DRUGS IN CONTEXT
RIGOROUS • RAPID • RESPONSIVE

A continuous publication, open access, peer-reviewed journal

ACCESS ONLINE

REVIEW

Dermatology: how to manage atopic dermatitis in patients with skin of colour

Muskaan Sachdeva[1], Marissa Joseph[2,3]

[1]Faculty of Medicine, University of Toronto, Toronto, ON, Canada; [2]Women's College Hospital, University of Toronto, Toronto, ON, Canada; [3]Section of Dermatology, Division of Pediatric Medicine, The Hospital for Sick Children, Toronto, ON, Canada

Abstract

Atopic dermatitis (AD) is a chronic inflammatory cutaneous disease prevalent in all skin types but can differ in pathogenesis and clinical presentation. It has been documented in the literature that AD is more prevalent in Asian and Black individuals than in white individuals. Genetic variations as well as cultural and socioeconomic factors have important implications for susceptibility to AD and response to treatment in skin of colour. In this narrative review, we discuss differences in the epidemiology, pathophysiology, clinical presentation and treatment of AD in skin of colour. Additionally, we highlight the need for greater inclusivity of non-white ethnic groups in clinical trials to develop targeted treatments for diverse populations. Moreover, awareness of differences in AD presentation amongst non-white individuals may encourage patients to seek medical care earlier, leading to timely management and improved outcomes.

Keywords: atopic dermatitis, eczema, management, skin of colour.

Citation

Sachdeva M, Joseph M. Dermatology: how to manage atopic dermatitis in patients with skin of colour. *Drugs Context*. 2022;11:2021-12-1. https://doi.org/10.7573/dic.2021-12-1

Introduction

Atopic dermatitis (AD) is a chronic inflammatory cutaneous condition that manifests as erythematous, pruritic and scaly lesions. It is typically localized to the flexural surfaces of the body such as the elbows and knees.[1] AD has a strong association with allergic rhinitis and asthma, which can occur as an atopic triad.[1] AD typically begins during early childhood and affects several ethnicities with varying prevalence.[1–3] However, limited data are available on the epidemiology, pathogenesis, clinical presentation and treatment of AD amongst patients with skin of colour.[2] The aim of this narrative review is to provide a thorough summary of current studies reviewing the characteristics of AD in individuals with skin of colour.

Epidemiology

AD has a high prevalence worldwide, with an increasing trend in most countries.[4] AD prevalence is estimated to be 13–25% in children but only 2–10% in adults.[2,5–8] Moreover, in the United States, Black people are affected at higher rates than Asians and Pacific Islanders (20.1% *versus* 16.1%).[9] Children in South Africa, Kenya, Nigeria and Morocco have a high prevalence of AD, of up to 20.9%, with a similar prevalence in Western Asia, South-East Asia, Eastern Asia and Oceania.[8]

One study found that Black individuals and Asian/Pacific Islanders were more likely to be affected with AD compared to white individuals.[9] Another study demonstrated that the prevalence of AD in 693 school children was disproportionately higher in Black Caribbean children compared to white, Indian or Pakistani children.[10] However, the exact prevalence of AD in various ethnic groups is still unknown.

Studies on the prevalence and geographical incidence of AD across the world can provide an estimate of how commonly AD occurs in diverse ethnic groups.[4] However, the intrinsic challenges in collecting data from patients of different races and the methodology used imply that the results should be interpreted with caution.[4] For example, many studies roughly estimate the prevalence of AD, whilst other studies predict its incidence.[4] Moreover, most studies are of European countries; however, Europe has people from many different races, making it difficult to conclude the epidemiology of AD in Europe across different races.[4]

Pathogenesis

The diverse genetic background of different racial populations may contribute to the varying prevalence.[8] AD has different

genetic mechanisms, making it a heterogenous disorder.[8] Loss-of-function mutations in filaggrin play an important role in AD onset.[11] *FLG*, encoding the epidermal barrier protein filaggrin, has an important role in barrier function and skin hydration through regulation of pH. The number of intragenic copies within the filaggrin gene can play a significant role in AD pathogenesis.[12] However, there is limited knowledge on the distribution of intragenic copy number variations as opposed to loss-of-function mutations in patients with AD.[8]

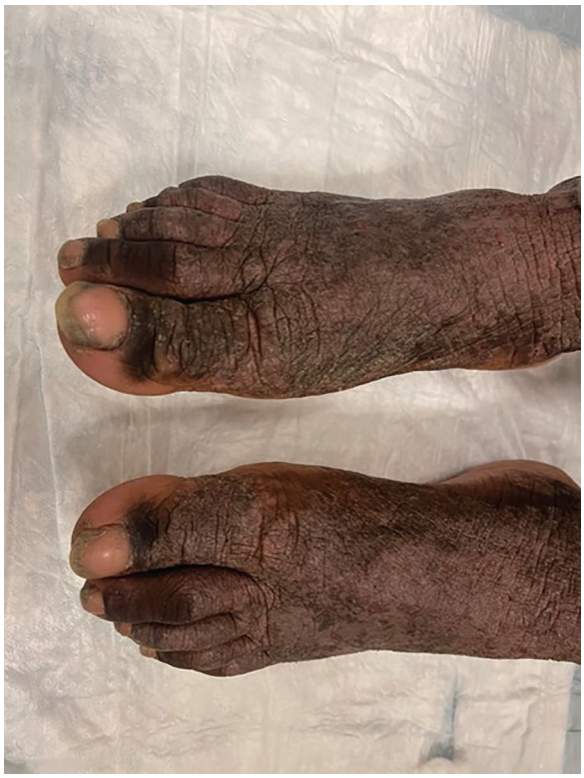
Loss-of-function *FLG* mutations differ in Asian, European and African populations.[11,13–17] In Europe, the most common filaggrin mutations are R501X and E2422X; however, these are rarely witnessed in Asian and African populations.[8] Moreover, the 3321delA mutation has been noted in Asian populations; however, it has not been seen in European populations.[8] Additionally, R501X and 2282del4 represented the most common mutations in Ireland (80% of mutations) but were reported to be prevalent in only 1% of the Singaporean Chinese population.[18] Additionally, in African Americans, *FLG* mutations are six times less likely to occur than in people of European American descent, even though AD is more prevalent in African American people.[7] Thus, the impact of the loss-of-function mutations on AD is not fully understood.[2]

Differences between white and non-white patients have also been observed regarding involved inflammatory pathways. T helper 2 (T_H2), T_H22, T_H17 and T_H1 pathways can be differently overexpressed.[19] One study revealed that, in Tanzanian people with AD, T_H1-related and T_H17-related markers may be upregulated compared to controls.[19]

Clinical presentation

AD can be classified into three distinct categories.[20] First, acute AD presents with a weeping, crusting, vesicular eruption, whereas subacute AD presents with erythematous, dry, scaly papules and plaques. Lastly, chronic AD presents with lichenification due to scratching.[20] AD typically involves the flexural surfaces of the body, dorsa of the feet, hands, anterior and lateral neck, forehead, face, eyelids, and wrists.[20] Important differences in the clinical manifestation of AD amongst ethnic groups are underrepresented in the literature and are mainly the result of differences in distribution and pigmentation of lesions.[21] Asian individuals typically have more well-demarcated lesions as well as more scaling and lichenification relative to white individuals (Figure 1).[22,23] African people are less likely to develop flexural dermatitis and instead, predominantly have extensor involvement.[21] Additionally, AD can manifest as perifollicular accentuation and distinct papules on the extensors and trunk in Black individuals.[24–26] A lichen planus-like presentation of AD has been seen only in dark-skinned patients, and this type of presentation responds more quickly to treatment.[27] According to a study conducted in Mexican children, 76% of children had at least one infrequent clinical sign of AD, which included nipple dermatitis, prurigo-type dermatitis, genital dermatitis and follicular dermatitis.[28]

Figure 1. Well-demarcated lesions, scaling and lichenification seen in a patient with skin of colour.



Picture taken by Dr Joseph with permission from the patient.

Moreover, erythema in darker skin commonly appears violaceous or is missed completely.[21,29] Oedema, warmth of the skin or overlying scale, may assist dermatologists in identifying the erythema. Scoring systems that consider erythema, such as Eczema Area and Severity Index and SCORing Atopic Dermatitis, significantly underestimate the severity of AD in dark skin.[7,21,29] Other classical findings that are more likely to be seen in skin of colour include Dennie–Morgan lines, diffuse xerosis and hyperlinearity of the palms.[24] Patients with darker skin are also more likely to present with prurigo nodularis than white patients.[21,24] Increased pruritus and thus greater rubbing and scratching may account for this type of presentation.[30,31] Patients with darker skin are also at an elevated risk for postinflammatory dyspigmentation.[32–35]

A large study in the United States indicated that there are ethnic differences in school absences amongst children with AD. The study found that children with skin of colour have more absent days than white children.[36] The authors also

Table 1. Atopic dermatitis treatment in skin of colour.

Generic name	Mechanism of action	Dosing	Vehicle	Considerations in skin of colour
Topical corticosteroids	- Interferes with antigen processing in many immune cells like T lymphocytes, dendritic cells, monocytes, macrophages - Suppresses pro-inflammatory cytokine release[40]	- 0.5 g with strength ranging from 0.05% to 1% applied to an area equal to 2 adult palms for 1–2 times a day - Paediatric: mid to high potency topical corticosteroids can be used during intense flare-ups; however, generally least potent corticosteroid must be used[40]	Topical (gel, cream, ointment)[40]	- Although topical steroids have similar efficacy in all skin colours, high potency topical steroids can cause hypopigmentation in darker skin[2]
Topical calcineurin inhibitors (tacrolimus, pimecrolimus)	- Block calcineurin-dependent activation of T cell activation - Reduce production of pro-inflammatory cytokines and atopic dermatitis mediators - Reduce number of dendritic cells and their ability to activity other immune cells - Reduce activation of mast cells[40]	- 0.03% and 0.1% strength topical tacrolimus ointment and 1% strength pimecrolimus cream applied twice daily - Paediatric: 0.03% strength tacrolimus ointment and pimecrolimus cream for children 2 years and older; 0.1% strength tacrolimus ointment for individuals older than 15 years[40]	Topical (ointment, cream)[40]	- Topical calcineurin inhibitors have similar efficacy across various skin types[2,68]
Phototherapy	- Ultraviolet light absorbed by nucleotides create DNA photoproducts and suppress DNA production - Ultraviolet light also leads to the formation of prostaglandins and cytokines involved in immune suppression[69]	- For broadband ultraviolet B: dosage based on minimal erythema dose and Fitzpatrick skin type ranging from an initial dosage of 20–60 mJ/cm^2 - Dosage administered 3–5 times a week - For narrowband ultraviolet B: dosage based on minimal erythema dose and Fitzpatrick skin type ranging from an initial dosage of 130–400 mJ/cm^2 - For oral psoralen plus ultraviolet A: dosage based on Fitzpatrick skin type ranging from an initial dosage of 0.5–3.0 J/cm^2 (ref.[6])	Light[6]	- Narrowband ultraviolet B requires greater doses in more pigmented skin types[2] - Ultraviolet A1 is equally effective for all Fitzpatrick skin types ranging from I to V[2] - In Asian cohorts, narrowband ultraviolet B and ultraviolet A/ narrowband ultraviolet B are effective in treating moderate to severe disease[2] - In darker skin, longer treatments may lead to build up of lead and causes atopic dermatitis flares[52]

(Continued)

Table 1. ***(Continued)***

Generic name	Mechanism of action	Dosing	Vehicle	Considerations in skin of colour
Cyclosporine A	- T cells and IL-2 production is suppressed[6]	- 150–300 mg/d - Paediatric: 3–6 mg/kg/d (ref.[6])	Oral[6]	- Black individuals have a 20–50% lower bioavailability of cyclosporine than white individuals; thus, they need higher doses[68]
Methotrexate	- Antifolate metabolite - Blocks the production of DNA, RNA and purines - Reduces T cell function[6]	- 7.5–25 mg/wk - Paediatric: 0.2–0.7 mg/kg/wk - Consider test dose: 1.25–5 mg (ref.[6])	Oral and injection[6]	- Black patients have a higher risk of alopecia when treated with methotrexate[68]
Azathioprine	- Reduces DNA production - As a result, it selectively affects B cells and T cells that are proliferating during inflammatory diseases like atopic dermatitis[6]	- 1–3 mg/kg/d - Paediatric: 1–4 mg/kg/d (ref.[6])	Oral[6]	- Deficiency of thiopurine methyltransferase (TPMT) enzyme is prevalent in Black patients; thus, these patients with low TPMT may be at risk of severe toxicity with the usual dosage of azathioprine[68] - Important to obtain TPMT levels and continue blood monitoring in Black patients before initiating azathioprine[68]
Mycophenolate mofetil	- Blocks purine biosynthesis pathway by inhibiting inosine monophosphate dehydrogenase - As other cells have purine scavenger mechanisms, it preferentially affects B cells and T cells[6]	- 1.0–1.5 g orally twice daily - Paediatric: 1200 mg/m^2 daily, which corresponds to 30–50 mg/kg/d (ref.[6])	Oral[6]	- Treatment efficacy is not affected by race[70]
Dupilumab	- Blocks IL-4 and IL-13 by targeting their alpha subunit[2]	- First dose of 600 mg (two 300 mg injections at different locations) - Afterwards, 300 mg biweekly is recommended[71]	Subcutaneous injection[71]	- Similar efficacy for white, Black and Asian skin[2,68]

Data taken from ref.[6]

found that Black children were 1.5 times more likely to be absent for 6 more days over a 6-month period compared to white children.[36] Additionally, Black children are 6 times more likely to have severe AD and treatment-resistant AD than white children.[7,29] Thus, it is hypothesized that AD may have a greater effect on the quality of life (QOL) of children with skin of colour, resulting in more school absences in these children.[36]

Treatment

There is limited evidence on the effectiveness of treatment options for AD in ethnically diverse groups due to under-representation of racial groups in clinical trials and lack of subset analyses by race.[37–39] Only 59.5% of AD clinical trials between the years 2000 and 2009 included ethnicity as part of their demographic information.[37] The current treatment guidelines for AD are similar across skin types, with minor differences due to variations in genetics, skin phototype and culture (Table 1).[2]

Patients with AD are recommended to use emollients liberally. Emollients, such as glyceryl stearate, glycol stearate and soy sterols, act as lubricants to soften the skin. Occlusive agents, such as petrolatum, mineral oil and dimethicone, function by forming a layer to limit water evaporation. Humectants, such as glycerol, urea and lactic acid, promote water retention.[40] The frequency of topical corticosteroids (TCs) can be greatly reduced by proper hydration from emollient use.[41]

As for topical treatments, a study of pimecrolimus cream 1% in white, Black, Asian and Hispanic populations showed similar outcomes between ethnic groups.[42] Pooled data on the efficacy of tacrolimus ointment in eight Asian countries showed 80% success in AD resolution, consistent with studies in Europe and the United States.[43] Although, clinical trials of tacrolimus in the United States included Black patients, treatment response was not stratified by race.[44] Phase III studies of crisaborole consisted of almost 40% non-white individuals, the majority being Black individuals. A statistically significant improvement in AD severity and QOL was found in Black and Hispanic populations.[45,46] Although it was not statistically significant due to small sample size, improvement was also seen in Asian/Pacific Islanders and American Indians.[46] TCs are also highly effective in different skin colours, although data are limited.[2] Unfortunately, TCs of high potency can cause hypopigmentation in darker skin types.[47] However, the risk for adverse effects is low if TCs are used properly.[47]

For recalcitrant AD, phototherapy may be used.[48–50] Narrowband (NB)-UVB and UVA/NB-UVB are recommended for the treatment of moderate-to-severe AD in Asian populations.[51] NB-UVB, which is typically used for AD treatment, requires higher doses in darker skin.[48,52,53] However, UVA1 is shown to be faster and more effective for the treatment of acute AD in Fitzpatrick skin types I–V without requiring dose modifications.[51,54] With phototherapy, patients with darker skin tend not to respond as well as those with lighter skin.[55] However, it is important to note that the notion to treat patients with dark skin with longer phototherapy treatments may lead to a heat build-up, which can actually cause a flare of their AD.[53]

Recent research has assessed the efficacy of biologics in diverse ethnic groups.[29,56–59] Dupilumab targets the α-subunit of the IL-4 and IL-13 receptors and has demonstrated improvement in severity and symptoms of AD.[60–64] Phase III trials of dupilumab consisted of 20–27% Asian individuals and 5–7% Black individuals; thus, the efficacy of dupilumab is consistent in diverse ethnic groups.[62–65] A subgroup analysis by race demonstrated comparable results between white, Black and Asian patients, although the number of Black individuals was limited.[63,65] For moderate-to-severe AD in patients 12 years and older, dupilumab is the only approved biologic.[66] A recent study demonstrated the effectiveness of dupilumab in improving QOL of patients with AD amongst various racial subgroups (i.e. white, Asian, Black/African Americans).[47] In addition, phase II and III clinical trials on tralokinumab, baricitinib and upadacitinib for the treatment of AD have been published.[67] Ethnicity data on these newer agents are not yet available. Generally, there are limited data on biologic agents in patients with skin of colour.

Regardless of skin type, the goals of AD treatment are to manage and prevent flares whilst improving skin barrier function.[40] Inclusion of various racial groups and subset analysis by race will be useful in clinical trials that evaluate novel AD therapies, both in regard to treatment modifications and placebo responses, and molecular phenotype changes in patients' skin.[2] Finally, further research must look for specific molecular targets in Black, Asians and Hispanic populations to assist with treatment development for diverse populations.[9,31,37,42,65]

Conclusion

Studies show that individuals with skin of colour have unique clinical and genetic features of AD. A thorough understanding of these characteristics is critical for caring for a multicultural patient demographic. Variations in the treatment of AD amongst varying ethnic groups are also likely influenced by genetic variability. Unfortunately, data are limited in diverse patient populations and future studies are needed to analyse the differences in treatment outcomes in various ethnic groups. Awareness of the differences in AD presentation in non-white patients is critical to encouraging individuals to seek medical help in a timely manner, which helps to ensure early diagnosis and treatment. Future studies should focus on developing personalized approaches for AD treatment in patients of varying ethnic and racial groups.

Key practice points

- Atopic dermatitis (AD) is more prevalent in Asian and Black than in white individuals.
- Differences between white and non-white patients have also been observed regarding involved inflammatory pathways.
- Scoring systems that consider erythema, such as Eczema Area and Severity Index and SCORing Atopic Dermatitis, significantly underestimate the severity of AD in dark skin.
- There is limited evidence on the effectiveness of treatment options for AD in ethnically diverse groups due to under-representation of racial groups in clinical trials and lack of subset analyses by race.

Contributions: All authors contributed equally to the preparation of this manuscript. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

Disclosure and potential conflicts of interest: MJ is a consultant for Abbvie, Amgen, Janssen, LeoPharma, Valeant, Pfizer, Pierre Fabre, Galderma, SunPharma, Johnson & Johnson, Sanofi Genzyme, UCB, Bausch Health and L'Oréal. MS has no conflicts of interest. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors is available for download at: https://www.drugsincontext.com/wp-content/uploads/2022/04/dic.2021-12-1-COI.pdf

Acknowledgements: None.

Funding declaration: There was no funding associated with the preparation of this article.

Article URL: https://www.drugsincontext.com/dermatology-how-to-manage-atopic-dermatitis-in-patients-with-skin-of-colour

Correspondence: Marissa Joseph, Women's College Hospital, 76 Grenville St, Toronto, ON M5S 1B2, Canada. Email: marissa.joseph@gmail.com

Provenance: Invited; externally peer reviewed.

Submitted: 9 December 2021; **Accepted:** 30 March 2022; **Publication date:** 31 May 2022.

Drugs in Context is published by BioExcel Publishing Ltd. Registered office: Plaza Building, Lee High Road, London, England, SE13 5PT.

BioExcel Publishing Limited is registered in England Number 10038393. VAT GB 252 7720 07.

For all manuscript and submissions enquiries, contact the Editorial office editorial@drugsincontext.com

For all permissions, rights and reprints, contact David Hughes david.hughes@bioexcelpublishing.com

References

1. Spergel JM. Epidemiology of atopic dermatitis and atopic march in children. *Immunol Allergy Clin North Am*. 2010;30(3):269–280. https://doi.org/10.1016/j.iac.2010.06.003
2. Kaufman BP, Guttman-Yassky E, Alexis AF. Atopic dermatitis in diverse racial and ethnic groups—Variations in epidemiology, genetics, clinical presentation and treatment. *Exp Dermatol*. 2018;27(4):340–357. https://doi.org/10.1111/exd.13514
3. Sangha AM. Dermatological conditions in SKIN OF COLOR—: managing atopic dermatitis. *J Clin Aesthet Dermatol*. 2021;14(3 Suppl. 1):S20.
4. Deckers IA, McLean S, Linssen S, Mommers M, Van Schayck CP, Sheikh A. Investigating international time trends in the incidence and prevalence of atopic eczema 1990–2010: a systematic review of epidemiological studies. *PloS One*. 2012;7(7):e39803. https://doi.org/10.1371/journal.pone.0039803
5. Feldman SR, Cox LS, Strowd LC, et al. The challenge of managing atopic dermatitis in the United States. *Am Health Drug Benefits*. 2019;12(2):83.
6. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71:327–349. https://doi.org/10.1016/j.jaad.2014.03.030

7. Brunner PM, Guttman-Yassky E. Racial differences in atopic dermatitis. *Ann Allergy Asthma Immunol*. 2019;122:449–455. https://doi.org/10.1016/j.anai.2018.11.015
8. Torrelo A. Atopic dermatitis in different skin types. What is to know? *J Eur Acad Dermatol Venereol*. 2014;28:2–4. https://doi.org/10.1111/jdv.12480
9. Janumpally SR, Feldman SR, Gupta AK, Fleischer AB. In the United States, blacks and Asian/Pacific Islanders are more likely than whites to seek medical care for atopic dermatitis. *Arch Dermatol*. 2002;138(5):634–637. https://doi.org/10.1001/archderm.138.5.634
10. Williams HC, Pembroke AC, Forsdyke H, Boodoo G, Hay RJ, Burney PG. London-born black Caribbean children are at increased risk of atopic dermatitis. *J Am Acad Dermatol*. 1995;32(2):212–217. https://doi.org/10.1016/0190-9622(95)90128-0
11. Brown SJ, Irvine AD. Atopic eczema and the filaggrin story. *Semin Cutan Med Surg*. 2008;27(2) 128–137. https://doi.org/10.1016/j.sder.2008.04.001
12. McGrath JA. Profilaggrin, dry skin, and atopic dermatitis risk: size matters. *J Invest Dermatol*. 2012;132(1):10–11. https://doi.org/10.1038/jid.2011.360 https://doi.org/10.1111/j.1365-2133.2009.09112.x
13. Hsu CK, Akiyama M, Nemoto-Hasebe I, et al. Analysis of Taiwanese ichthyosis vulgaris families further demonstrates differences in FLG mutations between European and Asian populations. *Br J Dermatol*. 2009;161(2):448–451. https://doi.org/ 10.1111/j.1365-2133.2009.09112.x
14. Akiyama M. FLG mutations in ichthyosis vulgaris and atopic eczema: spectrum of mutations and population genetics. *Br J Dermatol*. 2010;162(3):472–477. https://doi.org/10.1111/j.1365-2133.2009.09582.x
15. Osawa R, Konno S, Nishimura M, Shimizu H, Akiyama M. Japanese-specific filaggrin gene mutations in Japanese patients suffering from atopic eczema and asthma. *J Invest Dermatol*. 2010;130(12):2834–2836. https://doi.org/10.1038/jid.2010.218
16. Zhang H, Guo Y, Wang W, Yu X, Yao Z. Associations of FLG mutations between ichthyosis vulgaris and atopic dermatitis in Han Chinese. *Allergy*. 2011;66(9):1253–1254. https://doi.org/10.1111/j.1398-9995.2011.02597.x
17. Winge MC, Bilcha KD, Lieden A, et al. Novel filaggrin mutation but no other loss-of-function variants found in Ethiopian patients with atopic dermatitis. *Br J Dermatol*. 2011;165(5):1074–1080. https://doi.org/10.1111/j.1365-2133.2011.10475.x
18. Chen H, Common JE, Haines RL, et al. Wide spectrum of filaggrin-null mutations in atopic dermatitis highlights differences between Singaporean Chinese and European populations. *Br J Dermatol*. 2011;165(1):106–114. https://doi.org/10.1111/j.1365-2133.2011.10331.x
19. Lang CC, Renert-Yuval Y, Del Duca E, et al. Immune and barrier characterization of atopic dermatitis skin phenotype in Tanzanian patients. *Ann Allergy Asthma Immunol*. 2021;127(3):334–341. https://doi.org/10.1016/j.anai.2021.04.023
20. Berke R, Singh A, Guralnick M. Atopic dermatitis: an overview. *Am Fam Physician*. 2012;86(1):35–42.
21. Vachiramon V, Tey HL, Thompson AE, Yosipovitch G. Atopic dermatitis in African American children: addressing unmet needs of a common disease. *Pediatr Dermatol*. 2012;29(4):395–402. https://doi.org/10.1111/j.1525-1470.2012.01740.x
22. Noda S, Suárez-Fariñas M, Ungar B, et al. The Asian atopic dermatitis phenotype combines features of atopic dermatitis and psoriasis with increased TH17 polarization. *J Allergy Clin Immunol*. 2015;136(5):1254–1264. https://doi.org/10.1016/j.jaci.2015.08.015
23. Leung DY. Atopic dermatitis: age and race do matter! *J Allergy Clin Immunol*. 2015;136(5):1265–1267. https://doi.org/10.1016/j.jaci.2015.09.011
24. Nnoruka EN. Current epidemiology of atopic dermatitis in south-eastern Nigeria. *Int J Dermatol*. 2004;43(10):739–744. https://doi.org/10.1111/j.1365-4632.2004.02360.x
25. Kristal L, Klein PA. Atopic dermatitis in infants and children: an update. *Pediatr Clin North Am*. 2000;47(4):877–895. https://doi.org/10.1016/S0031-3955(05)70246-7
26. Lynfield YL. Prominent pruritic periumbilical papules. *Pediatr Dermatol*. 2000;17(6):490. https://doi.org/10.1046/j.1525-1470.2000.01837.x
27. Allen HB, Jones NP, Bowen SE. Lichenoid and other clinical presentations of atopic dermatitis in an inner city practice. *J Am Acad Dermatol*. 2008;58(3):503–504. https://doi.org/10.1016/j.jaad.2007.03.033
28. Julián-Gónzalez RE, Orozco-Covarrubias L, Durán-McKinster C, Palacios-Lopez C, Ruiz-Maldonado R, Sáez-de-Ocariz M. Less common clinical manifestations of atopic dermatitis: prevalence by age. *Pediatr Dermatol*. 2012;29(5):580–583. https://doi.org/10.1111/j.1525-1470.2012.01739.x
29. Ben-Gashir MA, Seed PT, Hay RJ. Reliance on erythema scores may mask severe atopic dermatitis in black children compared with their white counterparts. *Br J Dermatol*. 2002;147(5):920–925. https://doi.org/10.1046/j.1365-2133.2002.04965.x
30. Oh CC, Li H, Lee W, Tey HL. Biopsychosocial factors associated with prurigo nodularis in endogenous eczema. *Indian J Dermatol*. 2015;60(5):525. https://doi.org/10.4103/0019-5154.164451
31. Shaw FM, Luk KM, Chen KH, Wrenn G, Chen SC. Racial disparities in the impact of chronic pruritus: a cross-sectional study on quality of life and resource utilization in United States veterans. *J Am Acad Dermatol*. 2017;77(1):63–69. https://doi.org/10.1016/j.jaad.2017.01.016
32. Alexis AF, Blackcloud P. Psoriasis in skin of color: epidemiology, genetics, clinical presentation, and treatment nuances. *J Clin Aesthet Dermatol*. 2014;7(11):16.

33. Alexis AF, Sergay AB, Taylor SC. Common dermatologic disorders in skin of color: a comparative practice survey. *Cutis*. 2007;80(5):387–394.
34. Child FJ, Fuller LC, Higgins EM, Du Vivier AW. A study of the spectrum of skin disease occurring in a black population in south-east London. *Br J Dermatol*. 1999;141(3):512–517. https://doi.org/10.1046/j.1365-2133.1999.03047.x
35. Bolognia JL, Jorizzo JL, Rapini RP, et al. *Dermatology*. 2nd ed. London: Mosby Elsevier; 2008.
36. Wan J, Margolis DJ, Mitra N, Hoffstad OJ, Takeshita J. Racial and ethnic differences in atopic dermatitis–related school absences among US children. *JAMA Dermatol*. 2019;155(8):973–975. https://doi.org/10.1001/jamadermatol.2019.0597
37. Hirano SA, Murray SB, Harvey VM. Reporting, representation, and subgroup analysis of race and ethnicity in published clinical trials of atopic dermatitis in the United States between 2000 and 2009. *Pediatr Dermatol*. 2012;29(6):749–755. https://doi.org/10.1111/j.1525-1470.2012.01797.x
38. Charrow A, Di Xia F, Joyce C, Mostaghimi A. Diversity in dermatology clinical trials: a systematic review. *JAMA Dermatol*. 2017;153(2):193–198. https://doi.org/10.1001/jamadermatol.2016.4129
39. Bhattacharya T, Silverberg JI. Efficacy of systemic treatments for atopic dermatitis in racial and ethnic minorities in the United States. *JAMA Dermatol*. 2014;150(11):1232–1234. https://doi.org/10.1001/jamadermatol.2014.1674
40. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71(1):116–132. https://doi.org/10.1016/j.jaad.2014.03.023
41. Drucker AM, Eyerich K, de Bruin-Weller MS, et al. Use of systemic corticosteroids for atopic dermatitis: International Eczema Council consensus statement. *Br J Dermatol*. 2018;178(3):768–775. https://doi.org/10.1111/bjd.15928
42. Eichenfield LF, Lucky AW, Langley RGB, 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 out. *Int J Dermatol*. 2005;44:70–75. https://doi.org/10.1111/j.1365-4632.2004.02234.x
43. Kim KH, Kono T. Overview of efficacy and safety of tacrolimus ointment in patients with atopic dermatitis in Asia and other areas. *Int J Dermatol*. 2011;50(9):1153–1161. https://doi.org/10.1111/j.1365-4632.2011.04881.x
44. Hanifin JM, Paller AS, Eichenfield L, et al. Efficacy and safety of tacrolimus ointment treatment for up to 4 years in patients with atopic dermatitis. *J Am Acad Dermatol*. 2005;53(2):S186–S194. https://doi.org/10.1016/j.jaad.2005.04.062
45. Paller AS, Tom WL, Lebwohl MG, et al. Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults. *J Am Acad Dermatol*. 2016;75(3): 494–503. https://doi.org/10.1016/j.jaad.2016.05.046
46. Callender V, Alexis A, Stein Gold L, et al. Presented at The 26th Annual EADV Meeting, Geneva, Switzerland, 2017.
47. Silverberg JI, Gelfand JM, Margolis DJ, et al. Patient burden and quality of life in atopic dermatitis in US adults: a population-based cross-sectional study. *Ann Allergy Asthma Immunol*. 2018;121(3):340–347. https://doi.org/10.1016/j.anai.2018.07.006
48. Meduri NB, Vandergriff T, Rasmussen H, Jacobe H. Phototherapy in the management of atopic dermatitis: a systematic review. *Photodermatol Photoimmunol Photomed*. 2007;23(4):106–112. https://doi.org/10.1111/j.1600-0781.2007.00291.x
49. Slater NA, Morrell DS. Systemic therapy of childhood atopic dermatitis. *Clin Dermatol*. 2015;33(3):289–299. https://doi.org/10.1016/j.clindermatol.2014.12.005
50. Totri CR, Eichenfield LF, Logan K, et al. Prescribing practices for systemic agents in the treatment of severe pediatric atopic dermatitis in the US and Canada: the PeDRA TREAT survey. *J Am Acad Dermatol*. 2017;76(2):281–285. https://doi.org/10.1016/j.jaad.2016.09.021
51. Mok ZR, Koh MJ, Chong WS. Is phototherapy useful in the treatment of atopic dermatitis in Asian children? A 5-year report from Singapore. *Pediatr Dermatol*. 2014;31(6):698–702. https://doi.org/10.1111/pde.12405
52. Syed ZU, Hamzavi IH. Role of phototherapy in patients with skin of color. *Semin Cutan Med Surg*. 2011;30(4):184–189. https://doi.org/10.1016/j.sder.2011.08.007
53. Syed ZU, Hamzavi IH. Photomedicine and phototherapy considerations for patients with skin of color. *Photodermatol Photoimmunol Photomed*. 2011;27(1):10–16. https://doi.org/10.1111/j.1600-0781.2010.00554.x
54. 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(3):691–696. https://doi.org/10.1111/j.1365-2133.2008.08672.x
55. Tuchinda C, Kerr HA, Taylor CR, et al. UVA1 phototherapy for cutaneous diseases: an experience of 92 cases in the United States. *Photodermatol Photoimmunol Photomed*. 2006;22(5):247–253. https://doi.org/10.1111/j.1600-0781.2006.00245.x
56. Brunner PM, Guttman-Yassky E, Leung DY. The immunology of atopic dermatitis and its reversibility with broad-spectrum and targeted therapies. *J Allergy Clin Immunol*. 2017;139(4):S65–S76. https://doi.org/10.1016/j.jaci.2017.01.011
57. Khattri S, Brunner PM, Garcet S, et al. Efficacy and safety of ustekinumab treatment in adults with moderate-to-severe atopic dermatitis. *Exp Dermatol*. 2017;26(1):28–35. https://doi.org/10.1111/exd.13112
58. Malajian D, Guttman-Yassky E. New pathogenic and therapeutic paradigms in atopic dermatitis. *Cytokine*. 2015;73(2):311–318. https://doi.org/10.1016/j.cyto.2014.11.023

59. Lauffer F, Ring J. Target-oriented therapy: emerging drugs for atopic dermatitis. *Expert Opin Emerg Drugs*. 2016;21(1):81–89. https://doi.org/10.1517/14728214.2016.1146681
60. Hamilton JD, Ungar B, Guttman-Yassky E. Drug evaluation review: dupilumab in atopic dermatitis. *Immunotherapy*. 2015;7(10):1043–1058. https://doi.org/10.2217/imt.15.69
61. Hamilton JD, Suárez-Fariñas M, Dhingra N, et al. Dupilumab improves the molecular signature in skin of patients with moderate-to-severe atopic dermatitis. *J Allergy Clin Immunol*. 2014;134(6):1293–1300. https://doi.org/10.1016/j.jaci.2014.10.013
62. Beck LA, Thaçi D, Hamilton JD, et al. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. *N Engl J Med*. 2014;371(2):130–139. https://doi.org/10.1056/NEJMoa1314768
63. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375(24):2335–2348. https://doi.org/10.1056/NEJMoa1610020
64. Blauvelt A, de Bruin-Weller M, Gooderham M, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. *Lancet*. 2017;389(10086):2287–2303. https://doi.org/10.1016/S0140-6736(17)31191-1
65. Woo YR, Kim HS, Lee SH, et al. Systemic comorbidities in Korean patients with rosacea: results from a multi-institutional case-control study. *J Clin Med*. 2020;9(10):3336. https://doi.org/10.3390/jcm9103336
66. Katlin Poladian AB, Brianna De Souza MD, Amy JM. Atopic dermatitis in adolescents with skin of color. *Cutis*. 2019;104:164–168.
67. Newsom M, Bashyam AM, Balogh EA, Feldman SR, Strowd LC. New and emerging systemic treatments for atopic dermatitis. *Drugs*. 2020;80(11):1041–1052. https://doi.org/10.1007/s40265-020-01335-7
68. De Souza B, McMicheal AJ. Atopic dermatitis in patients with skin of color. *Dermatologist*. 2019. https://www.hmpgloballearningnetwork.com/site/thederm/nea-approved-features/atopic-dermatitis-patients-skin-color. Accessed April 12, 2022.
69. Bulat V, Šitum M, Dediol I, Ljubičić I, Bradić L. The mechanisms of action of phototherapy in the treatment of the most common dermatoses. *Coll Antropol*. 2011;35(Suppl. 2):147–151.
70. Waxweiler WT, Agans R, Morrell DS. Systemic treatment of pediatric atopic dermatitis with azathioprine and mycophenolate mofetil. *Pediatr Dermatol*. 2011;28(6):689–694. https://doi.org/10.1111/j.1525-1470.2011.01488.x
71. Din AT, Malik I, Arshad D, Din AT. Dupilumab for atopic dermatitis: the silver bullet we have been searching for? *Cureus*. 2020;12(4):e7565. https://doi.org/10.7759/cureus.7565