

exposure to endocrine-disrupting chemicals during pregnancy has been linked to altered growth trajectories in offspring.

The early life course also presents important windows of opportunity for prevention. Health and disease are full life-course processes and it is, today, widely recognised that the early parts of this course, from conception and even pre-conception, are especially vulnerable to environmental influences with life-long consequences. At least part of the origin of the most common NCDs lies in the first 18 years of life, and prevention during these periods will not just improve child health, but also benefit life-long health and disease trajectories. This means that building exposome tools and data for the future needs to start in the early life course.

4.2. EXPOSOME AND REPRODUCTIVE AND SEXUAL HEALTH: THE CASE OF ENDOCRINE DISRUPTORS

Recently, it has been demonstrated that certain compounds can act as endocrine disruptors, *interfering with the normal functioning of hormonal pathways*. These compounds have structures at the molecular level that resemble those of hormones and which replace them in carrying out their functions, ultimately causing alterations in the hormonal system. Exposure to these endocrine disruptors can be detrimental at any stage of life, but the effect is most marked during certain windows of susceptibility, particularly during pregnancy, lactation, and childhood, critical periods in an individual's development when their hormones play an essential role. Recent advances in omics technologies enable the characterisation of each of the molecules to which we are exposed and, thanks to this, the exposome can be seen to be playing a decisive role in determining the extent to which endocrine disruptors pose a risk to human health.

One example of a family of synthetic compounds that can act as endocrine disruptors are the phthalates, commonly found in plastics, PVC, cosmetics, and personal care products. When these compounds come into direct contact with blood or fluids containing lipids, they can readily enter the bloodstream and migrate to any part of the body. If these compounds reach the testes or ovaries, they can disrupt their hormone secretion function, leading to reproductive problems, spontaneous abortions, growth issues, and low birth weight, among others.

The role played by endocrine disruptors in the development of type II diabetes mellitus (DM) has also been well documented. While there is a genetic predisposition to DM, characterised by elevated blood glucose levels (hyperglycaemia) due to insulin resistance and a progressive failure in pancreatic insulin secretion, non-genetic factors such as poor diet, a sedentary lifestyle, and certain environmental pollutants can be critical in the development of this condition. Indeed,

exposure to these factors during the prenatal stage has been identified as a risk factor for future diabetes. Specifically, bisphenol-A (BPA) has been identified as a compound that acts as an endocrine disruptor and which is related to the development of DM. Since 2011, its use has been prohibited or restricted in certain applications in Europe.

While the number of such molecules to which we are exposed is low, studies show that the effects of these disruptive compounds can be potentiated, so even though we are exposed to low doses, their effect can be much greater. This underscores the importance of identifying those compounds that act as endocrine disruptors. Several European projects are currently addressing this very issue, including the EURION cluster. This initiative aims to identify endocrine disruptors related to an increased risk of certain diseases and to develop diagnostic tests based on that information.

4.3. EXPOSOME AND NON-COMMUNICABLE DISEASES

APOLLINE SAUCY

The association between environmental factors and non-communicable diseases (NCDs) is gaining increasing recognition. According to the WHO, 12.6 million deaths globally (24% of all deaths) can be attributed to the environment, of which two thirds (ca. 8.2 million deaths) are caused by NCDs (Prüss-Üstün et al., 2016). Air pollution contributes to 5 million deaths from cardiovascular diseases each year and is considered the 5th leading cause of death, ranking just after smoking (GBD 2017 Risk Factor Collaborators, 2018). Other environmental exposures are being increasingly recognised for their adverse effects on health, including climate (Vicedo-Cabrera et al., 2021; Watts et al., 2018), environmental noise (Münzel et al., 2021; Vienneau et al., 2015), urbanisation (World Health Organization, 2021), and green space (Barboza et al., 2021).

Cardiovascular diseases

Cardiovascular diseases (CVDs) – covering a range of health disorders of the heart and blood vessels, including coronary heart diseases and cerebrovascular diseases – make the largest contribution to the environmental burden of disease worldwide. In 2017, they contributed to 17.8 million deaths and 35.6 million disability-adjusted life years or DALYs worldwide, making it the leading cause of death globally (Wang et al., 2023). The action of environmental conditions on CVDs can be direct (e.g. the impact of air pollution on respiratory function and blood pressure) but it can also be mediated by changes in behaviour or in social

interactions, which may in turn lead to cardiovascular diseases. For instance, physical activity and a healthy lifestyle can be promoted by better access to public green spaces and public transport, and by improving street safety.

Mental health

Complex environments, including both environmental hazards and the social environment, have been shown to affect mental health and cause behavioural disorders. Wang et al. (2023) conducted exposome-wide association analyses in a twin cohort and found that more than half of the exposures were significantly associated with depressive symptoms in young adulthood. More specifically, influences from the family domain and the social exposome were particularly important drivers of depressive symptoms in late adolescence and early adulthood. Other environmental exposures such as environmental noise can also affect mental health, possibly via sleep alterations and effects on the central nervous system (Hahad et al., 2024). In a recent study conducted near a military airport, Wicki et al. (2024) showed a strong link between exposure to loud military aircraft noise events and symptom exacerbations and medical prescriptions in patients with psychiatric treatments.

NCDs and health disparities

The impact of environmental contaminants on health varies across regions, sexes, and age groups. The contribution of NCDs compared to infectious diseases is greatest in the adult and elderly population, and in high-income countries. However, the health impacts of modifiable environmental conditions globally have a disproportionate effect on low- and middle-income countries. With the epidemiological transition to an increasing prevalence of NCDs in developing countries and with a growing proportion of the population living in urban settings, environmental inequities are likely to grow in the future. Promoting healthy living environments is therefore essential in reducing mortality and morbidity from chronic diseases worldwide and in stemming the ever-increasing associated healthcare costs (Hajat & Stein, 2018).

4.4. EXPOSOME AND INFECTIOUS DISEASES

Environmental exposures, including exposures to endocrine disrupting chemicals (EDCs), can influence an individual's susceptibility to infection. Suspected to exert their effects via hormonal pathways, certain EDCs, including phthalates, bisphenols, organochlorine pesticides, and perfluorinated alkane