Pregnant women and the developing fetuses' unique vulnerabilities to environmental hazards

Fragile Beginnings

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for every child

Children face unique vulnerabilities to environmental hazards at every stage of life.

Children today face a new set of challenges that were unimaginable just a generation ago. Across the world, climate change and environmental degradation are threatening child survival, health and well-being. A fetus's developing cells, organs and tissues are uniquely vulnerable to damage from environmental hazards.

The Fragile Beginnings briefing note series provides a scientific stocktake of the growing body of research on the unique vulnerabilities in utero and at birth, during infancy and childhood, and throughout adolescence. This note focuses on the impact of environmental hazards on developing fetuses. The specific effects of environmental hazards on a pregnant woman's own health are critical but beyond the scope of this document.

Exposure to environmental hazards during pregnancy can have lifelong consequences on a child's health

- Every child has the right to a healthy start in life. But environmental hazards can cause harm before a child is born or even conceived.
- Environmental hazards can damage the egg or sperm cells long before conception takes place, and the effects can be passed down from generation to generation.
- The fetal period is critical as it shapes a child's lifelong health and development.
- There are critical windows of vulnerability to environmental hazards, particularly during the first trimester, when women might not be aware of their pregnancies.
- Adverse birth outcomes such as miscarriages, stillbirth, preterm births, birth defects and low birthweight have been linked to exposure to environmental hazards.
- A fetus's developing cells, organs and tissues are uniquely vulnerable to damage from environmental hazards.
- The consequences can last a lifetime, including health conditions like obesity, cognitive impairment, neurological disorders, lung disease and cancer which can arise in infancy into late adulthood.
- While all women are at risk, the heaviest burden falls upon women in low- and middle-income countries, especially those living in fragile and conflict-affected situations, deepening inequities between groups.
- Preventing exposure to environmental hazards can ensure that future generations live to their full potential. It can also prevent economic loss to countries, including to health systems.

Healthy Environments for Healthy Children

Examples of environmental hazards and how they affect pregnancy

Climate-related hazards

Malaria and Zika

Malaria infection rates in the first trimester of pregnancy are especially high. The parasites that cause malaria can cause severe anaemia in the pregnant woman, pregnancy loss and maternal death. Malaria can also cause babies to be born prematurely and have low birthweight. Children born after antenatal exposure to malaria may have impaired cognitive function.

While pregnant women are no more likely to acquire Zika virus than other women, the virus can seriously harm the fetus's developing nervous system.

Zika virus infection during pregnancy can be devastating, causing pregnancy loss or resulting in babies being born prematurely. Babies who survive may suffer from congenital Zika syndrome, which includes malformation of the head and eyes and significant developmental delays.

Even babies who do not have obvious defects at birth can still present with cognitive and language neurodevelopmental delay in childhood.

Cholera

Cholera is a severe diarrhoeal infection caused by ingesting food or water contaminated with the bacterium *Vibrio cholerae* and can cause dehydration. When a woman is pregnant, severe dehydration can cause problems for the pregnant woman and fetus, including compromised blood flow to the placenta and harmful levels of acid in the amniotic fluid, which can lead to pregnancy loss.

Extreme heat

During pregnancy, a pregnant woman's body adapts to many metabolic changes and maintains a steady and appropriate temperature. But in conditions of extreme heat, a pregnant woman's ability to regulate a healthy temperature can be overwhelmed.

Extreme heat can contribute to dehydration, which can reduce levels of amniotic fluid that protect the fetus.

Extreme heat is associated with preterm birth. It has also been linked to low birthweight, congenital anomalies and gestational diabetes.

Food insecurity

A pregnant woman is especially vulnerable to food insecurity because she needs more nutritious food (both in terms of quantity and quality) so her body can both support the growing fetus and continue to function properly. Climate hazards can reduce the amounts of nutritious food produced, the availability and the cost.

Undernutrition during pregnancy is linked to babies being born too early and too small. It is also linked to neural tube defects, including spina bifida, where the spine and spinal cord do not form properly. Children born to mothers who are experiencing undernutrition because of food insecurity have been shown to have impaired cognitive development.

Pollution

Air pollution

A pregnant woman can be exposed to higher levels of air pollution than a non-pregnant woman due to changes that occur in a woman's breathing system during pregnancy.

Chemicals in air pollution can directly affect a pregnant woman's lungs and create inflammation in her body. They can also enter a pregnant woman's circulation and then cross into the placenta.

Air pollution can affect the health of the pregnant woman (e.g., diabetes in pregnancy, high blood pressure), the ability for her to carry to term and the weight of the baby. It can cause pregnancy loss early on (miscarriage) or later in the pregnancy (stillbirth).

If a child is born after being exposed to air pollution in the womb, that child is at risk of developing neurodevelopmental disorders or asthma, the most common chronic childhood disease.

Lead

There is no safe level of lead exposure.

A fetus's developing brain is particularly vulnerable to lead.

Lead can compete for entry into a pregnant woman's body with important nutrients such as calcium and iron, which are needed at higher levels during pregnancy to support the growth and development of the fetus. Lead can also be released into the pregnant woman's bloodstream from her bones, which store lead from past exposures.

Antenatal exposure to lead is linked to reduced cognitive and behavioural development in children.

Pesticides

Exposure to pesticides can be harmful to a pregnancy, even if a woman is exposed before she gets pregnant.

Pesticides can contribute to impairment of DNA, which can harm the developing fetus. Antenatal exposure to pesticides is linked to birth defects and childhood cancers including neuroblastoma and leukaemia, the most common childhood cancer. Antenatal pesticide exposure can also negatively affect the development of a child's brain.

Arsenic

Arsenic is a toxic heavy metal that can contaminate drinking water and foods. Arsenic can accumulate at levels up to three times higher in the placenta than in a pregnant woman's body.

Arsenic exposure during pregnancy can cause pregnancy loss or premature birth. It is also associated with cognitive deficits in childhood.

Tobacco smoke

When a pregnant woman smokes or is around someone who smokes, her fetus can be exposed to over 7,000 toxic chemicals. There is no safe level of tobacco smoke.

Tobacco smoke can alter blood flow to the fetus, disrupting the delivery of oxygen and nutrients. Babies exposed to tobacco smoke may be born prematurely, have birth defects or die from sudden infant death syndrome. The effects of antenatal smoke exposure can also contribute to many chronic diseases in childhood.

Environmental exposures before and during pregnancy shape a child's lifelong health and well-being

Technical brief

Critical windows of vulnerability

During preconception, conception and all the months of pregnancy, there are critical windows of time where certain cells, organs and tissues are most susceptible to environmental hazards.[1] Understanding these windows can shed light on why environmental hazards can devastate a pregnancy or cause effects on health and development decades later. Protecting pregnant women from environmental hazards is an important step to ensure the health of future generations.

Preconception: The first exposure window

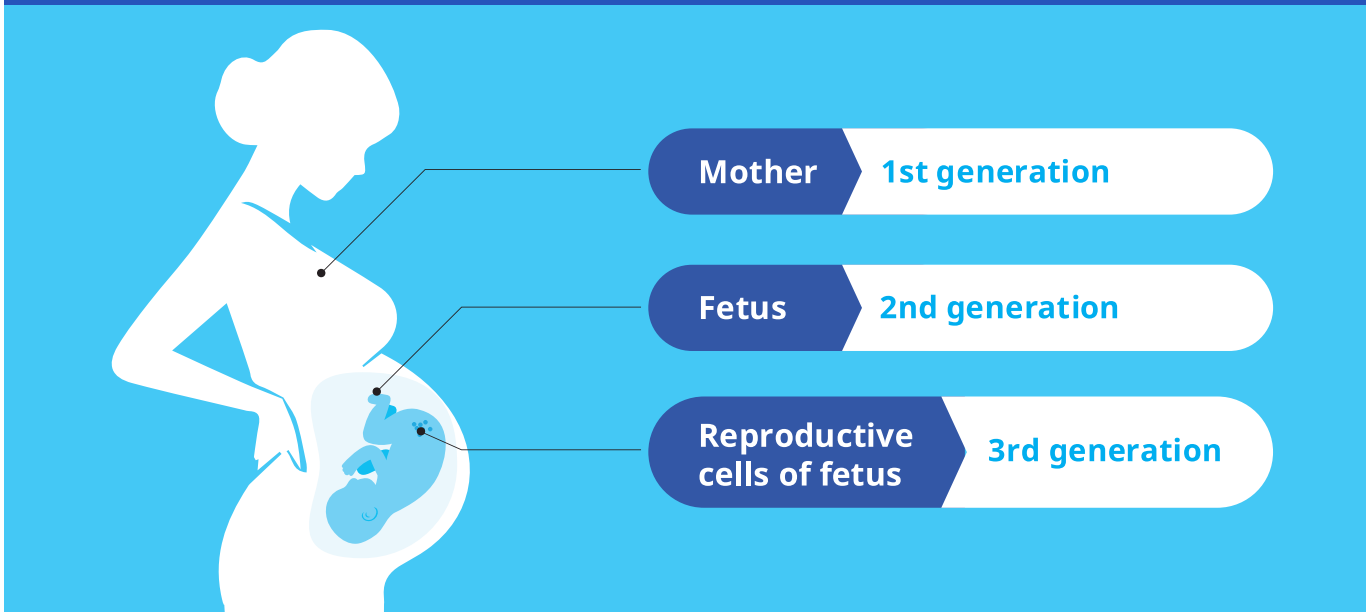
The health of both parents matters. The health of a sperm and egg which combine to create an embryo is foundational to the health of a pregnancy, the fetus and the baby after birth.[2] The weeks just before conception are particularly important.[3] But the impact of environmental hazards can be traced back several generations, and can occur even before a future parent is born.

The damage from direct exposure to environmental hazards to the reproductive cells of both men and women can happen decades before they conceive a child.[4] This is because a person's reproductive cells are already present when they are in the womb. It has been shown, for instance, that even when a woman does not smoke during pregnancy, her child is at increased risk of asthma if her own mother (the grandmother) smoked while pregnant with her.[5]

Damage can occur anytime, including before conception, continuing in utero, and persist through childhood and adolescence.[6] Egg and sperm cells also develop differently, which can affect when the windows of sensitivity to environmental hazards occur and, ultimately, fertility and health impacts.[7]

Changes to DNA in the reproductive cells can also be passed on to generations not directly exposed.[8] This means that a great-grandchild who did not have any direct exposure to an environmental hazard can still develop an environmentally related health condition, such as obesity.[9]

Intergenerational health impacts of exposure to environmental hazards



A closer look: How environmental hazards can change DNA instructions in the body

DNA is the genetic material that contains the instructions for a person to develop, survive and reproduce. Environmental hazards can change both the structure and function of DNA. Changes to the structure of DNA are called mutations. Changes to the function of DNA, where genes can be turned on or off, are more common and are called epigenetic changes.[10]

Mutations and epigenetic changes can occur in all cells in a body, including reproductive cells. If a mutation or epigenetic change caused by an environmental hazard takes place in a reproductive cell, the damage can be passed on to the next generation.

Epigenetic changes can occur at any point in a person's life but there are certain windows of increased vulnerability, such as during sperm and egg development, fertilization and the formation of an embryo.[11]

Pregnancy: The second exposure window

During pregnancy, a woman's body undergoes many changes to accommodate the metabolic and nutritional needs of the growing fetus and prepare for breastfeeding. Some of these changes can increase the vulnerability of a pregnant woman and fetus to environmental hazards. They can also alter key processes in a pregnant woman's body and change the way her body responds to physical stresses, such as extreme heat, putting both the woman and the fetus at risk of harm.

1. Increased food and fluid intake

A pregnant woman needs more food and fluids than a non-pregnant woman. This increases a pregnant woman's exposure to toxicants in contaminated food and drinking water. For instance, arsenic, a common contaminant of drinking water,[12] is linked to miscarriage, preterm birth and stillbirth,[13] as well as cognitive deficits in childhood.[14]

An increased need for fluids during pregnancy also puts a woman at risk of dehydration. This can cause low amniotic fluid levels, which limits fetal movement and creates pressure on the fetus from the umbilical cord.[15] Diseases like cholera, which make people lose fluids, make pregnant women especially susceptible to dehydration. Severe dehydration can compromise blood flow to the placenta and cause harmful levels of acid in the amniotic fluid, leading to fetal death.[16] Dehydration during heat waves may also contribute to growth restriction and low birthweight.[17]

Pregnant women have increased caloric and nutrient needs. This means they are more at risk of complications from food insecurity. Food insecurity is associated with a variety of adverse outcomes, including preterm birth, low birthweight and neural tube defects including spina bifida.[18] Food insecurity in pregnant women is also associated with impaired cognitive development in children.[19]

Consuming foods contaminated with fumonisins (mycotoxins found on corn and in corn flour) is associated with neural tube defects.[20] Climate change will increase the number of tropical regions susceptible to fungal growth, and this will likely lead to increased food contamination with fumonisins.

2. Changes to the respiratory system

Hormonal changes during pregnancy drive key changes in a pregnant woman's respiratory system, which can affect the body's response to environmental hazards such as air pollution.[21] Pregnant women inhale more air per minute, which means they will breathe in more air pollutants. Air pollutants can have a duel negative effect because they can both harm the fetus directly and act systemically by creating inflammation and reactive oxygen species, which are unstable molecules that can damage DNA.[22]

Antenatal air pollution exposure is associated with miscarriage,[23] preterm birth,[24] low birthweight[25] and stillbirth.[26] It is also linked to common chronic childhood conditions, including neurodevelopmental disorders[27] and asthma.[28] Exposure to wildfire smoke is linked to preterm birth and low birthweight.[29]

Exposure to second-hand smoke, which can contaminate children's environments when tobacco products are burned or when a smoker exhales smoke, contains over 7,000 chemicals, including approximately 70 that can

cause cancer.[30] Prenatal tobacco smoke exposure can alter blood flow and metabolism in the fetus and cause accumulation of chemicals both in the mother and the fetus.[31] Maternal smoking or second-hand smoke is linked to stillbirths, preterm births, birth defects and infant deaths.[32] The effects of prenatal smoke exposure continue through childhood and adolescence and include obesity, attention-deficit/hyperactivity disorder, mood disorders and childhood cancers.[33]

Increased demand for oxygen

Increased intake of oxygen necessary to meet the demands of the fetus can increase the production of reactive oxygen species, which are unstable molecules that can damage DNA.[34] Pregnancy alters the body's ability to detoxify these reactive oxygen species, and environmental factors can increase their production.[35] When there is an imbalance between the production and detoxification of these species, oxidative stress in cells occur.[36]

Increased oxidative stress in pregnancy is linked to adverse effects such as pre-eclampsia. It also is linked to the risk of developing cancer during childhood, and metabolic syndrome, cardiovascular disease and neurological diseases later in life.[37]

3. Changes in movement of substances in the body

The movement of substances, including chemicals, in a body can change during pregnancy. For example, a pregnant woman's bones will remodel to release calcium for the fetus, which can release lead into the bloodstream at the same time.

Other changes include the movement of fats in the body. Early in pregnancy, the storage of fat increases in a woman's body. Later in pregnancy, fat is broken down to provide energy for the fetus.[38] 'Fat-loving' (i.e., lipophilic) toxicants can be stored in this fat and then released into a woman's bloodstream, which can potentially reach the fetus.[39] Lipophilic chemicals include an array of harmful persistent pollutants, such as DDT, dioxins and heavy metals.[40]

4. Changes in metabolism

Other metabolic shifts to support fetal growth and development include changes in the metabolism of glucose and proteins. These changes are hormonally controlled and susceptible to endocrine-disrupting chemicals (EDCs) and other toxicants. When metabolism during pregnancy is negatively affected by EDCs, diseases such as gestational diabetes, hypertensive disorders or restricted fetal growth can occur. Miscarriage can also happen.[41]

5. Changes in the maternal heart, blood and circulation

During pregnancy, the heart increases the amount of blood it pumps per minute. The total volume of blood, including the plasma (i.e., the liquid portion of blood) is also increased.[42] Increased plasma volume is critical to maintain blood flow to the uterus. Low plasma volume is associated with gestational hypertension and other pregnancy complications.[43]

Red blood cell production also increases in pregnancy. As iron is a key component of these cells, pregnant women require more iron.[44] Conditions such as food insecurity, which may reduce availability of iron from dietary sources, can lead to iron deficiency and anaemia.

6. Changes in heat regulation

Changes in heat regulation to cope with the metabolic changes related to pregnancy include increased blood volume, dilation of blood vessels in the skin and increased sweating.[45] If a pregnant woman is exposed to extreme heat, she may not be able to transfer enough heat to the external environment. If this happens, her health and the fetus's health can be affected, with consequences for newborn and child health if the pregnancy goes to term.[46] Extreme heat experienced during pregnancy is associated with preterm birth and has been linked to gestational diabetes, low birthweight and congenital anomalies.[47]

7. Changes in immune function

During pregnancy, a woman's immune system will effectively suppress itself to enable the fetus to grow.[48] This increases a woman's susceptibility to certain infectious diseases and the severity of illness.[49] It also increases the risk of fetal death.[50] Research shows that pregnant women have an increased incidence of many types of infections, including some mosquito-borne illnesses that are increasing due to climate change, such as Zika virus infection and malaria.[51]

Malaria has significant impacts on the health of pregnant women and fetuses. Infections in the first trimester are especially high. The parasites that cause malaria can infect red blood cells and accumulate in the placenta, contributing to adverse pregnancy outcomes, including severe anaemia and death in the mother, miscarriage, stillbirth, preterm birth and low birthweight. Malaria during pregnancy has also been shown to be associated with impaired cognitive development in children.[52]

While Zika virus symptoms during pregnancy are usually mild and similar to those seen in non-pregnant people, Zika virus infection during pregnancy can cause miscarriage, stillbirth and preterm birth.[53] Zika virus can affect stem cells in the fetal nervous system.[54] Babies who survive may suffer from congenital Zika syndrome, which includes having a severely small head, brain and eye anomalies, congenital contractures, intrauterine growth restriction, seizures and neurodevelopmental delay.[55] Babies who are born without observable defects at birth can still present with cognitive and language neurodevelopmental delay in childhood.[56] Zika virus can also be transmitted sexually.

The placenta's dual role: Protector and pathway for pollutants and infections

The placenta is a remarkable organ. It takes on critical functions during pregnancy, acting like the lungs, gastrointestinal tract, kidneys and endocrine glands of the developing fetus.[57] A healthy placenta is essential to a healthy pregnancy.

While the main role of the placenta is to supply the fetus with oxygen and nutrients, the placenta also controls the adaptions a woman's body makes during pregnancy and acts like a barrier to minimize fetal exposures to toxicants and infectious agents.[58] Unfortunately, many harmful substances, such as lead, mercury, pesticides and other chemicals, can penetrate the placenta barrier and cross through it, harming the fetus and causing potentially lifelong effects to a child.[59] Some chemicals also concentrate in the placenta at higher levels than in the pregnant woman. For instance, arsenic can accumulate at levels up to three times higher in the placenta compared to the pregnant woman.[60]

Infectious agents, such as bacteria, parasites and viruses, can also cross the placenta and cause serious congenital infections, preterm birth and stillbirth.[61] For example, the Zika virus and a group of antenatal infections known by the acronym TORCH (*Toxoplasma gondii*, other, rubella virus, cytomegalovirus, herpes simplex virus) can devastate the health of the pregnancy and fetus.

A closer look: How environmental hazards affect placenta development and function

Researchers have recently begun to explore how environmental hazards might affect the development of a normally functioning placenta. The placenta has a large number of hormone receptors, which makes it vulnerable to chemicals that can disrupt the endocrine system, including heavy metals, some pesticides and per- and polyfluoroalkyl substances (PFAS).[62] Endocrine disruption in the placenta can cause oxidative stress and altered epigenetic programming, gene expression and placental function.[63]

Importantly, abnormal placenta development and function is associated with pre-eclampsia, a condition that includes high blood pressure and kidney damage in a pregnant woman. Pre-eclampsia is one of the most severe complications of pregnancy and can lead to maternal morbidity as well preterm birth and perinatal death.[64] In children who survive, it can also lead to neurodevelopmental delay and cardiovascular and metabolic disease later in life.[65] Antenatal air pollution exposure has been shown to be associated with pre-eclampsia.[66]

Exposure during the three pregnancy trimesters

The first trimester (weeks 1 to 13)

The first two weeks after fertilization: Even before a missed period would signal that a woman is pregnant, environmental hazards can interfere with implantation of the embryo into the womb and cause miscarriage.[67] Also during this period, the patterns of chemical tags on DNA, which can alter the function of DNA if affected by toxicants, are established.[68] By the time the embryo is implanted, the majority of DNA methylation tagging patterns are established.[69]

Weeks 4 to 8: Organs begin to form. By the eighth week of pregnancy, all major external and internal structures are formed, and organ systems have started to develop. During this time, the embryo's tissues and organs are rapidly developing, which makes them especially vulnerable to environmental hazards. As a result, weeks 4 to 8 is the window of time when major birth defects can occur.[70]

From week 9: This starts the fetal period. Until birth, organs continue to develop and mature and remain vulnerable to environmental hazards. Critical windows of development correspond to the periods of time that cells are dividing and changing into different types and tissues and the times that organs take on their shape.

For brain development, the critical period is from weeks 3 to 16. But brain development can continue to be affected by environmental hazards after this time as the brain will continue to grow and develop.

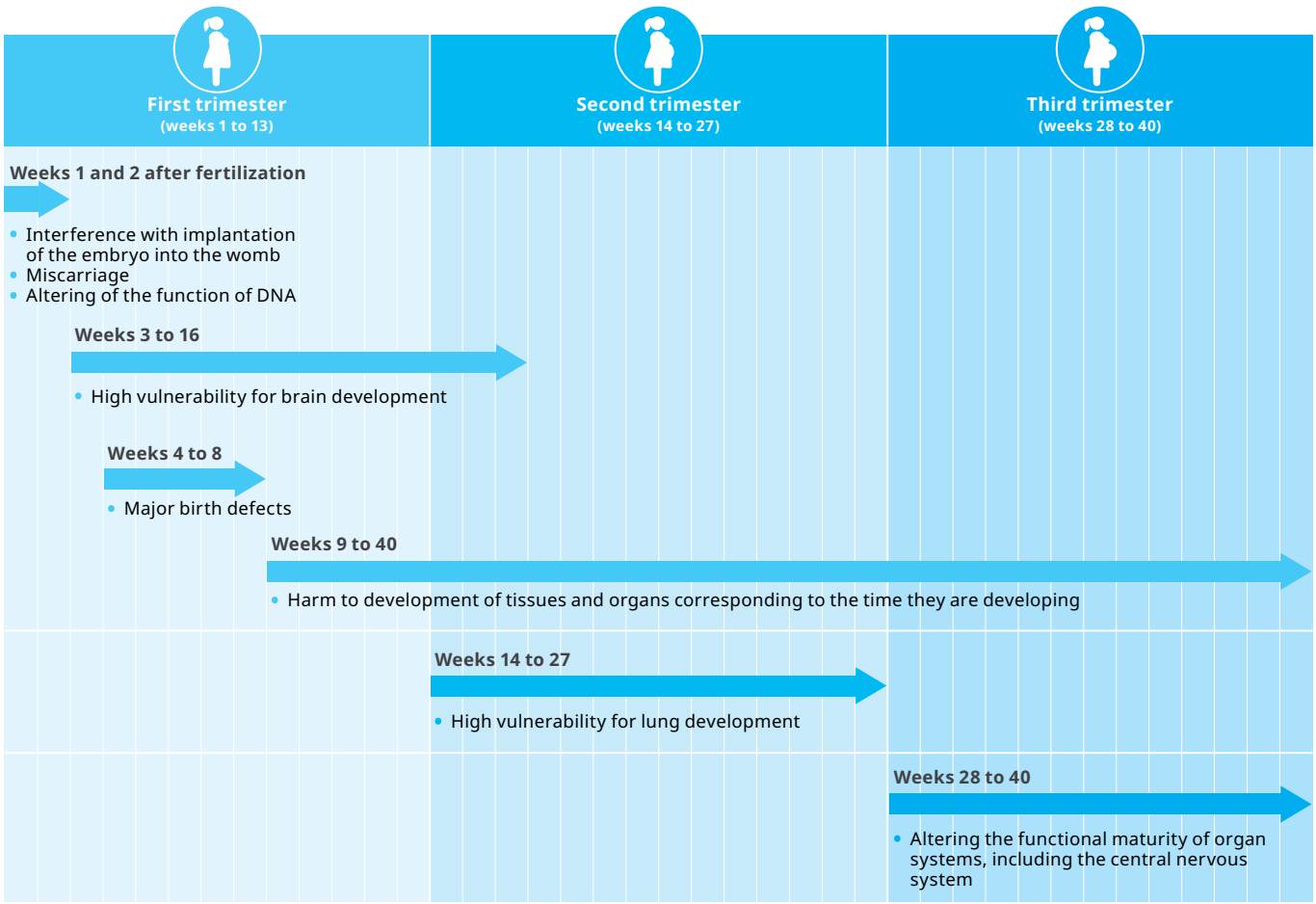
The second trimester (weeks 14 to 27)

This is a time of rapid growth and development. During the second trimester, lungs are most vulnerable to impairment from air pollution.[71]

The third trimester (weeks 28 to 40)

This is when fetal weight increases and organs continue to mature so they can be ready to function at birth.[72] During this time, environmental exposures can alter the functional maturity of organ systems, including the central nervous system.[73]

Timeline of health impacts from exposure to environmental hazards during trimesters



Note: An array of pregnancy-related disorders, including those caused by environmental hazards, can lead to the death of the embryo (miscarriage).

All women are at risk of environmental hazards during pregnancy – but some women are more at risk than others

Women in low- and middle-income countries, including fragile and humanitarian contexts

Women living in poverty and in low- and middle-income countries are more likely to suffer ill effects from environmental hazards.[74] A woman's health at the start of pregnancy and her genetic make-up can also play a role. Those particularly at risk include women who live in regions where unclean fuels are still used to cook, heat and light homes, as this generates high levels of household air pollution.[75] Others particularly at risk are those in regions where contamination of food crops with fumonisins (a group of mycotoxins) is common. Women working in dangerous jobs and without adequate workplace regulations, such as informal e-waste recycling, artisanal small-scale gold mining and in agricultural roles where pesticides are used, are also at great risk as they are regularly exposed to harmful chemicals.[76] Women can also be exposed to hazardous chemicals in female-dominated workplaces such as hairdressers and nail salons, or in daily living from cosmetics and household products (such as cleaning agents).[77]

The increased risk to health for pregnant women in urban slums

Living in an urban slum significantly affects the health of a pregnant woman and her developing fetus. Overcrowded and unsanitary conditions increase the prevalence of infectious diseases. Pregnant women in urban slums often experience inadequate nutrition and lack access to quality health care services. Air and water pollution are common, as slums are often located near industrial sites or waste dumps, exposing pregnant women to harmful chemicals.[78]

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How environmental hazards affect fetal, newborn and child health

Health outcome	Causes
Numerous health conditions in a pregnant woman can affect the pregnancy	The health status of a pregnant woman is critical to the health of the developing fetus and pregnancy. High blood pressure, gestational diabetes and obesity can contribute to adverse pregnancy outcomes and can be affected by environmental chemicals. For example, phthalates (chemicals added to plastics and found in many personal care and household products), PFAS, polychlorinated biphenyls (PCBs, a persistent organic pollutant formerly used in the electricity industry) and some flame retardants (such as polybrominated diphenyl ethers or PBDEs) significantly increase the risk of gestational diabetes.[79] Air pollution is also associated with gestational diabetes and high blood pressure.[80]
Death	Exposure to environmental hazards is associated with an array of pregnancy-related disorders that can lead to miscarriage, stillbirth and sudden infant death syndrome.[81]
Preterm birth	Many environmental hazards are linked to preterm birth (i.e., being born before 37 weeks of gestation).[82] Some examples include air pollution, lead, some pesticides, PFAS and phthalates.[83] Complications from preterm births are the leading cause of death among children under 5 years of age. Being born premature is also associated with many developmental problems in childhood.[84]
Low birthweight	The World Health Organization defines low birthweight as weight at birth less than 2,500 grams (5.5 pounds). Low birthweight can be caused by intrauterine growth restriction as well as prematurity. It is associated with fetal and neonatal morbidity and mortality as well as impaired growth and cognitive development in childhood.[85] It is also associated with chronic disease in adults, such cardiovascular disease, type 2 diabetes and metabolic syndrome.[86] Many environmental hazards are associated with low birthweight, including air pollution, tobacco smoke and pesticides.[87]
Birth defects	Air pollution, consumption of foods contaminated with fumonisins, extreme heat, hazardous waste and solvents are just some of the exposures that have been shown to be linked to various birth defects. These defects include malformation of the central nervous system, heart, abdominal organs, limbs and other structures.[88]
Numerous chronic conditions in childhood and adulthood	Beyond birth, diseases related to antenatal exposures can develop in childhood, adolescence and adulthood. Antenatal exposure to air pollution is associated with chronic childhood conditions, such as asthma, allergic disease, neurodevelopmental disorders, obesity and high blood pressure. It is also linked to adulthood diseases such as cardiovascular disease and chronic obstructive pulmonary disease, the third-leading cause of death worldwide.[89] Antenatal pesticide exposure is associated with neurodevelopmental disorders and childhood cancers including neuroblastoma and leukaemia, the most common childhood cancer.[90] Exposure to mercury during pregnancy can lead to devastating neurological outcomes in a child.[91]

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