Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Beyond *JAAD* October 2020: Articles of interest to dermatologists from the nondermatologic literature

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PATTERNS OF OMEGA-3 AND OMEGA-6 FATTY ACID DIETARY INTAKE AND MELANOMA THICKNESS AT DIAGNOSIS

The authors tested the hypothesis that a dietary pattern high in proinflammatory omega-6 fatty acids would be associated with thick melanomas. In 364 Australian patients with primary melanomas, they assessed prediagnosis consumption of 39 food groups by food frequency questionnaires completed within 2 months of diagnosis. Two major fatty acid dietary patterns were identified. The first, "meat, fish, and fat," positively correlated with intakes of all fatty acids. The second, "fish, low meat, and low fat," positively correlated with long-chain omega-3 fatty acid intake, and inversely with medium-chain omega-3 and omega-6 fatty acid intakes. Prevalence of thick melanomas was significantly higher in individuals in the highest tertile of meat, fish, and fat consumption. After adjustment for age, sex, skin examinations, and energy intake, patients in the highest tertile of meat, fish, and fat consumption had a prevalence ratio of thick melanoma versus those in the lowest tertile of 1.34. The positive association between meat, fish, and fat diets and melanoma thickness was observed more clearly among patients who reported serious comorbidities at melanoma diagnosis (prevalence ratio 1.83) and those with a family history of melanoma (prevalence ratio 2.32). The authors suggested that further studies may provide evidence for a role for diet to complement standard sun protection measures to reduce melanoma risk.

Mahamat-Saleh Y, Hughes M, Miura K, et al. Patterns of omega-3 and omega-6 fatty acid dietary intake and melanoma thickness at diagnosis [e-pub ahead of print]. *Cancer Epidemiol Biomarkers Prev*. 2020. https://doi.org/10.1158/1055-9965.EPI-20-0319.

MULTIPLE PRIMARY MELANOMA INCIDENCE TRENDS OVER FIVE DECADES, A NATION-WIDE POPULATION BASED STUDY

The authors identified patients receiving a diagnosis of a first primary cutaneous melanoma reported to the Swedish Cancer Registry and followed them for up to 10 years for a diagnosis of subsequent primary melanoma. A total of 54,884 patients with a primary melanoma were included, and within 10 years 2469 received a diagnosis of a subsequent primary melanoma. The study was conducted during 5 decades, the 1960s through and including the 2000s, and during those 5 decades there was a steady increase in frequency of second primary melanomas. In the 1960s cohort, less than 1% of men and 1.1% of women had a second primary melanoma, whereas in the 2000-2010 cohort, 6.4% of women and 7.9% of men had a second primary melanoma. The increase was observed independent of age, sex, invasiveness, or site of the melanoma. Furthermore, in patients who received a diagnosis of a second melanoma, the frequency of those having greater than 2 primary melanomas, which was observed to be 0% in the 1960s cohort, increased to 18% in the 2000-2010 cohort. The authors stressed the importance of the recognition of this trend and called for an annual full-body skin examination for at least 10 years after a patient's initial melanoma diagnosis.

Helgadottir H, Isaksson K, Fritz I, et al. Multiple primary melanoma incidence trends over five decades, a nation-wide population based study. *J Natl Cancer Inst*. 2020. https://doi.org/10.1093/jnci/djaa088.

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Funding sources: None.
Conflicts of interest: None disclosed.
Accepted for publication July 4, 2020.
Reprints not available from the authors.

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Published online July 8, 2020.
J Am Acad Dermatol 2020;83:1233-6.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2020.07.001

ASSOCIATION OF ANTIBIOTIC EXPOSURE WITH SURVIVAL AND TOXICITY IN PATIENTS WITH MELANOMA RECEIVING IMMUNOTHERAPY

In accordance with previous studies showing that gut microbial diversity is associated with improved response to immune checkpoint inhibitors (ICI), the authors tested the hypothesis that antibiotic receipt before treatment with ICI for metastatic melanoma would be associated with decreased survival. Patients with stage III and IV melanoma treated with ICI between 2008 and 2019 were selected from an institutional database, and those who received antibiotics within 3 months before the first infusion of ICI were identified. Primary outcome was overall survival, and secondary outcomes were melanoma-specific mortality and immunomediated colitis requiring intravenous steroids. Patients with stage III and IV melanoma who were exposed to antibiotics before ICI had statistically worse overall survival than unexposed patients. Patients with stage III disease had a hazard ratio of 2.78; those with stage IV disease, 1.81. The antibiotic group also had a greater incidence of colitis (hazard ratio 2.14), which, although associated with antibiotics, was *Clostridium difficile* colitis in only 3 cases. Given the finding of significantly worse overall survival in patients exposed to antibiotics before treatment with ICI, the authors called for caution when considering the prescription of antibiotics for patients who may be subsequent candidates for ICI.

Mohiuddin J, Chu B, Facciabene A, et al. Association of antibiotic exposure with survival and toxicity in patients with melanoma receiving immunotherapy [e-pub ahead of print]. *J Natl Cancer Inst*. 2020. https://doi.org/10.1093/jnci/djaa057.

HUMAN-COMPUTER COLLABORATION FOR SKIN CANCER RECOGNITION

The authors undertook in this study to examine the utility of diagnostic artificial intelligence (AI) in support of clinical decision making. Clinicians were divided into several groups based on experience, including board-certified dermatologists, dermatology residents, and general practitioners. Clinicians were tasked with diagnosing digital images, first without and then with AI support. The study showed an inverse relationship between the net gain from AI-based support and clinician experience. Clinicians in the least experienced group changed their initial diagnosis more often than experts (26.0% versus 14.7%). The authors recorded the time needed to reach a diagnosis, and used this as a surrogate marker for confidence. Expert raters benefited only marginally (net gain 13.4%) and only if they were not confident with their initial diagnosis, but not if they were confident. If experts were confident, they were usually correct and did not need support. The authors offered that this finding suggests that if experts have high confidence in their initial diagnosis, they should ignore AI-based support or not use it at all, whereas the least experienced clinicians gain the most from AI-based support.

Tschandl P, Rinner C, Apalla Z, et al. Human-computer collaboration for skin cancer recognition [e-pub ahead of print]. *Nat Med*. 2020. https://doi.org/10.1038/s41591-020-0942-0.

MANAGEMENT OF PRIMARY SKIN CANCER DURING A PANDEMIC: MULTIDISCIPLINARY RECOMMENDATIONS

The authors of this article, accepted for publication 6 weeks into the US coronavirus disease 2019 (COVID-19) pandemic, examined the marginal benefit of early physician intervention for skin cancer versus the marginal increased risk of contracting COVID-19 in the physician's office or clinic setting. The authors observed that the proper calculation and assessment of relative risks of early or deferred skin cancer treatment is particularly significant because the number of skin cancers diagnosed annually in the United States exceeds the number of all other cancers combined. The authors pointed out that COVID-19 infection has its highest morbidity and mortality in the elderly, and that the median age of diagnosis is 60 to 69 years for melanoma, 66 years for basal cell carcinoma, 75 to 79 years for Merkel cell carcinoma, and 78 to 80 years for squamous cell carcinoma. Taking into account and balancing the risks of early treatment and possible COVID-19 infection versus deferred treatment and avoidance of the possibility of COVID-19, with attendant possibility of progression of skin cancer, the authors arrived at several suggestions. For Merkel cell carcinoma, they suggested prioritization of treatment and delay of no more than 1 month. For melanoma, they recommended delay of no more than 3 months, depending on depth and biopsy findings. For basal cell carcinoma, they recommended delay for no more than 3 months "unless patients are highly symptomatic." For squamous cell carcinoma, they allowed for 2 to 3 months' deferral of treatment of T1 to T2a disease "unless there is rapid growth, or patients are symptomatic or immunosuppressed." They observed that "for the majority of patients at higher risk of COVID-19-related morbidity and/or mortality, the risk of contracting COVID-19 likely outweighs the benefits of early treatment for their skin cancer."

Baumann B, MacArthur K, Brewer J, et al. Management of primary skin cancer during a pandemic: multidisciplinary recommendations

[e-pub ahead of print]. *Cancer*. 2020. https://doi.org/10.1002/cncr.32969.

TREATMENT EFFECT OF OMALIZUMAB ON SEVERE PEDIATRIC ATOPIC DERMATITIS: THE ADAPT RANDOMIZED CLINICAL TRIAL

High immunoglobulin (Ig) E levels are associated with severe atopy, and atopic dermatitis lesions have been found to bear sizeable numbers of IgE-bearing cells. Receptor bound, these cells present allergens to primed T cells, leading to T-cell activation and cutaneous inflammation, and promote release of IgE-mediated histamine from mast cells, aggravating eczema through the itch-scratch cycle. The authors sought to support the hypothesis that an anti-IgE medication, omalizumab, would reduce IgE levels in children with severe eczema, alleviating symptoms. The authors studied 62 children, mean age 10.3 years, and randomized them into treatment with either omalizumab or placebo. Using the Scoring Atopic Dermatitis index as a metric for level of symptoms, the authors found a significant improvement with patients treated with omalizumab versus placebo, with a statistically significant reduction of Scoring Atopic Dermatitis indices, and also a statistically significant improvement of quality-of-life indexes, including the Children's Dermatology Life Quality Index and the Pediatric Allergy Quality of Life Questionnaire score. The authors noted that improvement occurred despite lower potent topical corticosteroid use in the omalizumab group compared with the placebo group. They offered its topical corticosteroid–sparing effect as a reason to consider omalizumab as a treatment option.

Chan S, Cornelius V, Cro S, Harper J, Lack G. Treatment effect of omalizumab on severe pediatric atopic dermatitis: the ADAPT randomized clinical trial. *JAMA Pediatr*. 2020;174(1):29-37.

ALLERGEN-SPECIFIC IMMUNOTHERAPY FOR PATIENTS WITH ATOPIC DERMATITIS SENSITIZED TO ANIMAL DANDER

The authors enrolled in a study atopic dermatitis (AD) patients who were sensitized to cat and dog dander, and prescribed a course of treatment with subcutaneous treatment of allergy-specific immunotherapy (AIT) with dog dander, cat dander, or both. A total of 19 patients underwent AIT. Average patient age was 31 years. The duration of AIT ranged from 2 to 58 months. The symptoms of 17 of the 19 patients were well controlled. Specific immunoglobulin E levels and IgG4 levels were obtained after 1 year in each patient who received AIT for more than 6 months. Specific immunoglobulin E levels to cat and dog dander were decreased after AIT compared with initial levels. These decreases were statistically significant. Specific IgG4 levels were found to be increased, but the difference was not significant. The authors cited this as the first study on the result of AIT in patients with atopic dermatitis sensitized to cat or dog dander, and offered it as a complement to other therapies such as dupilumab and dander avoidance.

Chu H, Park K, Kim S, et al. Allergen-specific immunotherapy for patients with atopic dermatitis sensitized to animal dander. *Immun Inflamm Dis*. 2020;1-5. https://doi.org/10.1002/iid3.291.

ENVIRONMENTAL FACTORS IN EPITHELIAL BARRIER DYSFUNCTION

The authors discussed epithelial barrier dysfunction as an effect of environmental stress. Citing the epithelium—respiratory, gastrointestinal, and cutaneous—as not just a barrier to the outside world but also a factor in maintaining homeostatic balance between host and environment, they systematically listed the many insults to our epithelium that have come about since the dawn of the industrial revolution and continue to emerge and proliferate in the 21st century. With respect to the skin, the authors described the various at-risk cellular actors of the cutaneous immune system, including keratinocytes, Langerhans cells, dendritic cells, melanocytes, macrophages, and several types of T cells. Among the insults cited were epithelial-barrier-damaging enzymes in allergens, along with detergents and cleaning products, ozone, particulate matter, and nanoparticles. With respect to the last, they called for a better understanding of cutaneous penetration mechanisms of nanoparticulates and their potential role in enhancing the penetration of other substances, including toxic or irritating ones, that abound in the exposome. The authors called for "international rapid action on the control of epithelial barrier-attacking environmental pollutants" and reminded dermatologists that even as we are custodians of the body's largest organ, that organ is itself part of a larger and more varied and extensive interface between us and a polluted world.

Sozener Z, Cevhertas L, Nadeau K, Akdis M, Akdis C. Environmental factors in epithelial barrier dysfunction [e-pub ahead of print]. *J Allergy Clin Immunol*. 2020. https://doi.org/10.1016/j.jaci.2020.04.024.

ERYTHRODERMA: A PROSPECTIVE STUDY OF 309 PATIENTS FOLLOWED FOR 12 YEARS IN A TERTIARY CENTER

The authors performed a prospective study at the University of São Paulo Medical School from 2007 to 2018 of 309 patients with acquired erythroderma. The aim was to find clues to the etiology and to propose a diagnostic approach to facilitate the

management of these patients. They found that median age at diagnosis was 57 years, with a male-to-female ratio of 2.2. Eczema was the most frequent etiology (20.7%), followed by psoriasis (16.8%), Sezary syndrome (12.3%), drug eruption (12.3%), atopic dermatitis (8.7%), and cutaneous T-cell lymphoma (5.5%). In 16.8% of patients, an underlying etiology was unable to be determined. Atopic dermatitis was associated with higher immunoglobulin E levels. Acute onset was associated with atopic dermatitis and drug reactions. The causative agents in drug-induced erythroderma were identified in 21 patients, with anticonvulsants (especially carbamazepine), antihypertensives, and anti-inflammatory drugs being the most common ones. This study supported the findings of previous studies that the exacerbation of preexisting dermatoses is the most prevalent cause of erythroderma. Forty percent of this study's patients had preexisting dermatoses. With respect to patients with idiopathic erythroderma, the authors called for a computed tomographic scan to search for internal malignancies causing paraneoplastic erythroderma.

Miyashiro D, Sanches J. Erythroderma: a prospective study of 309 patients followed for 12 years in a tertiary center. *Nat Sci Rep*. 2020 10:9774. https://doi.org/10.1038/s41598-020-66040-7.

TOPICAL TRIAMCINOLONE INDUCED CUSHING SYNDROME: A CASE REPORT

Although a single case report, this article is worth summarizing to remind practicing dermatologists that although "topical steroid phobia" is a real entity, so is actual topical steroid toxicity.

The authors, from the Departments of Dermatology and Pediatric Endocrinology at the University of Texas Southwestern Medical School in Dallas, TX, described a case of iatrogenic Cushing syndrome and adrenal insufficiency in a newborn secondary to overuse of triamcinolone cream 0.1% for the treatment of diaper dermatitis. The previously healthy female patient developed a diaper dermatitis at aged 2 months. Her pediatrician prescribed triamcinolone cream 0.1% twice daily. Her parents proceeded to apply the medication 4 to 5 times daily to 6% of her body surface area for 3 months. At aged 2 months, her weight and length had been at the 10th and 25th percentiles, respectively. At a consultation at aged 5 months, she was at the 90th percentile for weight and less than 1 percentile for length. She exhibited moon facies. Adrenocorticotropic hormone levels were below low normal, as was her serum cortisol level. Triamcinolone cream was promptly discontinued, and treatment of the patient's skin eruption was initiated with fluconazole systemically and topical clotrimazole cream with zinc oxide paste topically. At 10-month follow-up, the patient's Cushingoid appearance had improved, her height and weight had normalized, and her adrenocorticotropic hormone and serum cortisol levels were within normal range. The authors stressed the potential danger of the overuse of topical midstrength corticosteroids in infants.

Taylor O, Mejia-Otero J, Tannin G, Gordon K. Topical triamcinolone induced Cushing syndrome: a case report. *Pediatr Dermatol*. 2020;37:582-584.