Atopic Dermatitis in Skin of Color

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Atopic dermatitis (AD) is a common inflammatory skin disease which occurs worldwide. It is a chronic relapsing eczematous skin disorder associated with xerosis and pruritus. AD is widespread in industrialized countries with an overall prevalence of 10–20% among school children from the USA and parts of Europe. The countries in South Europe and the African continent show lower prevalence; however, it is a growing clinical problem in sub-Saharan Africa. In West Africa and other parts of the continent, the incidence of AD is considered to involve around 5% of the population, and this rate is still rising. Atopic dermatitis can occur at any age but usually develops in childhood. Its acute phase occurs during infancy and has a predilection for the face and extensors. As the children grow older, the skin lesions become chronic and lichenified, usually involving the flexural areas. There is often an association of AD with a personal or family history of atopy, e.g., asthma, allergic conjunctivitis, and allergic rhinitis.

3.1 Epidemiology

The varying prevalence of AD suggests that there are multiple environmental risk factors that occur in different regions of the globe, including climate [1], residence in an urban area [2], water hardness and increased water exposure [3], early-life infectious exposures [4], diet, obesity [5, 6] and skin care practices [7]. Many of these risk factors differentially impact some sociodemographic groups, e.g., those with higher consumption of Western diet, obesity, and less early-life vaccination in African-Americans than in Caucasians. Lower water quality is more likely in areas of poverty and lower socioeconomic status [8]. It is possible that ethnic differences with respect to the above risk factors contribute to regional disparities in AD. In addition, black-skinned individuals had lower levels of skin ceramides than Asians and Caucasians [9] and higher levels of transepidermal water loss than Caucasians [10, 11]. The prevalence of atopic dermatitis in African-American children is significantly higher than in Caucasians [12]. However, the severity of AD was found in multivariate analyses significantly associated with lower household income, but not with ethnicity [13].

3.2 Pathogenesis

There is a genetic link with AD although a clear mode of inheritance has not been established. The chromosomal regions 3q21 and 5q31 have been linked with high serum IgE levels as well as with the presence of skin lesions, associated with impaired barrier function and consecutive xerosis. In particular, baseline measurements of transepidermal water loss were found significantly higher in Asians and black-skinned individuals as compared to white Caucasians, suggesting that black skin is more susceptible to xerosis [14] and more sensitive to irritants than white skin [15]. Low levels of ceramides also contribute to dryness of the skin in AD; the disrupted epidermal barrier causes high susceptibility to irritants, microbial and other allergens, and environmental factors. Irritants in AD include harsh detergents and soaps, synthetic fabrics, as well fragrances, and most frequent allergens are dust mites, pollen, animal dander, and molds. Food allergies occur primarily in children younger than 2 years, the most common food allergens are cow's milk, eggs, peanuts, soya, and wheat.

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Staphylococcus aureus frequently colonizes eczematous skin and can also act as a super antigen bypassing antigen-presenting cells to directly activate T cells resulting in the induction of a Th2-dominant immune response in skin. Staphylococci are also implicated in causing secondary impetigo in AD; in addition, AD patients are predisposed to both herpes simplex and pox virus infections leading to eczema herpeticum and molluscum contagiosum, respectively.

Another player in the pathogenesis of AD is *filaggrin* (FLG) which is broken down into a natural moisturizing factor in stratum corneum playing an integral role in skin barrier function [16]. Mutations of FLG gene lead to deficiency of this factor [17] resulting in xerosis [18]. Multiple FLG mutations have been identified, shown to be a risk factor for AD [19]. FLG mutations were detected in 27.5% of white-skinned and only in 5.8% of African-American children with AD [20]. A follow-up study demonstrated common loss of function mutations of the FLG2 gene in African-Americans, not present in patients with European ancestry. Children with FLG2 loss of function mutations were less likely to be symptom free over time [21]. A study of 18 African-American children with AD and ichthyosis vulgaris and 17 African-American non-atopic controls found that only 22.2% of those with AD and 5.9% of the controls were heterozygous for FLG null mutations [22]. Taken together, these studies suggest that FLG2 may play an important role in AD in African-Americans but that one or more factors other than filaggrin mutations are responsible for AD in African-Americans and other patient subsets.

3.3 Clinical Picture

There are three classical stages of atopic dermatitis seen in early infancy, in children and in adults, each of which may show an *acute*, *subacute*, and *chronic skin reaction pattern*.

The *acute stage* usually predominates in the infantile form; the lesions are eczematous, exudative with edematous papules and plaques, often excoriated and intensely pruritic. Vesicles, oozing, and serous crusting are seen within affected areas (Fig. 3.1).

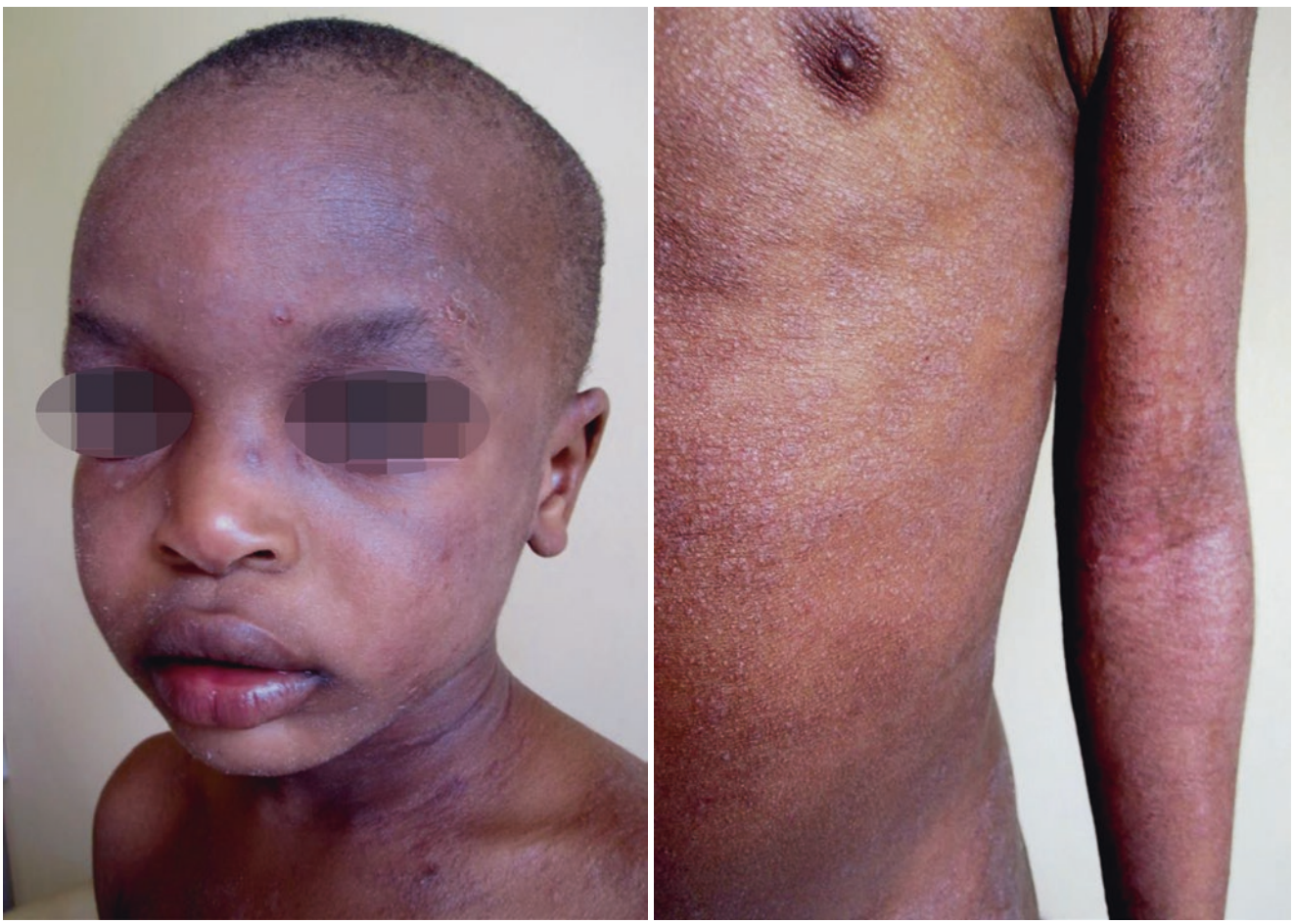

Fig. 3.1 *Atopic dermatitis*, early eczematous stage in childhood

In the *subacute stage*, erythematous papules and plaques are seen, with scaling and excoriations as secondary changes and beginning of lichenification. Staphylococcal impetigo may concomitantly appear as a complication (Fig. 3.2).

The final *chronic stage* is characterized by thickened, hyperkeratotic, and lichenified plaques with transient prurigo nodules. The disease may occasionally progress to erythroderma and/or to prurigo nodularis (Figs. 3.3, 3.4 and 3.5).

Pruritus is present regardless of the stage. In infants and young children, lesions are usually seen on the face, scalp, and extensor surfaces of the extremities and may be follicular; the diaper area is usually spared. As the child grows older, they tend to favor the flexural areas, the antecubital and popliteal fossae and posterior neck. In adults eczema is seen predominantly in a flexural distribution. For establishing the diagnosis, there are major and minor criteria, among them history of atopy, recurrent episodes of eczema with pruritus, xerosis, keratosis pilaris, Dennie-Morgan line, palmoplantar linearity, and presence of prurigo nodules.

The classical presentations of AD are essentially the same across all ethnic groups. However, there are a number of distinguishing features that occur more commonly in some populations than in others. In African black skin erythema often appears as a hyperpigmented or violaceous macule. A study in Nigeria documented that 54.1% of the patients had lichenoid lesions and 70.3% had a perifollicular, micropapular rash, on the extensor aspects of the joints [23]. Keloid formation may follow the chronic prurigo stage, and rashes of *follicular eczema* are sometimes seen on the trunk of dark-skinned African patients with AD, and this does not occur in white skin. When the lesions of AD resolve, they cause persistent dyschromia or pigmentary alterations resulting in either post-inflammatory hyperpigmentation or leukoderma which is always more pronounced in patients with darker skin phototypes [12]. These phenotypic differences may delay the diagnosis and treatment and allow for more severe disease to develop (Figs. 3.6 and 3.7).

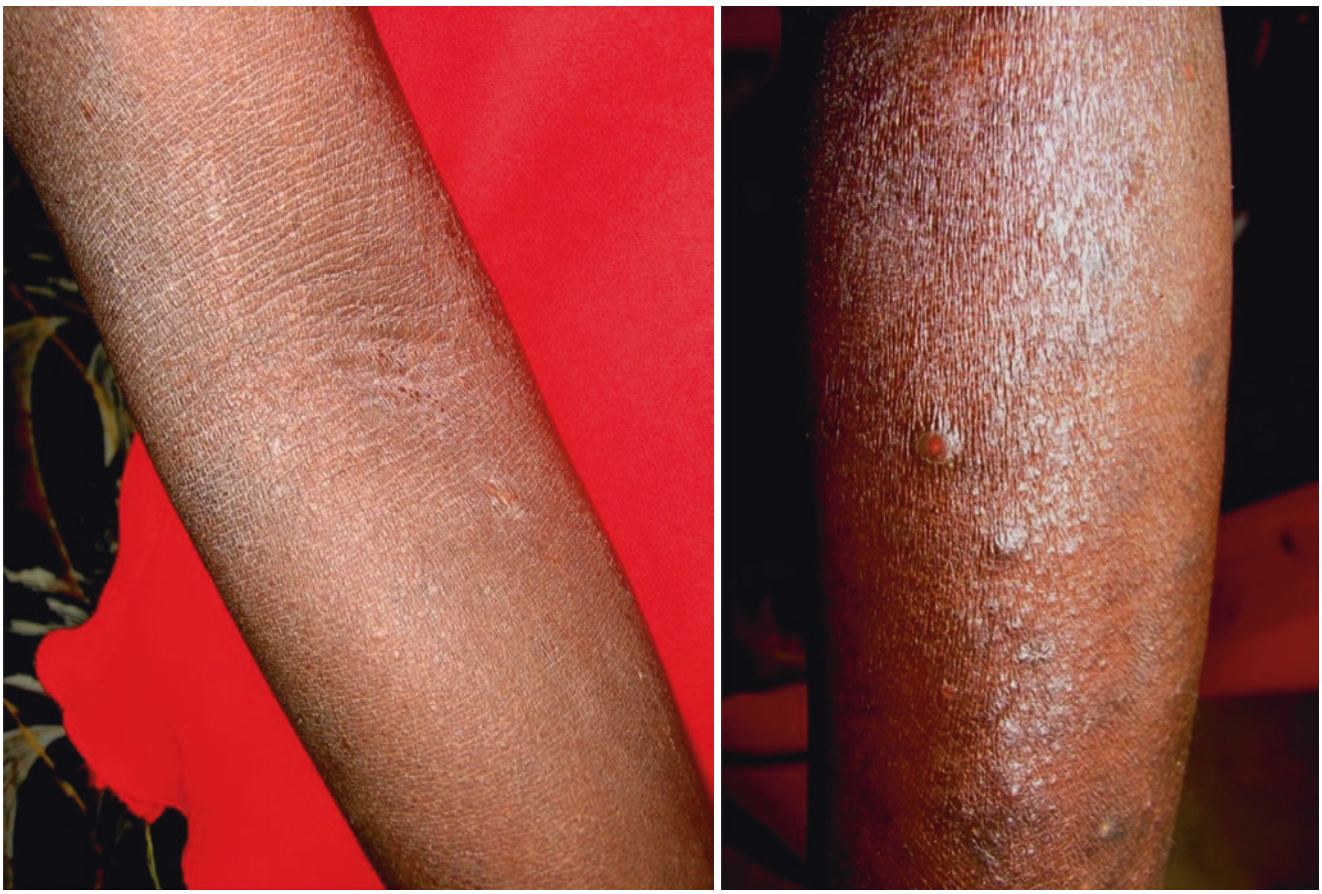

Fig. 3.2 Subacute stage of *atopic dermatitis* with flexural lichenification, perifollicular inflammatory reaction, and prurigo-like nodules in skin of color

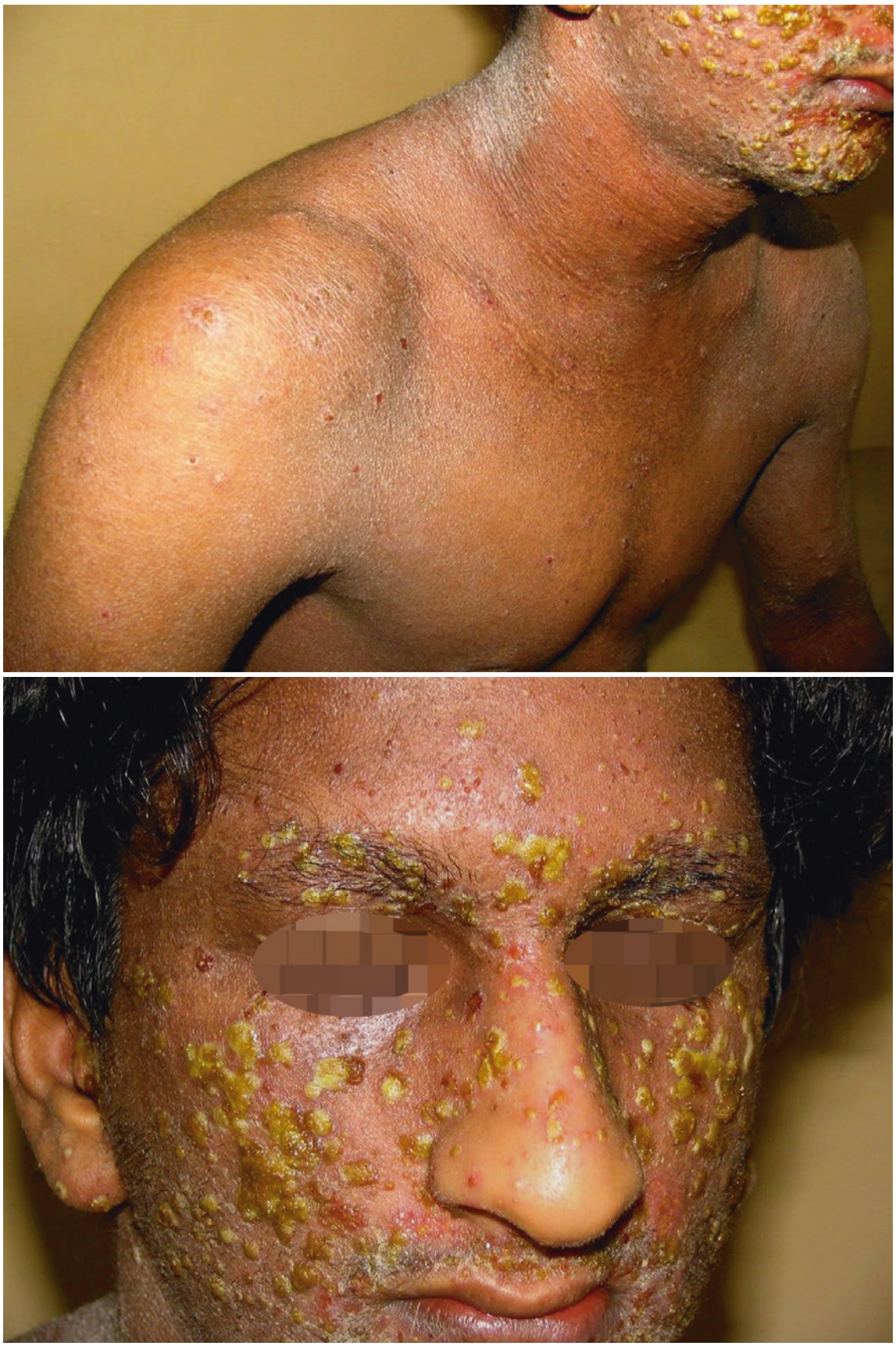

Fig. 3.3 Generalized, *chronic erythrodermic AD* with severe staphylococcal impetigo in face

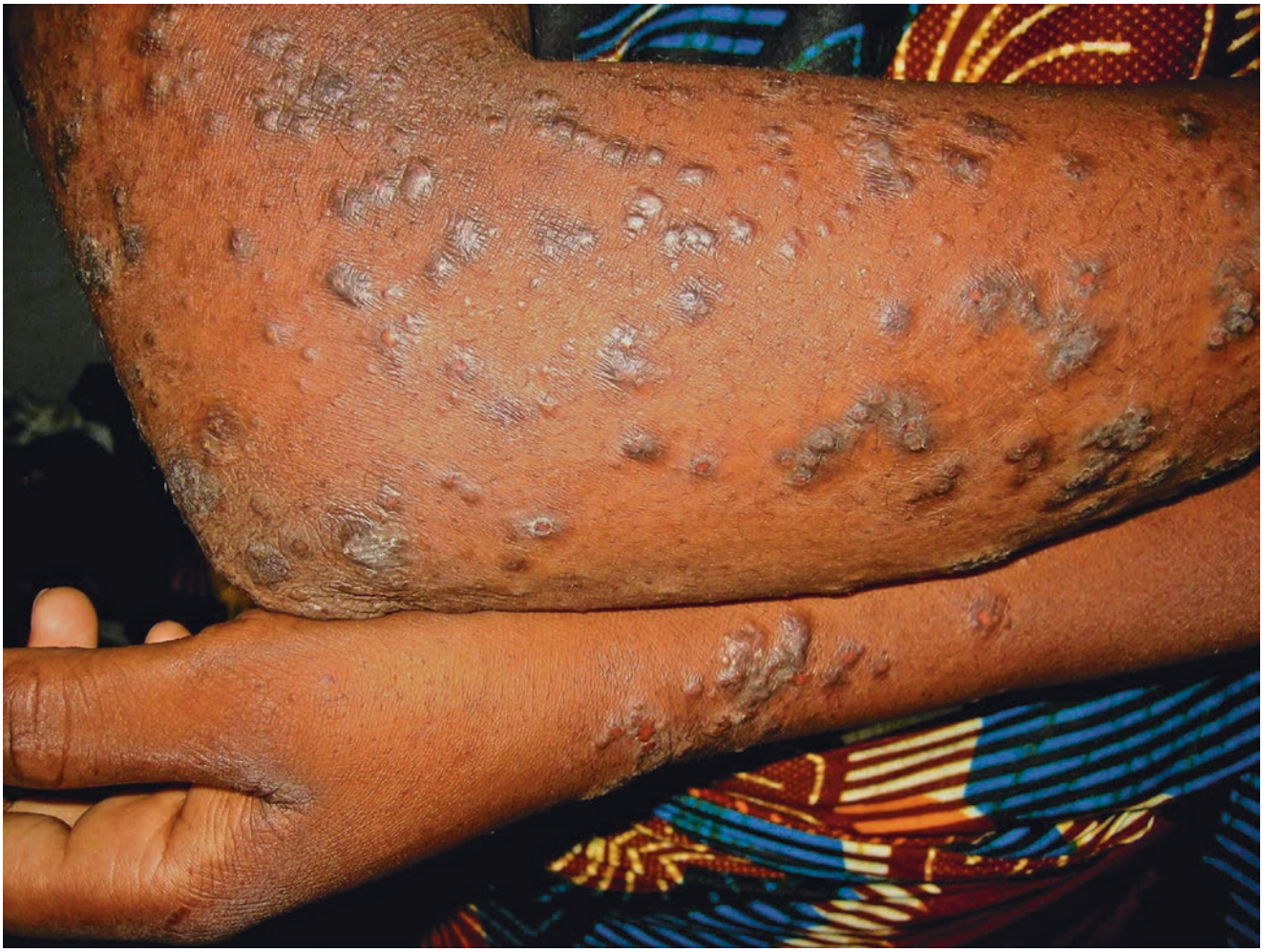

Fig. 3.4 *Chronic stage of AD* with extensive keloidal prurigo

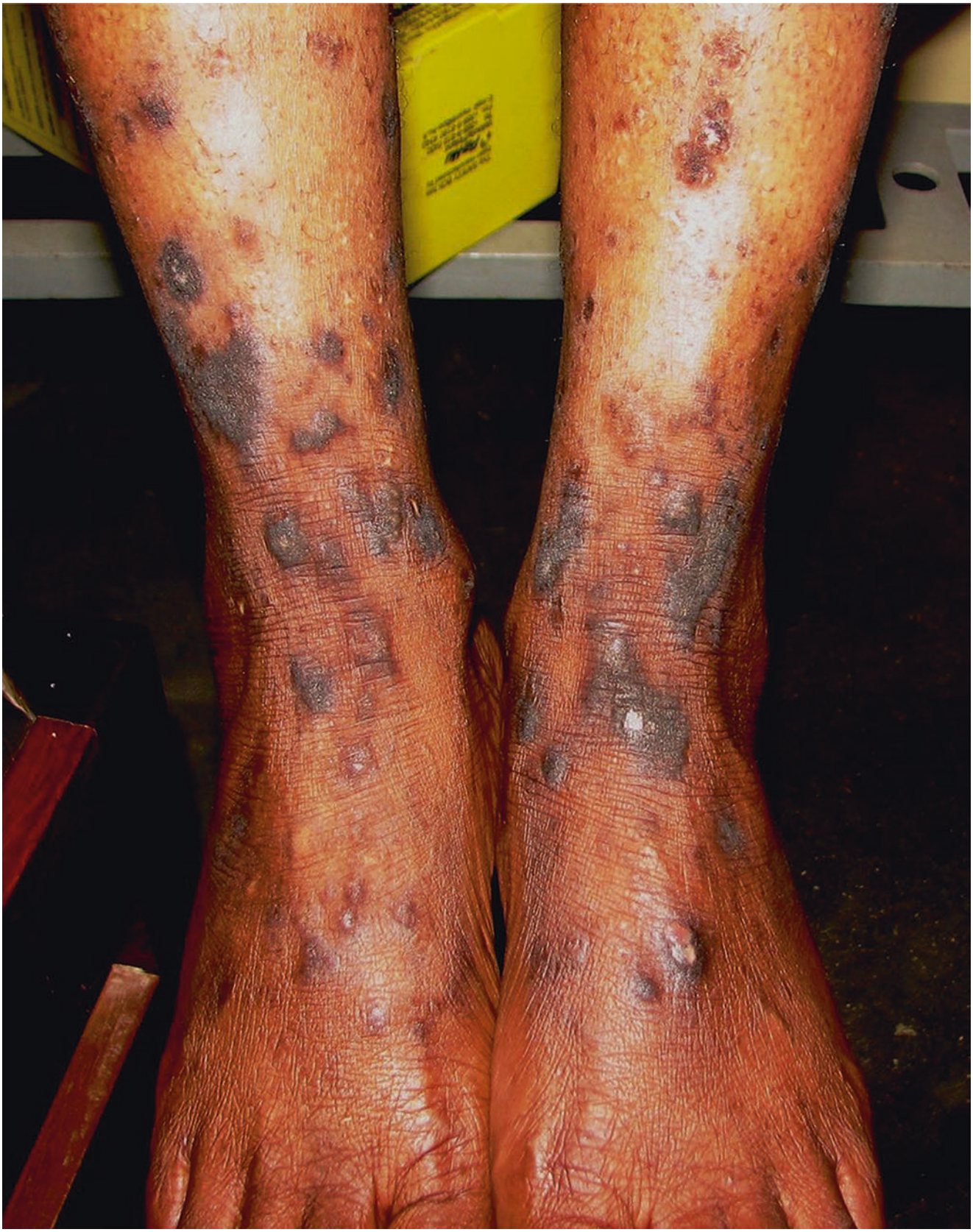

Fig. 3.5 Chronic atopic prurigo with transformation into prurigo nodularis

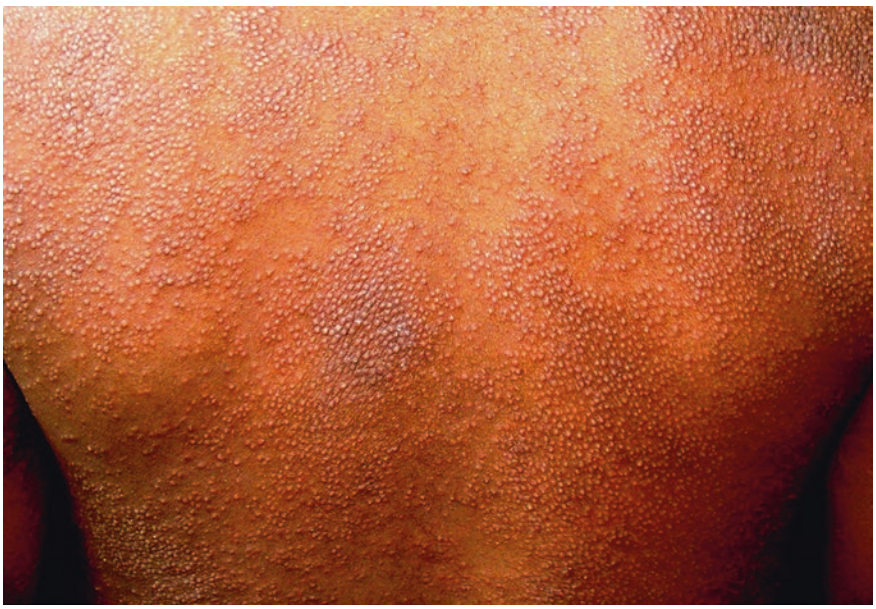

Fig. 3.6 Follicular eczematous rush on the trunk in an atopic patient (irritant dermatitis after local application of ointments of unknown composition)

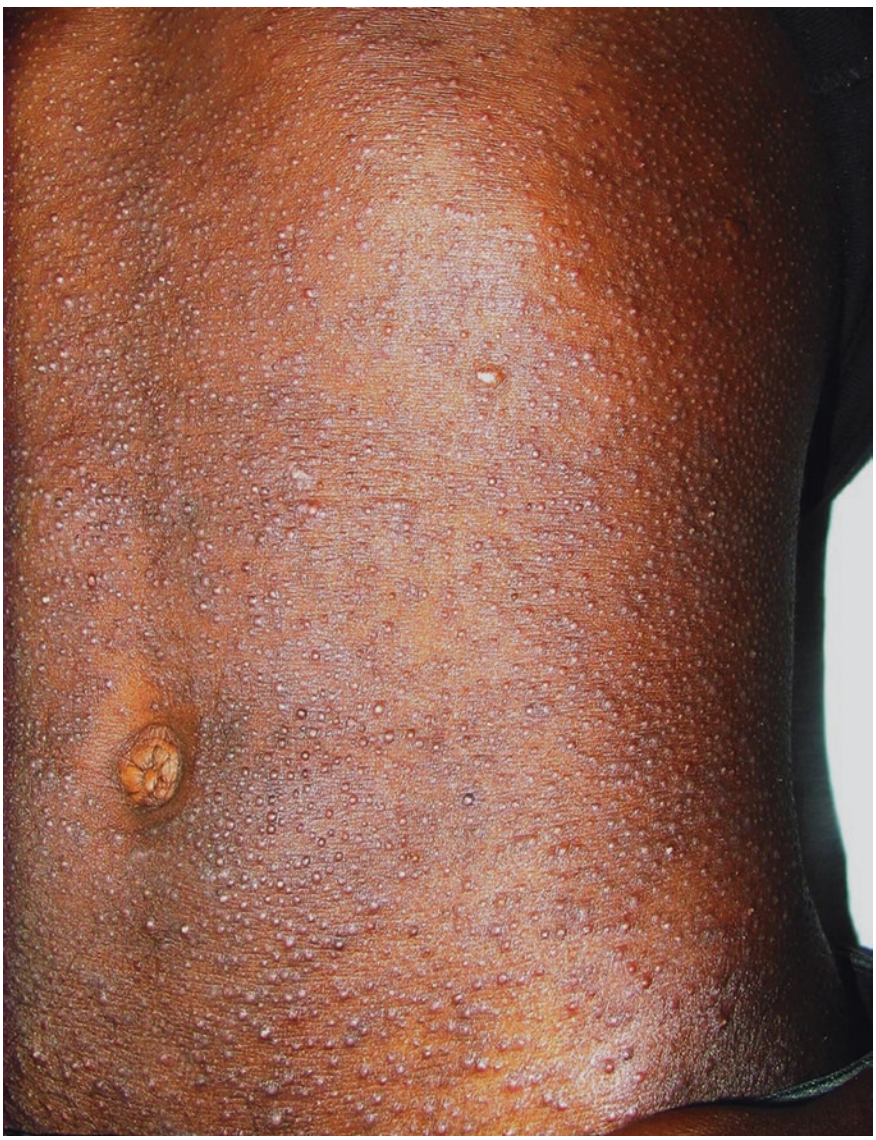

Fig. 3.7 *Follicular eczema*; 16-year-old boy (Uganda)

3.4 Course

In more than 50% of AD patients, the disease begins during infancy. It is a chronic condition with relapses and exacerbations which can also be seasonal, but the majority of patients report improvement as they grow older. It is difficult to assess how many cases progress to the adult form of the disease, but data may suggest that up to 40% of patients with childhood eczema have persistent or recurrent AD as adults.

3.5 Management

As a basic rule, the patients should be advised to avoid all type of possible skin irritants and allergens. They should bath less often, avoid hot water with harsh soaps and detergents, and opt for bath substitutes, e.g., glycerin-based soaps. Emollients must be applied soon after bathing to lock in moisture. *Topical moisturizers* are recommended to combat xerosis; alternatively agents such as petrolatum and mineral oils may be used to retard transepidermal loss of water. Liberal and frequent application of emollients is recommended also as prevention [7], together with oral sedating or non-sedating *antihistamines* to break the itch-scratch cycle and improve patients' quality of life. Extensive guidelines for care of AD are available [24, 25].

Topical corticosteroids are used in both adults and children and are the mainstay of anti-inflammatory management. For acute flares, daily use of topical steroids is recommended until the inflammatory lesions are significantly improved. After obtaining control, the goal is to prolong the period until the next flare by appropriate use of emollients. Low-potency preparations, e.g., 1% hydrocortisone, are recommended. Medium-potency steroids, e.g., betamethasone valerate and mometasone furoate, can be used for lesions on the trunk. More potent topical steroids should be avoided or tapered to less potent preparations.

Calcineurin inhibitors have the benefit of not carrying risk for cutaneous atrophy. They may be used at sensitive skin sites such as the face and the skin folds, topical tacrolimus ointment (0.03 and 0.1%) for moderate to severe disease, and pimecrolimus cream 1% for mild eczema.

Antimicrobials and antiseptics are frequently required, since atopic individuals are predisposed to skin infections. Bleach baths in conjunction with intranasal topical mupirocin can be used to eradicate colonization of staphylococci. They are preferred to topical antibiotics as there is less risk of resistance and contact dermatitis.

Phototherapies such as PUVA and narrowband UVB can be used alone or in combination with emollients and topical steroids [26]. No definitive recommendation can be made to differentiate between different forms of phototherapy in regard to efficacy. The use of light management may decrease the need for topical corticosteroids.

S*ystemic treatments* of AD are usually reserved for severe, acute flares [27]. *Corticosteroids* should be generally avoided because the risks outweigh the benefits. Immunosuppressives such as oral *cyclosporine* (3–6 mg/kg/day) is effective, but renal toxicity, hypertension, and increased risk for malignancy limit its use. *Azathioprine* is also efficacious (1–3 mg/kg/day), tapered or discontinued after clearance. Concomitant phototherapy is not advised because of increased risk of DNA damage and possible UV-induced carcinogenicity. *Methotrexate*, 2.5–25 mg/week depending on patient's age and weight, is also effective; liver functions should be monitored as well as full blood counts. *Mycophenolate mofetil* (25–50 mg/kg/day) can also be used. After all systemic therapies, laboratory monitoring is important before and during treatment.

Conclusions

Atopic dermatitis is a rising health problem in developing countries in African countries and their populations. Black skin seems to be more susceptible to dryness due to high transepidermal water loss and increased sensitivity to irritants and allergens leading to eczema. Post-inflammatory hyperpigmentation or leukoderma is a serious concern for dark-skinned patients, and clinicians should make an attempt to address it, as it affects the patient's quality of life. The socioeconomic conditions may play an additional role and explain the increasing prevalence. There is a need to support educational interventions together with programs for prevention and schedules for management adjusted to the environmental circumstances in hot climate zones.

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