA

Systemic contact eczema refers to development an eczema when a person with existing allergic-contact eczema is exposed to the allergen via a systemic route (oral, inhalation, injection or

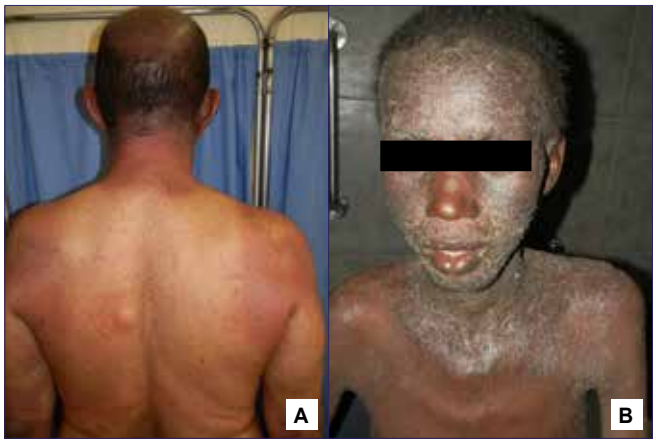


Figure 18: Photocontact eczema.

transmucosal). The most common feature is a flare-up at the site of previous contact or patch test, although the rash may become generalised. The spectrum of lesions is as wide as eczema itself but dyshidrotic eczema is particularly common. Another unique presentation of systemic contact eczema is baboon syndrome. In baboon syndrome, the erythematous rash is accentuated in the buttocks and upper inner thighs, hence the name. This should be differentiated from symmetrical drug-related intertriginous and flexural exanthema (SDRIFE), a form of cutaneous drug reaction with a similar clinical presentation.[25,26]

DISSEMINATED SECONDARY ECZEMA

Disseminated secondary eczema is also referred to as auto-eczematisation or ID reaction. It is a generalised acute eczema that follows another localised inflammatory skin disease. The lesions are intensely pruritic, symmetrical and usually affect the trunk and limbs. The morphology ranges from blisters, papules, nummular, follicular papules, morbilliform, targetoid and dyshidrotic. The preceding inflammatory diseases include other forms of eczema (stasis, nummular and acute contact), infections (fungal, bacterial and viral) and infestations (scabies and lice). The pathogenesis of disseminated secondary eczema is unknown. It is postulated to be an immune response to circulating antigens, skin components or messenger proteins. Treatment of the underlying condition is the mainstay of management. The secondary eczema should be managed based on the phenotype.[27]

CONCLUSION

Eczema is an umbrella term for multiple conditions with differing pathogenesis, clinical presentation and natural history. Clinicians need to be able to distinguish between the variants as this affects management and prognosis.

DECLARATION OF CONFLICT OF INTEREST
The author declares no conflict of interest.

This article has been peer reviewed.

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