4. Exposome and health

4.1. Early-life exposome and health development

The early stages of life are critical periods in an individual's health development, with environmental exposures during this time having profound and lasting effects. Indeed, the developmental origins of health and disease (DOHaD) hypothesis posits that environmental exposures during critical periods of early development – especially during prenatal and early postnatal life – can significantly influence long-term health outcomes. The suggestion is that adverse environmental exposures during sensitive developmental stages may programme physiological systems, leading to increased susceptibility to non-communicable diseases (NCDs) later in life.

One of the best known examples illustrating the DOHaD hypothesis is the Dutch famine study, conducted by Professor David Barker and colleagues. This landmark investigation examined individuals who had been exposed to severe undernutrition during gestation *in utero* during the Dutch famine of 1944-1945. Researchers found that individuals who had been prenatally exposed to famine exhibited higher rates of chronic diseases, including obesity, cardiovascular disease, and diabetes, later in life compared to unexposed individuals. These findings provided compelling evidence of the link between early-life exposures and subsequent health outcomes, and lay the foundations for further research testing the DOHaD hypothesis (Barker et al., 1989).

Numerous studies worldwide have since provided evidence both supporting and expanding the DOHaD hypothesis by studying the impact of various early-life exposures on health development. This body of research, among others, has explored the effects of maternal nutrition, exposure to environmental pollutants, stress, and other factors during pregnancy and infancy on the risk of NCDs in offspring.

In Spain, for example, the *INfancia y Medio Ambiente* (INMA) cohort profile is a large-scale birth cohort study that investigates the effects of environmental exposures on child health and development (Guxens et al., 2012).

FIGURE 12. The INMA birth cohort network.
SOURCE: INMA Project (2018), *INMA - INfancia y Medio Ambiente*, https://www.proyectoinma.org/en/inma-project/study-design/.

Some of the key findings to emerge from the INMA cohort include:

— *Prenatal exposures*: Various prenatal exposures, such as air pollution, tobacco smoke, and maternal diet, are associated with adverse health outcomes in children. For example, exposure to air pollutants during pregnancy has been linked to decreased birth weight and respiratory problems in infants.

— *Neurodevelopmental outcomes*: Prenatal exposure to certain environmental pollutants, such as polychlorinated biphenyls (PCBs) and organophosphate pesticides, may be associated with neurodevelopmental delays and cognitive impairments in children.

— *Childhood asthma*: Prenatal and early-life exposures to air pollution and tobacco smoke are risk factors for childhood asthma and respiratory allergies.

— *Growth and development*: Environmental exposures have an impact on growth patterns and physical development in children. For instance, maternal

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 preconception, 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,