Preamble

Pesticides, air pollution, lead, ultraviolet radiation, ozone, DDT, climate change… The full set of environmental factors with an impact on human health forms a vast jungle that is far from easy to navigate. Some of these factors and their related health effects result in all too *visible* environmental disasters – the case, for example, of Seveso, Chernobyl, Yusho, and Minamata, while others have been dubbed silent disasters associated with the *invisible* contaminants in our environment.

The epidemiological transition in industrialised societies and the Anthropocene have ushered in the era of chronic diseases (cancers, cardiovascular pathologies, mental disorders, etc.). These health problems are multifactorial by nature and pose a challenge to causality in medicine. Yet, understanding the complex interactions between environmental factors and health is fundamental for prevention and risk management; meanwhile, the debate rages as to whether we are best advised to prevent or cure, inform or prohibit, or act in accordance with the tenets of the precautionary principle. *Today, the conducting of environmental health research is more opportune than ever but it needs to find new research tools that can make the invisible visible.*

The Lancet Commission on Pollution and Health reported that pollution was responsible for 9 million premature deaths in 2022, corresponding to one in six deaths worldwide (Fuller et al., 2022), which makes it the world's largest environmental risk factor for disease and premature death. But while a reduction has been achieved in the number of deaths attributable to the types of pollution associated with extreme poverty (that is, household air pollution and water pollution), they have simply been offset by increased deaths attributable to ambient air pollution and toxic chemical pollution (most notably lead). Deaths from these "modern" pollution risk factors – the unintended consequences of industrialisation and urbanisation – have risen by 7% since 2015 and by over 66% since 2000.

Today, it is widely recognised that an individual's characteristics result from the combination of their genes and other non-genetic factors, and that only a small percentage of diseases are exclusively attributable to their genetic makeup. Yet, biomedical research in recent decades has continued to focus its efforts primarily on characterising genes. With the aim of correcting this imbalance, we have seen *the emergence of the exposome concept, defined as: "the integrated compilation of all of the environmental factors, whether they are the physical, chemical, biological or psychosocial factors, and their interactions, which have an impact on biology and health"* (adopted definition during the meeting at the Banbury Center at Cold Spring Harbor Laboratory, New York, USA, 3-6 December 2023).

Thanks to technology advances in both measurement and analysis in recent years, the exposome has gained a certain prominence in biomedical research for investigating the diseases. Indeed, causal relationships have been established between non-genetic factors that make up the exposome and specific pathologies, including, for example, exposure to solar UV radiation and the development of melanoma and the presence of endocrine disruptors and their involvement in individuals' hormonal and metabolic dysregulation, leading to a variety of developmental pathologies.

Despite these advances, studying the exposome is extremely complex. The diversity and quantity of molecules or agents involved, together with the fact that the exposome is dynamic (and as such varies over time), combine to complicate its study. This means efforts to understand the exposome must be multidisciplinary, drawing on knowledge from such disciplines as toxicology, epidemiology, clinical medicine, the omics sciences, and data science, to name just a few.

Through the integration of information from these disciplines within the broader framework of exposome studies, it should be possible to identify risk biomarkers for the development of certain pathologies associated with specific exposures, design initiatives for preventing specific diseases, and formulate recommendations for healthy habits (diet and physical exercise) both for population groups and individuals.

Although the application of information derived from exposome studies in clinical practice is currently limited to very specific cases, and many significant challenges have yet to be addressed, it seems likely that this valuable knowledge will be fundamental in designing preventive, diagnostic, and therapeutic actions in future medicine and an indispensable tool in public health policies.