

every event related to therapies. We believe that the observation of HR might be because these patients followed up with dermatologists, which highlights the importance of monitoring by a multidisciplinary team.

There must be different mechanisms in how the anti-PD-1 pathway works in different types of cancer and among different people. This might explain vitiligo-like reactions in patients with melanoma² and the opposite effect of HR in lung cancer, and now also in colorectal cancer or Hodgkin lymphoma. It also may explain why some patients show HR, and some others who also had gray hair do not have HR. One hypothesis could be the interaction of the immune system with tumor cells may release some inflammatory or proinflammatory mediators. There is evidence that inflammation can induce hair follicle pigmentation.³ The mechanisms of HR remain unclear. Further studies to clarify these questions are yet required.

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Allergen Concerns and Popular Skin Care Products

To the Editor We read with great interest the Original Investigation by Xu et al titled “Consumer Preferences, Product Characteristics, and Potentially Allergenic Ingredients in Best-Selling Moisturizers”¹ and published in a recent issue of *JAMA Dermatology*. In discussions with dermatology colleagues regarding this article,¹ we noticed another disturbing marketing trend: the labeling of skin care products marketed for babies.

In our experience, patients often consider baby skin care products to be safer and gentler. However, when we reviewed a sampling of popular adult skin care products compared with their counterparts marketed for babies, we found some surprising cases of misleading labeling.

For example, when comparing Vaseline original petroleum jelly to Vaseline baby petroleum jelly, the difference between the 2 products—besides the fact that Vaseline baby petroleum jelly has a pink label with the word “hypoallergenic” on it—is that Vaseline baby petroleum jelly contains

fragrance while Vaseline original does not. When comparing a product such as Aveeno baby daily moisture lotion to the counterpart marketed for adults (Aveeno daily moisturizing lotion), they contained identical potential allergens.

A study published in 2016² performed a systematic review of patch test results in children and adolescents with dermatitis and found that the top 5 most common allergens in children were nickel, thimerosal, cobalt, fragrance, and lanolin. Yet, we found that many popular baby products contain lanolin, including Aquaphor Baby Healing Ointment Advanced Therapy Skin Protectant, as well as many nipple skin protectants (which easily come into contact with a baby’s skin). In addition, many baby moisturizers, such as Johnson’s baby lotion; Cetaphil baby daily lotion with organic calendula, sweet almond oil, and sunflower oil; and Aveeno baby calming comfort lotion contain fragrance.

We think it is important to discuss with parents and patients that baby moisturizing products can differ in allergenicity and irritancy. We are curious to know if Xu et al saw any difference in the price of moisturizer products in their data when it comes to labeling skin care products marketed for babies or “approved for pediatric use.”

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1. Xu S, Kwa M, Lohman ME, Evers-Meltzer R, Silverberg JL. Consumer preferences, product characteristics, and potentially allergenic ingredients in best-selling moisturizers. *JAMA Dermatol*. 2017;153(11):1099-1105. doi:10.1001/jamadermatol.2017.3046
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To the Editor We read with great interest the article by Xu et al¹ published in a recent issue of *JAMA Dermatology* highlighting the high prevalence of contact allergens in common moisturizers. Their data mirror similar results in our recent study² investigating contact allergens in pediatric personal care products marketed as hypoallergenic, dermatologist recommended and/or tested, fragrance free, or paraben free.² Similar to the study by Xu et al,¹ which found that 88% of common moisturizers contained at least 1 common contact allergen, we found that 167 of 187 of our selection of pediatric products (89%) contained at least 1 allergen.

There are 2 further points that we think the *JAMA Dermatology* readership would appreciate. First, chronic exposure to cutaneous allergens through personal care products may to a certain degree have contributed to the global rise in atopic dermatitis (AD) incidence. While initial exposure to cutaneous allergens promotes T helper cell 1 (Th1)-skewed skin inflammation, which is characteristic of allergic contact

dermatitis (ACD), repeated and prolonged exposure to contact allergens drives a shift toward T helper cell 2 (Th2) inflammation, which is characteristic of AD. Similarly, initial contact allergen exposure in AD skin, in contrast to non-AD skin, shows increased Th2 programming, potentially altering risk of AD persistence and severity. Second, while overall risk of ACD does not seem to be increased in individuals with AD vs those without, there are likely differences in allergen-specific ACD risk in these 2 populations; for example, there is a strong association between compositae mix sensitization and AD status (compositae mix was found in 5% of moisturizers analyzed by Xu et al¹).³ Given these differences, there are likely objectively better and worse emollients to recommend to patients with AD. An additional concern, which has not been adequately examined yet, is the higher systemic exposure to endocrine disrupting chemicals in children who frequently use emollients, and perhaps in particular, individuals with AD.⁴

A solution to this problem of high prevalence of contact allergens in personal care products is unclear. As Xu et al¹ noted, there is currently very limited regulation of marketing terms such as “hypoallergenic” or “dermatologist-recommended.” An initial step to clarify the hypoallergenic definition has been undertaken by the North American Contact Dermatitis Group, a step that we commend, but translating this into regulation will be difficult.⁵ Chronic exposure to cutaneous allergens likely has far-reaching consequences in individuals with and without AD. Highlighting their use in common moisturizers is important and clinicians should be cognizant when recommending personal care products to their patients.

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In Reply We thank Hamann and Thyssen, as well as Harview and Hsiao, for their interest in our work and thoughtful commentaries. We agree that the safety and affordability of cosmetics and personal care products explicitly marketed toward the pediatric population is important to public health. In a recent publication of all adverse events (AE) submitted to the US Food and Drug Administration surrounding cosmetics and personal care products from 2004 to 2016, baby products were associated with the highest percentage of self-reported serious AEs (eg, death, serious injury, or hospitalization).¹

Labeling of cosmetics and personal care products as “baby safe” or “for pediatric use,” similar to “hypoallergenic” or “fragrance-free,”² is largely meaningless from a medical standpoint. We suspect that the label of “pediatrician-approved” is applied as inconsistently as “dermatologist-approved.” In our cohort of best-selling moisturizers,² 5 products were marketed for baby use. Although the label “pediatric use” did not have a higher average price (\$0.58/ounce) compared with the global average (\$0.59/ounce), these products all had at least 1 allergen in the 2012 North American Contact Dermatitis Group screening series. All 5 contained a fragrance or cross-reacting botanical ingredient, while 2 products had propylene glycol and tocopherol. Importantly, our study² did not explicitly investigate moisturizers for pediatric use. Specific investigations of best-selling moisturizers marketed explicitly for children would provide additional and important information. Ultimately, we agree that standardization of labeling (eg, “hypoallergenic”³) would be of high value for all consumers. A label (eg, “baby-safe”) without accompanying evidence and enforcement only causes further consumer confusion.

The most common AEs from personal care products are allergic and irritant contact dermatitis. Pediatric patients with atopic dermatitis have barrier dysfunction and aberrant innate and acquired immunity, suggesting an increased risk of cutaneous sensitization. Some have argued for preemptive avoidance of common cosmetics sensitizers for children with atopic dermatitis.⁴ This strategy may be difficult given the existing challenges in selecting truly hypoallergenic products and requires further validation with prospective studies. Beyond cutaneous AEs, there remains a challenge in definitively proving or disproving the relationship between common ingredients in cosmetics (eg, parabens, phthalates) with more serious adverse health outcomes such as cancer or endocrine disruption.

Regulation of the \$460 billion cosmetics industry⁵ in the United States has remained largely unchanged since 1938 when the Food, Drug, and Cosmetics Act was first enacted by Congress.⁶ In 2015, the Personal Care Products Safety Act (PCPSA) was introduced to the Senate, including provisions to increase ingredient transparency, mandatory manufacturer registration with the US Food and Drug Administration, and yearly review of 5 cosmetics ingredients to determine their appropriateness for inclusion in personal care products. With significant industry and medical organization support including the National Psoriasis Foundation, PCPSA is a step in the right direction to improving cosmetics regulation and oversight. Dermatologists represent the physician group most quali-

fied to comment on the safety and use of personal care products. As such, we have a responsibility to educate consumers, influence industry, and inform policy makers. Guiding the definition of evidence-based labeling and supporting their enforcement for key products such as moisturizers would positively benefit our patients.

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CORRECTION

Error in Figure Legend: In the article titled "Factors Associated With Clinical Remission of Skin Disease in Dermatomyositis" by Wolstencroft et al,¹ published online November 7, 2017, there was an error in the key for Figure 1B. This article was corrected online.

1. Wolstencroft PW, Chung L, Li S, Casciola-Rosen L, Fiorentino D. Factors associated with clinical remission of skin disease in dermatomyositis [published online November 7, 2017]. *JAMA Dermatol.* doi:10.1001/jamadermatol.2017.3758

NOTABLE NOTES

The Himba and Red Ochre—Aesthetics, Symbolism, and Adaptation

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The Himba are an indigenous, seminomadic tribe from Northern Namibia numbering around 50 000 members.¹ They are well known for their women applying a paste of butter, fat, and red ochre known as *otjize* to their skin and hair.¹ Red ochre is an earth-derived pigment obtaining its color from dehydrated hematite, or ferric oxide, which confers the Himba women a unique red hue on their skin.^{1,2}

The Himba largely describe the practice of applying *otjize* from an aesthetic stance as a makeup that women apply.^{1,2} It also likely has symbolic meaning across various global ancient societies that used the red pigment, signifying the earth and blood.^{2,3} The blood symbolized motherhood, menstruation, and reproduction.^{2,3} Some cultures using red ochre even thought of the red dye from iron ore as growing within the earth like a fetus grows within a uterus.³

The history of applying ochre dates back to the Upper Paleolithic Age, long before Namibia was ever established.³ The salience of the color red as found in ochre evokes an almost universal human behavioral response as hypothesized by anthropologists: feelings of excitement, power, and life through blood.³ As such, Neolithic farmers used red to bestow significance on representations of their gods, coating figurines of the God of rain and fertility in ochre.³

Additional hypotheses beyond cosmetic and symbolic appeal for the use of ochre have been suggested for the Himba women. Ochre may have repelled insects and offered sun protection as an ancient

sunscreen to tribes well beyond Namibia, extending into Ethiopia, Angola, and throughout southern Africa.^{1,2} Samples of various colors of ochre were analyzed in vitro from these regions and showed a mean (SD) sun-protectant factor (SPF) range of 0.9 (0.1) to 13.1 (1.3), with the highest values coming from red ochre.² The samples taken from the Himba women had the highest average SPF of 8.9 (1.2).² Samples were tested at 2 mg applied per cm², when the true average application of Himba women was 4.2 mg/cm², suggesting that the actual SPF conveyed is greater than measured.² Thus, Rifkin et al² suggested that the application of red ochre was also a cultural adaptation to a changing environment that included migration to lower latitudes with increased UV radiation exposure.² The Himba women seem to be making a fashion statement with a purpose.

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