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Correspondence to: Diamant Thaçi, MD, Research Institute and Comprehensive Center for Inflammation Medicine, University of Luebeck, Ratzeburger Allee 160, 23538 Luebeck, Germany

E-mail: *diamant.thaci@uksh.de* *and* *diamant. thaci@uni-luebeck.de*

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Association of particulate matter air pollution and itch: A digital epidemiology approach

To the Editor: Ambient air pollution secondary to industrialization is a growing health concern with the potential to cause exposure-related skin toxicity.[1] Among skin conditions, itch may be especially susceptible to environmental modulation, given that free nerve endings of sensory neurons are located in the epidermis.[2] Although several air pollutants are postulated to affect health, one well-studied marker of air quality is atmospheric particulate matter no larger than 2.5 μm ($PM_{2.5}$). Fine particulate matter of this size has important health effects, given its ability to penetrate the body systemically and serve as a carrier of pathogens and toxins.[1] We thus hypothesized that increasing levels of $PM_{2.5}$ are associated with increased population-level search interest in itch as a proxy for itch sensation.

Google Trends is an open-access database aggregating search queries across various regions that has been used for health care research, with successful validation against external data sets.[3] Search volume index (SVI) is a normalized value ranging from 0 to 100 that indicates the quantity of queries for a searched topic relative to all other queries within the given time frame. SVI data were
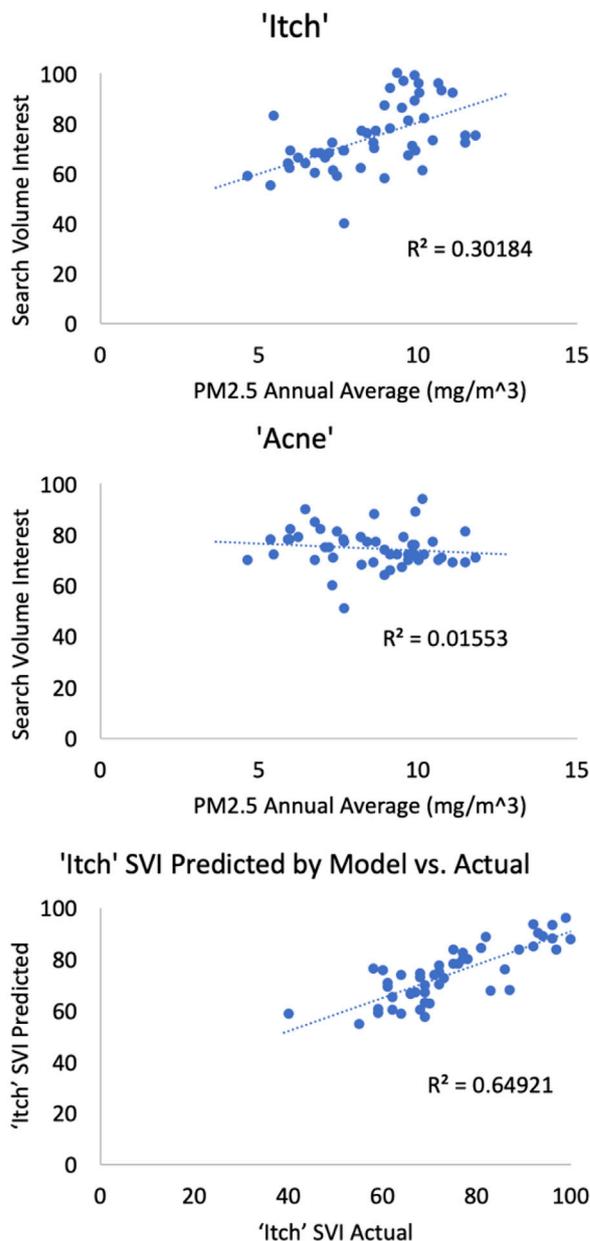

Fig 1. Air pollution and Google search volume index (SVI) for 49 States in the United States in 2014. $PM_{2.5}$. Particulate matter no larger than 2.5 μm.

evaluated within the United States in 2014 for the term *itch*, and for purposes of comparison, SVI data for the term *acne* were evaluated. We obtained data on annual state averages for $PM_{2.5}$ for 2014 from the US Centers for Disease Control and Prevention's National Environmental Public Health Tracking Network. Multivariate linear regression was conducted to examine the association between SVI for skin-related complaints and $PM_{2.5}$ adjusted for climate, population density, and percentage of population located in urban areas.

Across the United States, increased air pollution corresponded to increased queries for itch. The SVI for the term *itch* was correlated with concentration of atmospheric $PM_{2.5}$ ($R^2 = 0.30$; $P < .001$) (Fig 1), whereas the control SVI for the term *acne* was not ($R^2 = 0.016$; $P = .394$) (Fig 1). After adjustment for temperature, seasonality, and population density factors, itch SVI and $PM_{2.5}$ concentration still demonstrated a strong correlation ($\beta = 2.07$, $P = .016$, $R^2 = 0.6494$). Carbon dioxide emission levels were used as a negative control to demonstrate specificity between $PM_{2.5}$ and itch; no significant association between carbon dioxide levels and SVIs for any search terms was found.

Our results demonstrate that increasing levels of fine particulate matter air pollution are associated with higher search interest in itch, highlighting the potential role of environmental modulation in these conditions. In contrast, $PM_{2.5}$ air pollution did not show a similar correlation with search interest in acne. These findings may be explained by pollutant-induced sensitization and activation of cutaneous sensory nerves mediated by neurotrophin release from epidermal keratinocytes.[4] In addition, exposure to particulate matter was shown in an in vitro study of human epidermal keratinocytes to cause increased release of proinflammatory cytokines, which play a central role in itch transmission.[1] Lastly, itch was shown to result from ligand-mediated activation of the aryl hydrocarbon receptor pathway by particulate matter in an animal model of atopic dermatitis.[5] Future work in epidemiologic and clinical research can help further confirm the association between particulate matter air pollution and increased itch that was demonstrated in this study.

Katherine A. Whang, BS,[a] Amy H. Huang, MPH,[a,b] Lloyd S. Miller, MD, PhD,[a] Sewon Kang, MD,[a] and Shawn G. Kwatra, MD[a,b]

Department of Dermatology, Johns Hopkins University School of Medicine,[a] and Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland[b]

Ms Whang and Ms Huang are cofirst authors.

Correspondence to: Shawn G. Kwatra, MD, Cancer Research Building II, Johns Hopkins University School of Medicine, Suite 206, 1550 Orleans St, Baltimore, MD 21231

E-mail: skwatra1@jhmi.edu

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Timing of mucocutaneous symptoms and medication discontinuation in patients with Stevens-Johnson syndrome and toxic epidermal necrolysis in the United States

To the Editor: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe mucocutaneous reactions commonly triggered by medications. Although small single-institution studies have demonstrated improved outcomes with shorter time to admission and earlier discontinuation of the causative drug, the precise timing of initiation and discontinuation of suspected medications has not been evaluated in a large cohort.[1,2] We conducted a retrospective cohort study using a multi-institutional cohort of patients from the United States in whom SJS/TEN had been diagnosed, as previously described.[3] The causative drug was determined by expert clinical judgment at the time of dermatology consultation. Available criteria from the algorithm of drug causality for epidermal necrolysis were used to exclude cases with unlikely or doubtful causality on the basis of "delay from initial drug component intake to onset of reaction" and "drug present in the body on index day" (n = 50).[4] Descriptive statistics were used to evaluate timing between medication initiation, symptom onset, and medication discontinuation. Univariate logistic regression was used to identify factors associated with discontinuation of the medication at the time of symptom onset and to examine the relationship between drug discontinuation and mortality, adjusted for age and sex.