

Call to action: Air pollution, asthma, and allergy in the exposome era



Isabella Annesi-Maesano, MD, PhD, DSc,^a Cara Nichole Maesano, PhD,^a Benedetta Biagoni, MD,^b Gennaro D'Amato, MD,^c and Lorenzo Cecchi, MD, PhD^d *Montpellier, France; and Bologna, Naples, and Florence, Italy*

Key words: Asthma, allergy, air pollution, climate, exposome

According to the World Health Organization, by 2050, approximately 50% of the world's population will have had asthma and/or allergy at least once in life.¹ Increasing evidence suggests that air pollution is a primary risk factor that can help explain the increase in incidence of these diseases.²

AIR POLLUTION IS A UBIQUITOUS RISK FACTOR

Although air quality has improved in many regions over recent decades, the levels of certain air pollutants still exceed the World Health Organization guidelines in most countries, with 9 of 10 people on the Earth breathing polluted air. Various air pollutants (nitrogen dioxide [NO₂], ozone [O₃], volatile organic compounds, and particulate matter [PM] of varying size and composition) are emitted from a multiplicity of sources, including stationary sources (power plants, oil refineries, industrial facilities, factories, and domestic heating), mobile sources (cars, buses, trucks, planes, and trains), anthropogenic sources (agricultural activities, cities, wood burning fireplaces, and indoor settings), and natural sources (windblown dust, wildfires, and volcanic eruptions). As a result, individuals across the globe are continually exposed to pollutants as they breathe. This exposure is expected to grow as urbanization increases and also as a consequence of climate change-related phenomena such as continued fossil fuel emissions, excess heat, wildfires, drought, and increased confinement indoors. Compounding this issue, individuals are also regularly exposed to air pollutants that are not yet regularly monitored, such as ultrafine PM, 1,3-Butadiene, and mobile persistent pollutants, which have also been associated with adverse health effects.

From ^athe Desbrest Institute of Epidemiology and Public Health, INSERM, and Montpellier University, Montpellier; ^bthe Allergy Outpatient Clinic, Division of Internal Medicine, IRCCS Azienda Ospedaliera Universitaria Bologna; ^cthe Division of Respiratory and Allergic Diseases, Department of Chest Diseases, High Specialty A, Cardarelli Hospital, and Medical School of Specialization in Respiratory Diseases, University of Naples Federico II; and ^dthe Centre of Bioclimatology, University of Florence.

Disclosure of potential conflict of interest: I. Annesi-Maesano reports grants for the European Commission's Horizon 2020 Framework Programme and the French National Agency for Research outside the submitted work. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication March 2, 2021; revised May 24, 2021; accepted for publication May 25, 2021.

Corresponding author: Isabella Annesi-Maesano, MD, PhD, DSc, Desbrest Institute of Epidemiology and Public Health, INSERM and Montpellier University, URC, 641 Avenue du Doyen Gaston Giraud, 34093 Montpellier, France. E-mail: isabella.annesi-maesano@inserm.fr.

J Allergy Clin Immunol 2021;148:70-2.

0091-6749/\$36.00

© 2021 Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaci.2021.05.026>

AIR POLLUTION DOES CONTRIBUTE TO ASTHMA AND ALLERGY DEVELOPMENT

Recent data indicate that air pollution is responsible not only for exacerbations of asthma and allergy but also for their development. A causal relationship between new onset of childhood asthma and long-term exposure, especially to metrics of traffic-related air pollution such as NO₂, O₃, PM_{2.5} (fine particles less than 2.5 μm in diameter), and black carbon, has been established.^{2,3} The impact of air pollution starts in early life and continues onward, as revealed by recent data demonstrating that long-term exposures to PM_{2.5}, NO₂, and black carbon causally contribute to new-onset asthma in adulthood. Regarding mortality, new data indicate that at the population level short-term exposures to PM_{2.5}, NO₂, and O₃ may increase risk of mortality due to asthma.³ For the first time, this year a UK court recognized that air pollution was a causal factor in a 9-year-old London girl's induction, progression, and death due to asthma. Various experimental and epidemiologic studies have well demonstrated the association between air pollution (particularly PM) and the rising prevalence of allergic rhinitis.³ Several mechanisms plausibly explain how air pollution can induce new-onset asthma and allergic rhinitis, including the action of oxidative stress on the mucous membrane of the respiratory tract and its subsequent inflammation, remodeling, and immune changes, which then induce sensitization to aeroallergens and allergic inflammation.^{2,4} Air pollution is also a risk factor for skin diseases such as atopic dermatitis, the occurrence of which, according to data available in the literature, can be linked to exposure to many air pollutants, including cigarette smoke, volatile organic compounds, NO₂, and PM.⁵ Again, the underlying mechanism seems to be due to oxidative stress that affects the integrity of the barrier by inducing epithelial damage.⁵ Finally, widely used emerging industrial chemicals such as phenols and phthalates, which are commonly used in plasticization, have also been shown to play a role in asthma and allergies.^{6,7} New evidence shows that effects are induced even at low air pollutant concentrations, including concentrations that are sometimes below even standard air quality levels and are predominant in subjects already predisposed to atopy.²

AIR POLLUTION INTERACTS WITH OTHER FACTORS

To fully explain the increase in the prevalence of asthma and allergy observed worldwide, however, air pollution has to be considered as a part of the exposome, namely, the set of all exposures to the external environment (Fig 1) to which a given individual is subjected from preconception onward and the consequences of these exposures at the cellular and organ levels (the internal exposome).³

Environmental exposures prenatally and early in life appear to play a very important role in the etiopathogenesis of asthma and

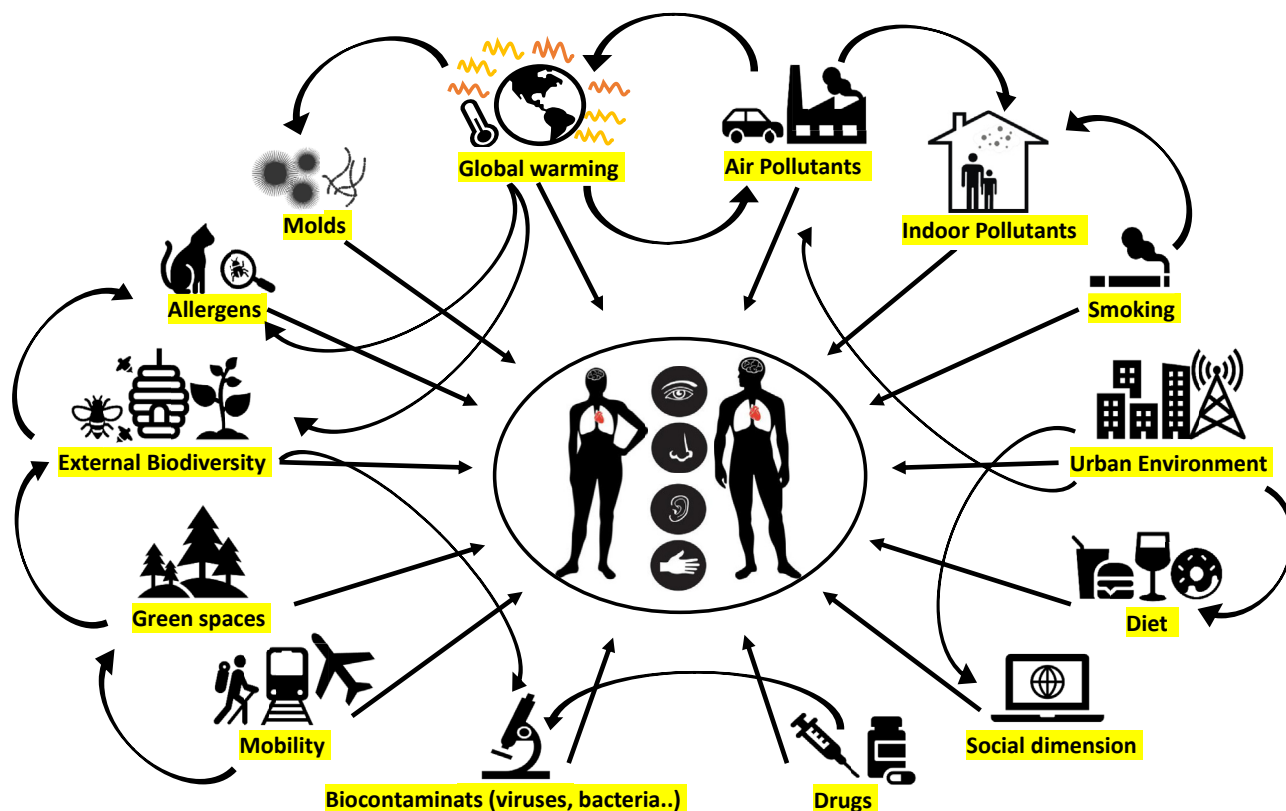


FIG 1. The surrounding environment involved in asthma and allergy.

allergy. This is the period of life in which a child's airways and immune system develop.

A growing body of scientific evidence confirms that air pollutants interact with aeroallergens (pollen, molds, house dust mites, etc), increasing the risk of atopic sensitization.⁴ Furthermore, several experimental studies have shown that O₃, NO₂, and diesel particulate emissions have the ability to increase bronchial epithelium permeability and reduce mucociliary clearance, facilitating the residence of allergens and irritants at the level of the epithelium and allowing their entry at the level of the submucosa.^{1,3} This facilitates encounter between antigen and immune cells as well as initiation of the allergic response. Air pollutants can also increase the ability of pollen-derived allergens to induce an IgE response (allergenicity) in sensitized subjects, thus putting susceptible individuals at higher risk of aggravation or development of allergic diseases.^{1,4} Evidence suggests that diets rich in carotenoids, vitamin D, and vitamin E help protect against air pollution damage that can trigger asthma. Vitamin C, curcumin, choline, and omega-3 fatty acids may also play a role.⁸

Nonspecific external factors of the exposome that interact with air pollution include climate conditions and surrounding biodiversity.³ Climate change, urbanization, and loss of biodiversity affect the sources, emissions, and concentrations of many aeroallergens and air pollutants,³ and they are among the most critical challenges facing the health and quality of life of the ever-increasing number of patients with allergy, both today and in the coming decades. Policy perspectives in this context should include prevention and mitigation in regard to climate, air pollution, and pollens, with improvement of environmental monitoring methods and alerts directed toward the at-risk groups. Poverty and

lifestyle factors are also crucial aspects in the relationship between air pollution and asthma and allergy development, and they must be considered when addressing prevention through multidisciplinary efforts to eliminate detrimental environmental exposures while promoting a healthy lifestyle and implementing all components of high-quality health care (prevention, screening, diagnosis, and treatment).⁹ Overall, environment- or lifestyle-driven aberrancies in the composition of the gut and skin microbiome represent key mediators of allergic diseases.¹

Building the exposome is challenging in various respects. In terms of assessments, it requires reliable assessment of the maximum number of environmental factors at different periods of life in the different settings attended by the individual (home, school, work, transportation, community, etc) so as to be representative of individual exposures across the entire lifespan or at least in those life periods identified as critical in the lifespan. These assessments rely on technologies that need to be validated to avoid exposure misclassification, which can be time-consuming and expensive. In terms of statistical analysis to identify those factors among the several hundred being considered that are significantly related to the studied outcome, the challenge consists of use of sophisticated methods to account for the heterogeneity of the assessments and the multitude of testing in the context of big data. The last challenge consists of identification of the avoidable exposome at the individual, family, and community levels to promote prevention.

Although it has been used rarely so far, the exposome approach has been applied successfully, for instance, in the Canadian Healthy Infant Longitudinal Development Study, which observed an association between first-trimester exposure to traffic-related

air pollution and increased risk of allergic sensitization at 12 months of age. In a smaller Canadian birth cohort study, it was found that regular use of air fresheners and presence of mold in the residence were associated with early childhood wheezing and cough.¹⁰ Further studies are needed, however.

CALL TO ACTION

To conclude, we can no longer ignore the fact that the impact of air pollution on asthma and allergy development has to be considered within the larger context of the exposome. Air pollution interacts with allergens, pollen, molds, climate, green-space, and lifestyle, among others. Therefore, efforts to reduce exposure to air pollution to protect the public's health, especially against emissions resulting from both fossil fuel combustion and biomass combustion, are needed urgently. Tackling both air pollution and climate change simultaneously would bring substantial benefits for public health and should not be underestimated.⁸ This should be advocated through green-friendly industrial, agricultural, and vehicle renovations, as well as through interventions at the population level, including public health prevention strategies and individualized interventions to lower personal exposures. At the same time, it is necessary to improve nature relatedness; revegetate urban areas; reforest, protect, and conserve natural elements; and organize traffic and mobility infrastructure to promote bicycling, walking, and emissions avoidance. Efforts to electrify indoor cooking methods and

promote other healthy indoor habits should be considered. In addition, more research is needed to better understand the involved phenomena and the effectiveness of these actions.

REFERENCES

1. Cecchi L, D'Amato G, Annesi-Maesano I. External exposome and allergic respiratory and skin diseases. *J Allergy Clin Immunol* 2018;141:846-57.
2. Thurston GD, Balmes JR, Garcia E, Gilliland FD, Rice MB, Schikowski T, et al. An official American Thoracic Society workshop report. *Ann Am Thorac Soc* 2020;17:387-98.
3. Annesi-Maesano I, Forastiere F, Balmes J, Garcia E, Harkema J, Holgate S, et al. The clear and persistent impact of air pollution on chronic respiratory diseases: a call for interventions. *Eur Resp J* 2021;57:2002981.
4. Pfeffer PE, Mudway IS, Grigg J. Air pollution and asthma: mechanisms of harm and considerations for clinical interventions. *Chest* 2021;159:1346-55.
5. Ahn K. The role of air pollutants in atopic dermatitis. *J Allergy Clin Immunol* 2014;134:993-9.
6. Vernet C, Pin I, Giorgis-Allemand L, Philippat C, Benmerad M, Quentin J, et al. In utero exposure to select phenols and phthalates and respiratory health in five year-old boys: a prospective study. *Environ Health Perspect* 2017;125:097006.
7. Soomro MH, Baiz N, Philippat C, Vernet C, Siroux V, Maesano CN, et al. Prenatal exposure to phthalates and the development of eczema phenotypes in male children: results from the EDEN Mother-Child Cohort Study. *Environ Health Perspect* 2018;126:027002.
8. Whyand T, Hurst JR, Beckles M, Caplin ME. Pollution and respiratory disease: can diet or supplements help? A review. *Respir Res* 2018;19:79.
9. Celedón JC, Roman J, Schraufnagel DE, Thomas A, Samet J. Respiratory health equality in the United States. The American Thoracic Society perspective. *Ann Am Thorac Soc* 2014;11:473-9.
10. Baluch N, Gallant M, Ellis AK. Exposomal research in the context of birth cohorts: what have they taught us? *Ann Allergy Asthma Immunol* 2020;125:639-45.