

Atopic Dermatitis in African American Children: Addressing Unmet Needs of a Common Disease

Vasanop Vachiramon, M.D.,*,†,‡ Hong Liang Tey, MRCP (UK),*,‡, Amy E. Thompson, M.D.,* and Gil Yosipovitch, M.D.*

**Department of Dermatology, School of Medicine, Wake Forest University, Winston-Salem, North Carolina,*

†Division of Dermatology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand,

‡National Skin Center, Singapore City, Singapore

Abstract Recent published data suggest that the prevalence of atopic dermatitis (AD) in African American children is significantly higher than in Caucasians. There are certain characteristics in the presentation of AD in African Americans that seem to differ from those in other racial groups, but there is a paucity of information on this topic. In this review, we highlight the differences in pathophysiology, clinical presentation, and treatment of AD between African Americans and Caucasians. It is important for dermatologists to understand these differences in order to provide better care for African American children with AD.

Atopic dermatitis (AD) is a common skin condition in children worldwide, and untreated or undertreated AD can have a devastating effect on quality of life for affected individuals and their families. Children with AD have sleep disturbances due to nocturnal itching that result in daytime exhaustion and difficulties at school. A recent publication, using data from the 2003 National Survey of Children's Health, which involved more than 102,000 families in the United States, demonstrated an overall prevalence of AD of 10.7% of children in the United States and found that AD is more prevalent in African Americans than Caucasians (15.9% vs 9.7%) (1), affirming that AD places a high burden on the AA population.

We used a systematic approach to search all available literature from January 1970 through August 2011 from the electronic databases PREMEDLINE and MEDLINE using the search terms of "atopic dermatitis," "atopic eczema," "dermatitis," "Africans," "African Americans," "blacks," "black skin," "ethnic skin," "itch," and "skin barrier." The references of relevant studies were also checked. The goals of this review are to highlight the differences in the pathophysiology, clinical presentation, and therapeutic consideration of AD in AAs and to encourage research on this largely unstudied topic. For the purposes of this article, we will define blacks as individuals of African descent, which includes African, African American, and African Caribbean people.

Address correspondence to Gil Yosipovitch, M.D., Department of Dermatology, Neurobiology and Anatomy, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, or e-mail: gyosipov@wakehealth.edu.

DOI: 10.1111/j.1525-1470.2012.01740.x

DIFFERENCES IN PATHOPHYSIOLOGY

AD is a multifactorial inflammatory skin disease involving epidermal permeability and antimicrobial barriers, host immune response, and the neural network in the skin. The precise pathogenesis of AD is unclear, although the new paradigm holds that AD is an outside-inside-outside disease (2). In addition, scratching and excoriations create further defects in the epidermis, representing another potentially important vicious cycle in AD pathogenesis.

BARRIER FUNCTION

Failure of permeability and antimicrobial function is well recognized in individuals with AD. Deficiency of stratum corneum (SC) ceramides has been reported as an important etiologic factor of dry skin and barrier disruption in AD. A study examining the ceramide-to-cholesterol ratio of populations from different ethnic groups demonstrated that black subjects had the lowest values, with a median ratio of 0.8, compared with 2.1 for Asians and 1.7 for Caucasians (3). High transepidermal water loss (TEWL) in nonlesional and, to a greater extent, in lesional skin has been demonstrated in AD (4). TEWL has been found to be greater in normal African American skin than in Caucasian skin (5). Together with lower SC ceramides, this may account for greater risk of skin dryness and may explain higher rates of AD in African American children.

A recent breakthrough in the quest to understand the etiology of AD has been the identification of genetic defects in filaggrin (6). A 2009 meta-analysis demonstrated that filaggrin haploinsufficiency increases the risk of developing AD and is associated with greater severity of disease (7). The prevalence of the two most common *FLG* mutations, R501X and 2282del4, were significantly lower in Africans than in Caucasians (6) suggesting that the genetic basis for susceptibility to AD in blacks may differ from that in other populations.

Higher skin pH in lesional and normal skin has been found in individuals with AD (8,9). Higher pH has been shown to impair restoration of the permeability barrier after an acute insult (10), allowing more opportunities for antigens and microbes to reach the deeper layers of the epidermis and perpetuate the outbreak. Furthermore, the higher pH levels correlate with the severity of dryness, itching, and eczematous skin symptoms (8). Skin pH in African Americans has been found to be lower in the superficial layers of the SC on the volar forearms and cheeks (5), suggesting that the difference in skin pH does not explain the higher prevalence of AD in African Americans, although no studies were conducted on skin

pH in African American and Caucasian patients with AD.

A higher rate of *Staphylococcus aureus* colonization has been found in individuals with AD. Up to 65% of *S. aureus* strains isolated from patients with AD express superantigens, which polyclonally activate T cells, resulting in high cytokine production and greater presentation of allergen by keratinocytes to T-helper 2 cells (11). An exotoxin from *S. aureus* can induce the production of superantigen-specific immunoglobulin (Ig)E, which degranulates mast cells and contributes to inflammation in AD. The resulting increase in histamine and leukotriene C₄ leads to late-phase reactions and pruritus (12).

Although no studies have investigated the possible differences in the prevalence of Staphylococcal colonization in AD skin between different races, nasal carriage of *S. aureus* has been found to be significantly higher in whites than blacks (13,14), suggesting that *S. aureus* colonization does not explain the higher prevalence of AD in African Americans.

IMMUNE SYSTEM

Several studies have demonstrated that AD keratinocytes produce low levels of antimicrobial peptides (e.g., human β -defensins and cathelicidins), which may predispose individuals with AD to skin colonization and infection with *S. aureus*, viruses, and fungi (4). A significant difference in single-nucleotide polymorphisms (SNPs) in human β -defensin genes (*DEFB1* and *DEFB2*) has been demonstrated between racial groups (15), although the functional significance of this difference has yet to be determined.

Grundbacher (16) measured serum IgE levels in 326 normal subjects aged 5 and older of different races. IgE levels were found to be higher in African Americans than in Caucasians. The difference presumably results mainly from genetic differences, although a possible effect of socioeconomic or environmental factors is not entirely excluded.

Microscopic evaluation has revealed that mast cell granules in African American skin are larger than those in Caucasian skin and has shown differences in mast cell structure and enzymes. These variations may account for differences in pruritus that individuals in these racial groups experience (17).

Although the data regarding immunopathogenesis of AD in different racial groups are limited, the differences in genetic and immunologic background may account, at least in part, for the differences in clinical manifestation and disease severity. Moreover, individuals of African descent with asthma have more severe disease, higher IgE

levels, a higher degree of steroid dependency and more severe clinical symptoms than individuals of European descent with asthma (18).

ITCH RESPONSE

A prominent characteristic of and source of morbidity in AD is pruritus. Although no studies have compared variations in the characteristics of itch in AD of racial groups, differences in the mechanisms of itch transmission have been identified. Mas-related G protein-coupled receptors (Mrgprs) mediate chloroquine-induced itch, and polymorphic variations of Mrgpr genes may account for chloroquine-induced itch being much more common in blacks than in whites (19). As mentioned earlier, skin pH in blacks was found to be lower than in whites, and this may result in less activation of serine proteases and lower protease activated receptor-2-mediated itch signaling (20). These differences may account for an initially less symptomatic disease presentation in African American children and may partly explain why they are often diagnosed at a later stage of disease.

African Americans display a lower degree of hypersensitivity to capsaicin, a substance that activates transient receptor potential vanilloid subtype 1 (TRPV1), than other racial groups (21). The TRPV1 receptor has recently been shown to be an important mediator of the itch of allergic rhinitis and of histamine-induced itch (22). These findings suggest that polymorphisms of itch receptors such as TRPV1 may exist in African Americans. As a result of differences in neural functions, African Americans with AD may experience and report itch that is quantitatively and characteristically different from that of other races. A summary of pathophysiologic

differences of AD between African Americans and Caucasians is presented in Table 1.

DIFFERENCES IN CLINICAL PRESENTATION

African American children with AD are at risk of being diagnosed at a later stage of disease because of the challenge of recognizing early-stage AD. These children can present with subtle findings and different disease patterns than children of other populations. Because the symptoms of advanced disease are more difficult to bring under control, it is essential that practitioners be able to diagnose early AD in children whose presentation varies from the norm.

MORPHOLOGY

Scattered papular lesions on the extensors and trunk with annular configuration is commonly observed in black patients with AD (Figs. 1 and 2) (23,24). The main differential diagnosis is lichen nitidus, but lichen nitidus is usually less pruritic and is distributed on the trunk, flexors, and genitalia. The presence of the Koebner phenomenon and distinct histopathologic findings allow for the accurate diagnosis of lichen nitidus. Lesions that are nearly indistinguishable from classic lichen planus (lichen planus-like AD) were found to be more common in African Americans with AD (25), but the distribution of lichen planus-like AD is the extensors and there is limited mucosal or genital involvement. The histopathology of such lesions reveals spongiosis, mild superficial perivascular lymphocytic infiltration with occasional eosinophils, and scattered melanophages (25). The

TABLE 1. Pathophysiologic Differences in Atopic Dermatitis Between African Americans and Caucasians

Pathophysiologic differences	African Americans	Caucasians
Barrier		
Ceramides-to-cholesterol ratio (3)	Lower	Higher
Transepidermal water loss (5)	Higher	Lower
Skin pH (5)	Lower	Higher
Percutaneous absorption (38–41)	May be lower	May be higher
<i>Staphylococcus aureus</i> colonization (13,14)	Lower	Higher
Immune response		
Serum IgE (16)	Higher	Lower
Mast cell granules (17)	Larger	Smaller
Itch response		
Protease activated receptor-2-mediated Itch signaling (20)	Lower	Higher
Response to capsaicin (21)	Lower	Higher

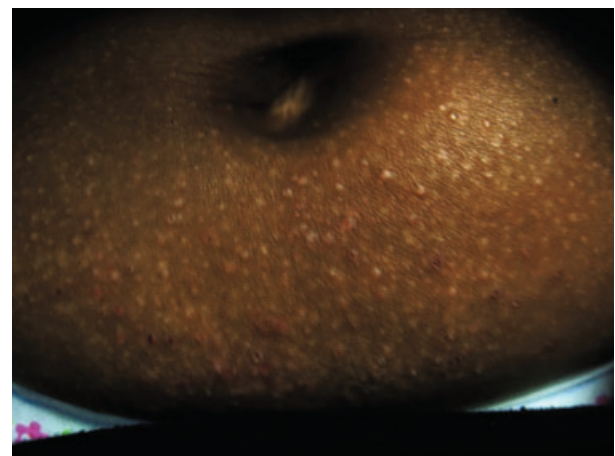


Figure 1. Scattered papular lesions on periumbilical area in adolescent African Americans with atopic dermatitis, mimicking nickel contact dermatitis.



Figure 2. Extensor involvement in a 14-year-old African American patient with atopic dermatitis.

combination of melanophages and increased pigmentation of the basal keratinocytes in dark-skinned patients may account for the violaceous color observed clinically.

Prurigo nodularis and lichenification can be associated with AD and may represent its dominant manifestation (26,27). Although there are no reports suggesting that they are more common in African Americans with AD, we have observed that African Americans have a higher tendency to present with prurigo nodularis and lichenification than other ethnic groups (Fig. 3).

COLOR

The response of different races to cutaneous irritants has been well documented, and black skin has been shown to be less likely to develop erythema when exposed to irritants (28). One study examined the effect of inclusion versus exclusion of erythema scores on disease severity in



Figure 3. Prurigo nodularis in an 11-year-old African American patient with atopic dermatitis.

black and white children with AD; the data including erythema scores showed a nonsignificantly lower risk of severe disease in black children, whereas a highly significantly greater risk of severe disease was found after exclusion of erythema score (29). It can be difficult to discriminate erythema within the context of pigmented skin. When evaluating dark-skinned patients, practitioners may need to rely on patients' reports of reddened skin, which may be a more reliable indication of erythema.

Postinflammatory hyperpigmentation and hypopigmentation are common sequelae of inflammatory dermatoses that tend to affect darker-skinned patients. Several factors can enhance the degree of pigmentary change as determined by individual chromatic tendency (30). Because of the color contrast, postinflammatory hypopigmentation is more obvious in darkly pigmented individuals. In addition, persistent hypopigmentation is commonly seen in dark-skinned patients with severe, long-standing AD (31).

DISTRIBUTION

The Hanifin and Rajka criteria, developed in 1980 (32), remain the hallmark criteria for diagnosing AD. The criteria include typical lesions and distribution based on age, with facial and extensor involvement seen in infants and young children and flexor involvement seen in older children and adults. In the African Americans with AD at our clinic, we have noted that, in older children and adolescents, involvement of the extensor surfaces of the extremities is more predominant than flexural involvement. Similar observations have been reported in studies from Nigeria and the United Kingdom (23,33).

Pruritic eczematous lesions on periumbilical areas have been described in African Americans with AD (34). These lesions can coincide with or mimic allergic contact dermatitis due to nickel. A chronic course, family history of atopy, negative patch test result, and other characteristic findings of AD suggest a diagnosis of AD.

OTHER FEATURES

Ichthyosis vulgaris, hyperlinear palms, and keratosis pilaris have also been found to vary according to racial group (35,36). The frequency of ichthyosis vulgaris in AD ranges from 1.6% to 37% and has been found to be higher in blacks (23).

A prominent infraorbital crease has been described as a minor criterion for the diagnosis of AD and is associated with eyelid dermatitis in individuals with AD (32). According to a study by Williams et al (37), a prominent infraorbital crease was common in black children (49%),

even in the absence of AD. Therefore, this physical finding may be less suggestive of AD in African Americans.

DISEASE SEVERITY

Using the Eczema Area and Severity Index (EASI) and Investigator Global Assessment (IGA) scoring tools, we conducted a survey to evaluate the severity of AD in our pediatric patients. Of 60 consecutive African Americans with AD recruited in a 2-week period in our clinic, 75% had moderate to severe disease, whereas of 100 Caucasians with AD, only 40% had moderate to severe disease (unpublished data, G.Y., 2010), although the severity prevalence from our study may not apply to the general population because it was conducted in a tertiary center.

A study in the United Kingdom showed that black children with AD are approximately six times more at risk of having severe AD than white children (29). In that study, 50% of the black children's parents were unemployed, which was a much higher unemployment rate than in parents of white children (29). Poorer access to medical care, a problem among African Americans in the United States, may be another explanation for the high prevalence of severe disease in African American patients with AD. In addition, difficulties of assessment of erythema can lead to a delay in diagnosis and treatment, which results in greater disease severity at presentation. A summary of clinical differences between AD in African Americans and Caucasians is presented in Table 2.

TABLE 2. Clinical Differences in Atopic Dermatitis in Children (aged > 4) and Adolescents Between African Americans and Caucasians

Clinical difference	African Americans	Caucasians
Morphology		
Scattered papular lesions	++	+
Lichen planus-like lesions	++	0
Prurigo nodularis	++	+
Lichenification	+++	+ to ++
Color		
Noticeable erythema	+	+++
Postinflammatory hyperpigmentation	+++	++
Postinflammatory hypopigmentation	+++	++
Distribution		
Extensor involvement	+++	+
Flexor Involvement	++	+++
Associated features		
Ichthyosis vulgaris	+++	++
High disease severity	++ to +++	+ to ++

0, absent; +, occasional finding; ++, common finding; +++, very common finding.

DIFFERENCES IN TREATMENT

Regardless of race, successful treatment of AD requires several different approaches, including skin hydration, pharmacologic therapy, and the identification and elimination of aggravating factors (e.g., irritants, allergens, infection, and emotional stressors). Adherence is particularly important in AD treatment, but there were no published data regarding the difference in adherence to AD treatment between ethnic groups.

Studies on interracial variation in percutaneous absorption have produced conflicting results (38). Although no difference in percutaneous absorption was noted in some studies, lower cutaneous absorption in African Americans has been reported in others (39,40). Stoughton (41) measured percutaneous absorption of fluocinolone acetonide through normal-appearing white and black cadaveric skin and found poorer absorption in black than white skin.

Topical therapies, including emollients, topical corticosteroids, and topical calcineurin inhibitors, are the mainstay of treatment, but the data regarding the difference in response to these agents between racial groups are limited.

Topical corticosteroids are frequently the first line of pharmacologic therapy for AD. As mentioned earlier, postinflammatory hypopigmentation is obvious in dark-skinned patients; prolonged use of topical corticosteroids may cause further hypopigmentation (42), but hypopigmentation in dark-skinned patients with AD is less likely to be associated with corticosteroids use and more likely to be related to postinflammatory changes.

Topical calcineurin inhibitors have been shown to be safe and effective in the management of pediatric AD. Eichenfield et al (43) evaluated the racial difference in response to pimecrolimus in children and infants with AD. According to their study, ethnic origin has no effect on treatment outcome.

Regarding systemic medications, differences between racial groups in the metabolism, clinical effectiveness, and side-effect profiles of drugs must be considered. Sedating antihistamines are helpful in breaking the "itch-scratch cycle" in AD, especially when given at bedtime. Hepatic cytochrome P₄₅₀ (CYP) enzyme 3A4 metabolizes H₁ antihistamines. A remarkable variation of the CYP 3A4 genotype has been demonstrated in African Americans and Caucasians (44), but no clinically important difference in enzyme activity has been found between racial groups (45).

Cyclosporine, a potent immunosuppressive drug that acts primarily on T cells by suppressing cytokine transcription, is usually given for a limited duration in severe, recalcitrant AD. Many factors influence cyclosporine

pharmacokinetics, including concurrent medications, ethnicity, liver function, genetics, intake of grapefruit juice, and formulation. CYP3A5, one of the main cytochromes, is variably expressed in different racial groups. CYP3A5 is more frequently expressed in AAs than in Caucasians (46). In addition, oral bioavailability of cyclosporine in AAs is 20% to 50% lower than in Caucasians, leading to a higher dose requirement to maintain adequate concentrations (47).

Azathioprine, an immunosuppressant commonly used in dermatology, is useful in stabilizing severe AD (48). Thiopurine methyltransferase (TPMT) enzyme activity is a major factor determining azathioprine metabolism. Several studies have clearly demonstrated that patients with low TPMT activity are at high risk of severe toxicity if treated with conventional dosages of azathioprine (49). African Americans have a higher prevalence of TPMT deficiency than Caucasians (50). Thus, dosage adjustments and frequent monitoring of possible side effects are required, especially in African Americans.

Methotrexate is an effective alternative treatment for AD, but a significant number of patients experience toxic side effects. Genes encoding enzymes in the methotrexate cellular pathway partly determine this. Of these, methotrexate transporter gene has been studied in racial groups. The SNP in adenosine triphosphate-binding cassette transporter C2 (ABCC2) 1058 G → A was associated with hepatotoxicity, and SNP in methylenetetrahydrofolate reductase 677 C → T was associated with alopecia in African Americans (51).

Although the use of mycophenolate mofetil (MMF) and dapsone in AD is off label, the antiinflammatory

effects make them a useful second-line treatment for AD. The data regarding racial differences in MMF pharmacokinetics are controversial, and further study is needed for clarification (47). For dapsone, hemolytic anemia, which is related to glucose-6-phosphate dehydrogenase (G6PD) deficiency, is important, and the prevalence of G6PD deficiency in African Americans is higher than in Caucasians (52). Assessment of G6PD level and blood count monitoring are recommended in African Americans receiving dapsone.

Numerous phototherapy regimens have been reported to improve AD. Ultraviolet A (UVA) 1 phototherapy is highly effective in acute, severe AD, whereas broadband UVB, broadband UVA, narrowband UVB, and combined UVA and UVB are effective for chronic mild to moderate AD (53,54). It is plausible that the higher levels of pigmentation present in African Americans may impede the ability of UV radiation to reach its target, but this question is unaddressed in the literature, and thus the therapeutic efficacy of phototherapy in relation to skin pigmentation is unknown.

Ravnbak et al (55) determined a minimal melanogenic dose (MMD) in individuals with different skin types using different light sources. A higher dose of narrowband UVB was required in darker skinned individuals, but this higher dose requirement was not seen with UVA1, in which the MMD was independent of preexposure pigmentation. A study by Jacobe et al (56) supported this observation, determining that Fitzpatrick skin type does not significantly influence the efficacy of UVA1 phototherapy for different skin conditions. Thus, Fitzpatrick skin type may be a factor for determining narrowband UVB but not UVA1 dosage.

TABLE 3. Key Points and Proposed Recommendations for the Treatment of Atopic Dermatitis in African Americans

Key points	Recommendations
Greater risk of skin dryness in African Americans due to lower ceramide to cholesterol ratio and higher transepidermal water loss	Effective emollient and hydration therapy (e.g., lukewarm soaking baths, wet dressing) are recommended. A high-potency topical corticosteroids or occlusive techniques (e.g., polythene occlusion, wet wrap therapy) should be used on these lesions.
Conflicting results of studies on the interethnic variation in percutaneous absorption	Because of conflicting data, we recommend the use of topical medicines in African American patients in a similar way as in patients from other ethnic groups.
20% to 50% lower oral bioavailability of cyclosporine in African Americans than in Caucasians	A higher dose of cyclosporine is required in African American patients.
Higher prevalence of TPMT deficiency in African Americans	Dosage adjustments and frequent monitoring of side effects are required in African American patients.
Higher prevalence of G6PD deficiency in African Americans	Assessment of G6PD level and blood count monitoring are required in African American patients.
Lacking data regarding the use of antihistamines, methotrexate, and mycophenolate mofetil in different racial group	There are no specific recommendations regarding the use of these agents in African Americans.
Correlation between the dosage of narrowband UVB and skin type and preexposure skin pigmentation	A higher dose of narrowband UVB is required in African-American patients.

UVB, ultraviolet B.

PROPOSED TREATMENT GUIDELINE FOR AD IN AFRICAN AMERICANS

Guidelines for the treatment of AD in African Americans is proposed in Table 3.

CONCLUSION

Atopic eczema commonly affects African American children and adolescents. It is imperative to diagnose and treat atopic eczema correctly in this group because it is associated with significant morbidity. The clinical characteristics of AD in African Americans differ from the classical definitions of AD, and the treatment may need to be tailored. We hope this article will increase awareness among practitioners of the unmet needs of AD in this population. More research is needed to further define the biological, psychosocial, and lifestyle variation that exist in African Americans with AD.

REFERENCES

- Shaw TE, Currie GP, Koudelka CW et al. Eczema prevalence in the United States: data from the 2003 National Survey of Children's Health. *J Invest Dermatol* 2011;131:67–73.
- Elias PM, Hatano Y, Williams ML. Basis for the barrier abnormality in atopic dermatitis: outside-inside-outside pathogenic mechanisms. *J Allergy Clin Immunol* 2008;121:1337–1343.
- Jungersted JM, Hogh JK, Hellgren LI et al. Ethnicity and stratum corneum ceramides. *Br J Dermatol* 2010;163:1169–1173.
- Proksch E, Folster-Holst R, Brautigam M et al. Role of the epidermal barrier in atopic dermatitis. *J Dtsch Dermatol Ges* 2009;7:899–910.
- Wesley NO, Maibach HI. Racial (ethnic) differences in skin properties: the objective data. *Am J Clin Dermatol* 2003;4:843–860.
- Palmer CN, Irvine AD, Terron-Kwiatkowski A et al. Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. *Nat Genet* 2006;38:441–446.
- Rodriguez E, Baurecht H, Herberich E et al. Meta-analysis of filaggrin polymorphisms in eczema and asthma: robust risk factors in atopic disease. *J Allergy Clin Immunol* 2009;123:1361–1370.
- Eberlein-Konig B, Schafer T, Huss-Marp J et al. Skin surface pH, stratum corneum hydration, trans-epidermal water loss and skin roughness related to atopic eczema and skin dryness in a population of primary school children. *Acta Derm Venereol* 2000;80:188–191.
- Rippke F, Schreiner V, Doering T et al. Stratum corneum pH in atopic dermatitis: impact on skin barrier function and colonization with *Staphylococcus aureus*. *Am J Clin Dermatol* 2004;5:217–223.
- Mauro T, Holleran WM, Grayson S et al. Barrier recovery is impeded at neutral pH, independent of ionic effects: implications for extracellular lipid processing. *Arch Dermatol Res* 1998;290:215–222.
- Bieber T. Atopic dermatitis. *N Engl J Med* 2008;358:1483–1494.
- Wehner J, Neuber K. *Staphylococcus aureus* enterotoxins induce histamine and leukotriene release in patients with atopic eczema. *Br J Dermatol* 2001;145:302–305.
- Noble WC. Carriage of *Staphylococcus aureus* and beta haemolytic streptococci in relation to race. *Acta Derm Venereol* 1974;54:403–405.
- Kuehnert MJ, Kruszon-Moran D, Hill HA et al. Prevalence of *Staphylococcus aureus* nasal colonization in the United States, 2001–2002. *J Infect Dis* 2006;193:172–179.
- Jurevic RJ, Chrisman P, Mancil L et al. Single-nucleotide polymorphisms and haplotype analysis in beta-defensin genes in different ethnic populations. *Genet Test* 2002;6:261–269.
- Grundbacher FJ. Causes of variation in serum IgE levels in normal populations. *J Allergy Clin Immunol* 1975;56:104–111.
- Sueki H, Whitaker-Menezes D, Kligman AM. Structural diversity of mast cell granules in black and white skin. *Br J Dermatol* 2001;144:85–93.
- Barnes KC, Grant AV, Hansel NN et al. African Americans with asthma: genetic insights. *Proc Am Thorac Soc* 2007;4:58–68.
- Tey HL, Yosipovitch G. Itch in ethnic populations. *Acta Derm Venereol* 2010;90:227–234.
- Steinhoff M, Neisius U, Ikoma A et al. Proteinase-activated receptor-2 mediates itch: a novel pathway for pruritus in human skin. *J Neurosci* 2003;23:6176–6180.
- Wang H, Papoiu AD, Coghill RC et al. Ethnic differences in pain, itch and thermal detection in response to topical capsaicin: African Americans display a notably limited hyperalgesia and neurogenic inflammation. *Br J Dermatol* 2010;162:1023–1029.
- Alenmyr L, Hogestatt ED, Zygmunt PM et al. TRPV1-mediated itch in seasonal allergic rhinitis. *Allergy* 2009;64:807–810.
- Nnoruka EN. Current epidemiology of atopic dermatitis in south-eastern Nigeria. *Int J Dermatol* 2004;43:739–744.
- McLaurin CI. Pediatric dermatology in black patients. *Dermatol Clin* 1988;6:457–473.
- Summey BT, Bowen SE, Allen HB. Lichen planus-like atopic dermatitis: expanding the differential diagnosis of spongiotic dermatitis. *J Cutan Pathol* 2008;35:311–314.
- Pugliarello S, Cozzi A, Gisondi P et al. Phenotypes of atopic dermatitis. *J Dtsch Dermatol Ges* 2011;9:12–20.
- Tanaka M, Aiba S, Matsumura N et al. Prurigo nodularis consists of two distinct forms: early-onset atopic and late-onset non-atopic. *Dermatology* 1995;190:269–276.
- Berardesca E, Maibach H. Ethnic skin: overview of structure and function. *J Am Acad Dermatol* 2003;48:S139–S142.
- Ben-Gashir MA, Hay RJ. Reliance on erythema scores may mask severe atopic dermatitis in black children compared with their white counterparts. *Br J Dermatol* 2002;147:920–925.
- Ruiz-Maldonado R, Orozco-Covarrubias ML. Postinflammatory hypopigmentation and hyperpigmentation. *Semin Cutan Med Surg* 1997;16:36–43.

31. Ortonne J. Vitiligo and Other disorders of Hypopigmentation. In: Bologna J, Jorizzo J, Rapini R, eds. *Dermatology*, 2nd ed. Spain: Elsevier, 2008:913–938.
32. Hanifin J, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol* 1980;92(Suppl):44–47.
33. Williams HC, Pembroke AC, Forsdyke H et al. London-born black Caribbean children are at increased risk of atopic dermatitis. *J Am Acad Dermatol* 1995;32:212–217.
34. Rencic A, Cohen BA. Prominent pruritic periumbilical papules: a diagnostic sign in pediatric atopic dermatitis. *Pediatr Dermatol* 1999;16:436–438.
35. Uehara M, Hayashi S. Hyperlinear palms: association with ichthyosis and atopic dermatitis. *Arch Dermatol* 1981;117:490–491.
36. Wells RS. Some genetic aspects of dermatology: a review. *Clin Exp Dermatol* 1980;5:1–11.
37. Williams HC, Pembroke AC. Infraorbital crease, ethnic group, and atopic dermatitis. *Arch Dermatol* 1996;132:51–54.
38. Taylor SC. Skin of color: biology, structure, function, and implications for dermatologic disease. *J Am Acad Dermatol* 2002;46:S41–S62.
39. Berardesca E, Maibach HI. Racial differences in pharmacodynamic response to nicotines in vivo in human skin: black and white. *Acta Derm Venereol* 1990;70:63–66.
40. Wedig JH, Maibach HI. Percutaneous penetration of dipyrithione in man: effect of skin color (race). *J Am Acad Dermatol* 1981;5:433–438.
41. Stoughton R. Bioassay methods for measuring percutaneous absorption. In: Montagna W, Stoughton RB, vanScott EJ, eds. *Pharmacology of the Skin*. New York: Appleton-Century-Crofts, 1969:542–544.
42. Hengge UR, Ruzicka T, Schwartz RA et al. Adverse effects of topical glucocorticosteroids. *J Am Acad Dermatol* 2006;54:1–15.
43. Eichenfield LF, Lucky AW, Langley RG et al. Use of pimecrolimus cream 1% (Elidel) in the treatment of atopic dermatitis in infants and children: the effects of ethnic origin and baseline disease severity on treatment outcome. *Int J Dermatol* 2005;44:70–75.
44. Zhou X, Barber WH, Moore CK et al. Frequency distribution of cytochrome P450 3A4 gene polymorphism in ethnic populations and in transplant recipients. *Res Commun Mol Pathol Pharmacol* 2006;119:89–104.
45. Wandel C, Witte JS, Hall JM et al. CYP3A activity in African American and European American men: population differences and functional effect of the CYP3A4*1B5'-promoter region polymorphism. *Clin Pharmacol Ther* 2000;68:82–91.
46. Kuehl P, Zhang J, Lin Y et al. Sequence diversity in CYP3A promoters and characterization of the genetic basis of polymorphic CYP3A5 expression. *Nat Genet* 2001;27:383–391.
47. Dirks NL, Huth B, Yates CR et al. Pharmacokinetics of immunosuppressants: a perspective on ethnic differences. *Int J Clin Pharmacol Ther* 2004;42:701–718.
48. Meggitt SJ, Gray JC, Reynolds NJ. Azathioprine dosed by thiopurine methyltransferase activity for moderate-to-severe atopic eczema: a double-blind, randomised controlled trial. *Lancet* 2006;367:839–846.
49. Escousse A, Rifle G, Sgro C et al. Azathioprine toxicity, 6-mercaptopurine accumulation and the "poor" 6-thiopurine methylator phenotype. *Eur J Clin Pharmacol* 1995;48:309–310.
50. McLeod HL, Lin JS, Scott EP et al. Thiopurine methyltransferase activity in American white subjects and black subjects. *Clin Pharmacol Ther* 1994;55:15–20.
51. Ranganathan P, Culverhouse R, Marsh S et al. Methotrexate (MTX) pathway gene polymorphisms and their effects on MTX toxicity in Caucasian and African American patients with rheumatoid arthritis. *J Rheumatol* 2008;35:572–579.
52. Serpa JA, Villarreal-Williams E, Giordano TP. Prevalence of G6PD deficiency in a large cohort of HIV-infected patients. *J Infect* 2010;61:399–402.
53. Krutmann J, Czech W, Diepgen T et al. High-dose UVA1 therapy in the treatment of patients with atopic dermatitis. *J Am Acad Dermatol* 1992;26:225–230.
54. Scheinfeld NS, Tutrone WD, Weinberg JM et al. Phototherapy of atopic dermatitis. *Clin Dermatol* 2003;21:241–248.
55. Ravnbak MH, Wulf HC. Pigmentation after single and multiple UV-exposures depending on UV-spectrum. *Arch Dermatol Res* 2007;299:25–32.
56. Jacobe HT, Cayce R, Nguyen J. UVA1 phototherapy is effective in darker skin: a review of 101 patients of Fitzpatrick skin types I–V. *Br J Dermatol* 2008;159:691–696.