

Factsheet on environmental exposure and female reproductive health

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Key facts

- Human fertility rates are declining globally and have been below the population replacement rate in the EU for decades.
- One in six people globally will experience involuntary infertility at some point in their lives.
- Besides age, factors such as diseases of the reproductive and endocrine systems, genetic conditions, lifestyle, and environmental, including workplace, exposures affect female fertility.
- Environmental exposures, including air pollution and human-made chemicals, correlate with altered puberty onset, increased risk of miscarriage, endometriosis, ovulatory disorders, infertility, and earlier menopause.
- Animal experiments support a causal link between exposure to common human-made chemicals and adverse reproductive outcomes.
- Everyone faces lifelong exposure to human-made chemicals and air pollution, which can reach the ovaries, exposing the finite reserve of oocytes, and can also cross the placenta, thereby exposing the foetus.
- The production and use of chemicals are increasing.
- Most chemicals on the market have not been tested for reproductive toxicity.

Background information

As human females age, there is a natural decline in both the quantity and quality of their oocytes, leading to a gradual but inevitable depletion of the ovarian reserve and the onset of menopause, typically occurring between the ages of 45 and 55. This process poses a challenge for those who wish to start a family later in life, a trend that is becoming increasingly common globally. In Europe, for instance, the average age of females giving birth now exceeds 30 years. This delay in starting a family results in a narrower window of opportunity for conception, as the number and quality of oocytes decline rapidly during the fourth decade of life.

Furthermore, the healthy development of reproductive organs during the foetal stage is crucial for future fertility and reproductive health in adulthood. Disruptions in these early developmental stages can potentially lead to reproductive disorders in adulthood, such as ovulatory disorders, endometriosis, and infertility.

Exposure to human-made chemicals and air pollution

It is estimated that there are approximately 100,000 different synthetic chemicals on the market today. Roughly 70% of these chemicals have not been adequately assessed for toxicity [1]. Reproductive toxicity testing is required only for chemicals produced or imported in significant quantities, leaving a substantial portion of chemicals unchecked for their potential effects on reproduction. Even when testing is conducted, the reliability of standard tests in predicting effects on human reproduction remains a subject of debate.

Beyond chemical pollutants, air quality also emerges as a significant factor influencing female fertility. Air pollution comprises a complex mixture of particulate matter, nitrogen oxides, sulphur oxides, ozone, metals, and volatile organic compounds. Air pollution contributes to millions of deaths worldwide annually. In 2020, 96% of the urban population in the EU was exposed to levels of fine particulate matter exceeding the health-based thresholds set by the World Health Organization [2].

Furthermore, studies have revealed the presence of chemical mixtures and air pollution particles in ovarian follicular fluid, highlighting direct exposure of developing human oocytes [3-5].

In essence, individuals are continuously exposed to mixtures of chemicals from various sources, including occupational and household activities, indoor and outdoor air, water and food consumption, and the use of consumer products [6]. This exposure spans all life stages, from germ cells and foetuses to children and adults.

Exposure to human-made chemicals and air pollution: links with female fertility

→ Environmental exposures affect the development of the reproductive system.

- Early development is inherently susceptible to external disturbances, as evidenced by diethylstilbesterol (DES), identified as an endocrine disruptor. While the pregnant mothers who took these medications were relatively unharmed, their exposed foetuses faced an increased risk of cancer and infertility later in life.
- The period before birth is recognised as a critical window of vulnerability, during which environmental exposures can profoundly impact the developing brain, reproductive organs, and ovarian follicle reserve. Alterations in development may manifest as an elevated risk of birth defects, as well as disruptions in puberty, ovulatory function, menstrual irregularities, increased susceptibility to miscarriage, infertility, and premature reproductive aging, collectively termed ovarian dysgenesis syndrome [7].

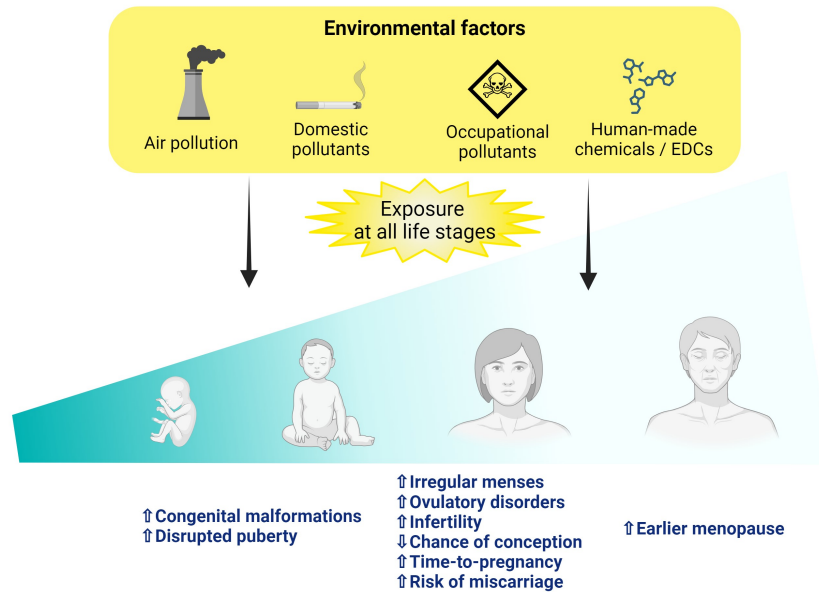


Figure 1: Potential effects of exposure to environmental factors on female health. EDCs, Endocrine Disrupting Chemicals (Created with BioRender.com).

→ **Environmental exposures in adulthood can affect reproductive health.**

- Air quality has been shown to have a correlation with female fertility. Poor air quality is linked to reduced levels of anti-Müllerian hormone in females of reproductive age, indicating an accelerated depletion of ovarian reserve. Cohort studies further demonstrate significant associations between air pollution levels and decreased rates of both spontaneous and medically assisted conception, along with an increased incidence of miscarriages [8].
- Additionally, levels of human-made chemicals have been associated with diminished fertility markers in females. Exposure to environmental chemicals has been linked to a decrease in ovarian reserve and earlier onset of menopause. Furthermore, chemical exposures have been implicated in an elevated risk of developing conditions such as polycystic ovary syndrome and endometriosis.
- Most females of reproductive age are active in the workforce, potentially facing heightened exposure to harmful substances before and during pregnancy. Concerningly, there is a lack of understanding regarding whether current occupational safety standards adequately safeguard fertility and the developing foetus.
- All individuals are subject to complex mixtures of chemicals and air pollution, but the extent of exposure to these environmental factors varies depending on lifestyle, socio-economic status, geographic location, and occupation. This variability poses challenges in comprehensively evaluating environmental influences in cohort studies. Female fertility remains an area with limited number of studies, hampering efficient risk assessment.

Time for action: policies to mitigate environmental impact on female fertility.

Facilitate Research

- ✓ Promote and finance research aimed at identifying environmental factors, including occupational exposures, contributing to reproductive diseases and infertility.
- ✓ Establish and maintain a Europe-wide digital healthcare data collection system for long-term monitoring of reproductive health trends.

Promote Awareness

- ✓ Educate the public about the potential risks posed by environmental contaminants.
- ✓ Provide training for healthcare professions to enhance their understanding and ability to communicate about the impact of environmental factors to patients.
- ✓ Support policymakers in recognising and acting on the urgency and importance of addressing reproductive health concerns linked to environmental factors.

Support Prevention

- ✓ Develop and enforce prevention strategies at both institutional and individual levels to effectively mitigate environmental and health risks.
- ✓ Fulfil the commitment to implement the European Chemicals Strategy for Sustainability.

References¹

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¹Only key papers were included, but further detailed references on individual studies can be requested from ESHRE by contacting guidelines@eshre.eu

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