## Editorial

# The Impact of Environmental Factors on Cardiopulmonary Health*

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Cardiovascular and respiratory diseases, which frequently progress to heart failure, have become a major and growing cause of morbidity, disability, and mortality worldwide. Data from the Global Burden of Disease 2021 show that cardiovascular and respiratory diseases accounted for 28.6% and 6.5% of the global deaths, respectively, with the corresponding proportion of 45% and 11.4% in China. It is estimated that around 330 million adults suffer from cardiovascular diseases (CVD), 8.9 million from heart failure[1-3], and 100 million from chronic respiratory diseases in China[4], representing a substantial burden and major increasing challenge for the healthcare system. Therefore, a comprehensively understanding the health effects of risk factors and their potential pathogenic mechanisms is essential for the prevention of cardiopulmonary diseases.

Environmental factors play a crucial role in the occurrence and progression of cardiopulmonary diseases. A growing body of evidence indicates that environmental exposures, such as fine particulate matter and smoke, significantly increase the risk of coronary heart disease (CHD), strokes, and chronic respiratory diseases. A suitable climate is essential to health. Health effects of ambient temperature have been well studied. However, atmospheric humidity has received relatively little attention in environmental health research. In fact, ambient humidity is an increasing public health concern in the context of climate change. Long-term exposure to higher humidity has been positively associated with the risks of CVD, CHD and cerebrovascular disease hospitalizations among the US Medicare population[5]. Ambient temperature and humidity have also been reported to be associated with mortality in China[6]. In this issue, Congyi Zheng et al. explored the relationship between ambient humidity and CVD and concluded that unsuitable (too high or low) humidity increased the risk of CVD by over 30% compared to suitable humidity based on a prospective study of 24,510 adults, and the strong relationship were found in women, older adults, and those living in the south[7]. This will undoubtedly play a positive supporting role in the formulation of healthy environment strategies.

On the other hand, rapid global development and the growth in human needs have led to the continuous introduction of new substances, which escalate environmental pollution and pose a serious threat to human health. New contaminants, also known as emerging contaminants (ECs), include pharmaceuticals, per- and poly-fluoroalkyl substances (PFAS), pesticides, industrial and household chemicals, micro- and nanoplastics, and other exogenous substances. Although their harmful impacts on human health are not well understood, governments worldwide have implemented policies to minimize environmental contamination. For example, the Action Plan for Controlling Emerging Contaminants was issued by the State Council of China on May 4, 2022. To better understand the pollution caused by ECs and their detrimental impacts on human health, numerous researchers have focused on this emerging concern. In humans, micro- and nanoplastic particles have been detected in the lower respiratory tract[8], atherosclerotic plaques, epicardial adipose tissues, myocardium, and other cardiovascular tissues[9], providing increasing evidence and crucial insights into an emerging issue in cardiopulmonary health. The relationship between household chemical exposures and cardiovascular and respiratory diseases has gradually attracted attention in recent years. This issue presents results from the 2018 China Longitudinal Health and Longevity Survey (CLHLS) database reported by

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Yongbin Zhu et al., which demonstrate that regular use of repellents and oil removers is associated with increased risks of respiratory diseases in a dose-dependent manner[10].

Both genetic factors and environmental exposures contribute to the development of chronic cardiopulmonary diseases. Environmental risk factors can modify the effect of genetic susceptibility. For instance, gene-by-environment interactions increase the risk of multiple sclerosis associated with exposure to household chemicals[11]. Individuals with high genetic risk may exacerbate the responses to environmental pollutants, leading to increased risks of CVD[12] and respiratory diseases that vary across ethnic groups[13]. However, genetic variants only partially explain the variability of cardiopulmonary risk, suggesting the presence of other mechanisms that play an important role.

The interaction between environmental and genetic factors in influencing cardiopulmonary health remains incompletely understood. Epigenetic mechanisms have been considered as the missing link between the genetic and environmental risk factors. Epigenetic changes, such as DNA methylation, chromatin remodeling, histone modifications and RNA modifications, are influenced by genetic factors, exposures to environmental pollutants, aging and disease processes. N6-methyladenosine ($m^6A$), one of the most common RNA modifications in eukaryotes, plays a significant role in gene regulation. In recent years, epigenetic regulators have increasingly become targets for the prevention and treatment of cardiopulmonary diseases. Ziyi Yang et al. integrate multiple omics data, including genomics, transcriptomics, and proteomics, and demonstrate the effect of $m^6A$ associated single nucleotide polymorphisms (SNPs) on heart failure, providing new evidence for the involvement of epigenetic mechanisms in the gene-environmental interaction[14]. Somatic mutations in genes involved in epigenetic regulation, such as DNMT3A and TET2, lead to clonal hematopoiesis of indeterminate potential which is a risk factor for cardiovascular diseases. The recent studies demonstrated the effects of clonal hematopoiesis on the risk of CHD and chronic obstructive pulmonary disease and provided a better understanding of this emerging risk factor[15,16]. In addition, using internal chemical exposure and multi-omics methods allows for a thorough assessment of measurable environmental factors, helping to reveal the underlying molecular mechanisms and biological pathways[17].

Emerging environmental factors are gradually considered as the determinants of health, particularly concerning cardiopulmonary diseases. To address the challenges posed by these factors, we recommend emphasizing the following aspects in future research: 1) Conducting longitudinal cohort studies and multiple-generation population studies to elucidate temporal patterns of epigenetic signatures and determine whether epigenetic changes cause or result from diseases. 2) Epigenetic research holds great promise as biomarkers for epigenetic changes can be valuable tools for assessing environmental exposure and may serve as potential targets of prevention and treatment. Integrating exposomics, genomics, epigenomics, proteomics, and even metabolomics data will further transform to promote advances in biomedical and population health sciences. Animal models and functional experiments will provide crucial evidence for the causal relationship of environmental factors with diseases. 3) Illustrating the effects of emerging environmental factors, particularly in vulnerable populations, will enhance our understanding of their role in the development of cardiopulmonary diseases and aid in developing personalized interventions. In addition, there is an urgent need to validate these targeted interventions in large clinical trials.

In conclusion, the complex relationship between environmental factors and the development of cardiopulmonary diseases is increasingly evident. To tackle these emerging environmental risks, future research is urgently needed to better understand their impact on cardiopulmonary health. By clarifying these mechanisms, we can develop targeted interventions to mitigate the effects of harmful exposures and promote preventive strategies to improve overall public health.

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