SnapshotDx Quiz: July 2019

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**WHAT IS YOUR DIAGNOSIS?**

![Figure 1](image_url)  
*Figure 1.* Image credit: Emily Y. Chu, MD, PhD, Department of Dermatology, University of Pennsylvania.

*Editorial note:* Welcome to the *Journal of Investigative Dermatology (JID)* Snapshot Dx Quiz. In this monthly online-only quiz, the first question (“What is your diagnosis?”) relates to the clinical image shown, while additional questions concern the findings reported in the JID article by Kim et al. (2019) (https://doi.org/10.1016/j.jid.2018.10.029).

**QUIZ QUESTIONS**

1. **What is your diagnosis?**
   a. Mycosis fungoides
   b. Psoriasis
   c. Atopic dermatitis
   d. Erythema annulare centrifugum
   e. Subacute cutaneous lupus erythematosus

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2. Which of the following is TRUE regarding the results of the longitudinal prospective cohort study by Kim et al. (2019)?
   a. Non-Hispanic black children and Hispanic children had greater odds of persistent atopic dermatitis than non-Hispanic white children even after adjustment for sociodemographic factors and maternal plasma vitamin D levels.
   b. Maternal plasma 25(OH)D levels were lower among mothers of non-Hispanic white children than among mothers of non-Hispanic black, Hispanic, and other non-Hispanic children.
   c. The odds ratio of incident atopic dermatitis in early childhood among non-Hispanic black children decreased after adjusting for child sex, maternal education, parental atopy, neighborhood income, and maternal blood 25(OH)D levels.
   d. They determined there was a positive association between Hispanic ethnicity and incident atopic dermatitis after adjustment for sociodemographic factors and maternal plasma vitamin D levels.
   e. Other non-Hispanic children showed statistically significant increased odds of persistent atopic dermatitis compared with non-Hispanic white children.

3. In the article by Kim et al. (2019), which of the following is NOT a proposed contributing factor to racial/ethnic differences in atopic dermatitis persistence in mid-childhood?
   a. Pattern of health care—seeking behavior
   b. Differences in innate and adaptive immunity dysfunction among different races
   c. Presence of FLG2 mutations in African Americans
   d. Parental history of atopy
   e. Higher rates of vitamin D deficiency in individuals with darker skin

See following pages for detailed answers.
Atopic dermatitis (AD) is a common chronic inflammatory skin disease often associated with other atopic disorders such as asthma and allergic rhinitis. It results from a complex interaction of epidermal barrier dysfunction, immune dysregulation, and environmental factors. This skin disease is clinically characterized by pruritus and a chronic relapsing course that usually begins in infancy but occasionally develops in adulthood. In general, the prevalence of AD is higher in urban and high-income areas. About 50-60% of AD is evident within the first year of life. AD has a broad clinical spectrum that can be divided into acute and chronic presentations. At any age, patients can develop acute lesions characterized by edematous, erythematous papules and plaques that may exhibit vesication, oozing, and crusting. Chronic lesions present as thickened plaques with lichenification and scale. Nummular lesions, such as the one depicted in the image presented here, may develop on the extremities in children and adults, appearing as coin-shaped eczematous plaques, usually 1-3 cm in diameter, and often with prominent oozing, scaling, and crusting (Bolognia et al., 2018). In early phases, histopathology shows parakeratosis, mild spongiosis, and exocytosis of lymphocytes. Subacute lesions are characterized by hyperkeratosis, acanthosis, and parakeratosis with less prominent spongiosis and inflammatory cell infiltrate. Chronic lesions resemble those of lichen simplex chronicus with pronounced epidermal thickening (Elder et al., 2015).

Discussion of incorrect answers:

a. **Mycosis fungoides:** Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma and estimated to account for approximately 50% of all primary cutaneous lymphomas. Although typically it is a disease of older adults with a median age at diagnosis of 55-60 years, children and adolescents may also be affected. MF is characterized by variably sized erythematous patches and plaques with fine scale that may evolve to nodules or tumors. Anatomically, it favors the buttocks and sun-protected areas of the trunk and extremities. The patch/plaque stage results from intraepidermal and superficial dermal infiltration of neoplastic T cells. MF may follow an indolent course over many years; associated features include pruritus, poikiloderma, and tumor ulceration. Several variants of MF with distinctive clinicopathologic features have been described and include folliculotropic MF, pagetoid reticulosis, and granulomatous slack skin (Bolognia et al., 2018). The etiology of MF remains unclear, although genetic, environmental, and immunologic factors are thought to play a role. Early lesions of MF may show a patchy band-like lymphocytic infiltrate in the papillary dermis. Small- to medium-sized lymphocytes with characteristic cerebriform nuclear contours may be seen, although early stages may reveal only a few of these atypical T cells. Lymphoid epidermotropism, in which pagetoid infiltrate of atypical lymphocytes into the epidermis is observed, is seen more frequently in later plaque MF stages (Elder et al., 2015). Multiple biopsies may be required to establish the diagnosis.

b. **Psoriasis:** Psoriasis is a chronic inflammatory skin condition affecting 2% of the world’s population. It typically presents as raised, well-demarcated erythematous oval plaques with thick silvery scales that result from hyperproliferation of the epidermis with premature maturation of keratinocytes and retention of nuclei in the stratum corneum (Nestle et al., 2009). Commonly involved sites include the scalp, intergluteal fold, umbilicus, extensor surfaces, such as the elbows and knees, the nails, hands, feet, and trunk. Psoriasis can also affect other major body folds (axilla, inguinal crease, inframammary fold) and the genitalia. Psoriasis is driven by various classes of T cells and their complex interactions with dendritic cells and cells involved in innate immunity (Bolognia et al., 2018). Histopathology of well-developed psoriasis lesions demonstrate acanthosis with regular elongation of rete ridges, diminished to absent granular layer, confluent parakeratosis, Munro microabscesses, and dilated blood vessels at the tips of the dermal papillae (Elder et al., 2015).

d. **Erythema annulare centrifugum:** Erythema annulare centrifugum refers to erythematous annular lesions that expand centrifugally, resulting in a characteristic pink papule or plaque with “trailing” white scale and central clearing. In deeper lesions, there may be no associated scaling. Erythema annulare centrifugum has been postulated to be the result of a hypersensitivity reaction to a foreign antigen. Although infections, drugs, systemic diseases, malignancy, and pregnancy have been associated occasionally with erythema annulare centrifugum, no etiologic agent is ever identified in most cases. Lesions are more common in adults and may persist anywhere from a few days to a few months (Bolognia et al., 2018). Histopathology of superficial erythema annulare centrifugum is characterized by superficial perivascular lymphohistiocytic infiltrate with endothelial cell swelling, extravasation of erythrocytes in
the papillary dermis, and focal epidermal spongiosis and parakeratosis (Elder et al., 2015).

e. **Subacute cutaneous lupus erythematosus:** Subacute cutaneous lupus erythematosus is a form of cutaneous lupus that manifests as a photosensitive non-scarring erythematosus annular eruption or papulosquamous eruption. Lesions last longer than acute cutaneous lupus and favor the sun-exposed skin of the lower neck, upper trunk, back, and extensor surfaces of the arms (Alniemi et al., 2017). Although the etiology is poorly understood, certain drugs have been reported to trigger subacute cutaneous lupus erythematosus, including hydrochlorothiazide, calcium channel blockers, angiotensin-converting enzyme inhibitors, terbinafine, tumor necrosis factor-α inhibitors, proton-pump inhibitors, taxanes, and nonsteroidal anti-inflammatory drugs (Bologna et al., 2018). There is a strong association with the presence of anti-SSA/Ro autoantibodies and many studies show that a high percentage of patients with subacute cutaneous lupus erythematosus fulfills four or more of the American College of Rheumatology criteria for systemic lupus erythematosus diagnosis (Alniemi et al., 2017). Histopathology shows a sparse mononuclear inflammatory infiltrate in the upper dermis, pronounced dermal edema, continuous subepidermal vacuolization, focal hemorrhage, and mucin deposition (Elder et al., 2015).

2. Which of the following is TRUE regarding the results of the longitudinal prospective cohort study by Kim et al. (2019)?

**CORRECT ANSWER:** a. Non-Hispanic black children and Hispanic children had greater odds of persistent atopic dermatitis than non-Hispanic white children even after adjustment for sociodemographic factors and maternal plasma vitamin D levels.

The above statement is true according to the article by Kim et al. (2019). A total of 58 of 392 children (14.8%) with incident atopic dermatitis (AD) in early childhood were found to have persistent AD in mid-childhood. The authors found that non-Hispanic black children (OR = 3.23, 95% confidence interval [CI] = 1.64–6.35) and Hispanic children (OR = 3.24, 95% CI = 1.35–7.73) had higher odds of persistent disease in mid-childhood than non-Hispanic white children. This association was strengthened after multivariable adjustment for sociodemographic factors (non-Hispanic black children: OR = 6.07, 95% CI = 2.63–14.00; Hispanic children: OR = 5.77, 95% CI = 2.14–15.57) and maternal 25(OH)D levels (non-Hispanic black children: OR = 6.26, 95% CI = 2.32–16.88; Hispanic children: OR = 6.42, 95% CI = 1.93–21.41).

**Discussion of incorrect answers:**

b. Maternal plasma 25(OH)D levels were lower among mothers of non-Hispanic white children than among mothers of non-Hispanic black, Hispanic, and other non-Hispanic children: This is false based on the data presented by Kim et al. (2019). The characteristics of the study participants, as outlined in Tables 1 and 2, illustrate that maternal plasma 25(OH)D levels were higher among mothers of non-Hispanic white children (mean = 63.3 nmol/L) than among mothers of non-Hispanic black (mean = 48.5 nmol/L), Hispanic (mean = 50.1 nmol/L), and other non-Hispanic children (mean = 52.1 nmol/L).

c. The odds ratio of incident atopic dermatitis in early childhood among non-Hispanic black children decreased after adjusting for child sex, maternal education, parental atopy, neighborhood income, and maternal blood 25(OH)D levels: This is false according to the results presented by Kim et al. (2019). The odds ratio of incident AD in early childhood among non-Hispanic black children (OR = 2.12, 95% CI = 1.55–2.90) increased after adjusting for child sex, maternal education, parental atopy, neighborhood income (OR = 2.67, 95% CI = 1.86–3.83), and maternal blood 25(OH)D levels (OR = 2.71, 95% CI = 1.75–4.19).

d. They determined there was a positive association between Hispanic ethnicity and incident atopic dermatitis after adjustment for sociodemographic factors and maternal plasma vitamin D levels: This is false. The authors found no association between Hispanic ethnicity and incident AD after adjustment for sociodemographic factors (OR = 1.23, 95% CI = 0.82–1.86) and maternal plasma vitamin D levels (OR = 1.10, 95% CI = 0.66–1.84).

e. Other non-Hispanic children showed statistically significant increased odds of persistent atopic dermatitis compared with non-Hispanic white children: This is false according to the results presented by Kim et al. (2019). Although children with other non-Hispanic race did show increased odds of persistent AD compared with non-Hispanic white children, the result was not statistically significant (OR = 2.06, 95% CI = 0.81–5.25, after adjustment for sociodemographic factors; OR = 1.19, 95% CI = 0.39–3.91, after adjustment for maternal vitamin D levels). The authors postulate this was because of small sample size.
3. In the article by Kim et al. (2019), which of the following is NOT a proposed contributing factor to racial/ethnic differences in atopic dermatitis persistence in mid-childhood?

CORRECT ANSWER: d. Parental history of atopy

Parental history of atopy is not proposed as a contributing factor to the racial/ethnic differences observed in atopic dermatitis (AD) persistence in mid-childhood in the article by Kim et al. (2019). Although the authors did collect data showing that 65.5% of children with AD persistent in mid-childhood had one or more parents with history of atopic disease, strong parental history of atopic disease was seen among all races/ethnicities examined in the study (non-Hispanic white, 68.5%; non-Hispanic black, 59.5%; Hispanic, 67.6%; and other non-Hispanic, 62.2%).

Discussion of incorrect answers:

a. Pattern of health care-seeking behavior: In fact, the authors do discuss differences in health care-seeking behavior as one factor that may contribute to racial/ethnic disparities in AD persistence. A study by Fischer et al. (2017) evaluated health care utilization for childhood eczema among different racial/ethnic groups in the USA and found that non-Hispanic blacks were less likely to report an ambulatory visit for eczema than non-Hispanic whites. Although overall health care utilization by non-Hispanic black children was lower, those who accessed medical care reported more visits, more prescriptions obtained for eczema, and were more likely to report a dermatology visit than non-Hispanic whites. This finding was independent of sociodemographic factors, insurance status, and presence of atopic comorbidities, suggesting greater AD disease severity in this group (Fischer et al., 2017).

b. Differences in innate and adaptive immunity dysfunction among different races: The authors acknowledge that there may be differences in innate and adaptive immunity dysfunction among different races as another factor that may contribute to racial/ethnic disparities in AD persistence. Pointing to strong evidence in the literature that supports the hypothesis that the immune system plays a mediating role in the association between psychosocial stress and health outcomes, Dowd et al. (2014) examined associations between race/ethnicity, socioeconomic status, stress, and immune function using Epstein-Barr virus IgG levels as an indirect marker of cell-mediated immunity. In their results, they found those with black race/ethnicity to have Epstein-Barr virus antibody levels 13.6% higher than those with white race/ethnicity after adjusting for education and income, confirming the presence of racial differences in markers of immune function (Dowd et al., 2014).

c. Presence of FLG2 mutations in African Americans: The authors do propose the presence of FLG2 mutations in African Americans as one possible contributing factor to racial/ethnic differences in AD persistence. FLG is a structural protein involved in the skin barrier function. Loss-of-function mutations and reduced FLG levels are associated with increased odds of developing AD (Bolognia et al., 2018). Results of a multi-year prospective cohort study by Margolis et al. (2014) demonstrated that African-American children with certain loss-of-function mutations in FLG2 were more than 50% more likely to have persistent AD than African-American children without these variants.

e. Higher rates of vitamin D deficiency in individuals with darker skin: The authors do propose higher rates of vitamin D deficiency in individuals with darker skin as a possible contributing factor to racial/ethnic differences in AD persistence. The study by Kim et al. (2019) demonstrated that the maternal plasma 25(OH)D levels among mothers of non-Hispanic black, Hispanic, and other non-Hispanic children were lower than the levels in mothers of non-Hispanic white children, further supporting findings in various other studies that suggest a link between vitamin D deficiency and childhood AD. Individuals with darker skin tend to have higher rates of vitamin D deficiency in part because greater pigmentation reduces vitamin D production (Harris, 2006).

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REFERENCES