Environmental Agents and their Impact on Placental and Gestational Development

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Conflicts of Interest
The author declares that there are no conflicts of interest.

Outline

- Background
- Birth Outcomes and the Environment
- Environmental Influences on Fetal Health
- Potential Mechanisms
- The Placenta
“Environmental Agents and their Impact on Placental and Gestational Development”
Alaeddin Abukabda, PhD


“The periods of embryonic, fetal and infant development are remarkably susceptible to environmental hazards. Toxic exposures to chemical pollutants during these windows of increased susceptibility can cause disease and disability in infants, children and across the human lifespan.

Among the effects of toxic exposures recognized in the past have been spontaneous abortion, congenital malformations, lowered birthweight and other adverse effects.”

2007 Nordic Pharmacological Society. Basic & Clinical Pharmacology & Toxicology. 10273–75

Examples of Environmental Agents

- Air pollutants (ozone, particulate matter)
- Cigarettes
- Bisphenol-A (BPA), phthalates
- Lead, mercury
Environmental Agents and Birth Outcomes

- Exposure of nonsmoking pregnant women to environmental tobacco smoke may be a risk factor for preterm birth, low birth weight, fetal death or miscarriage.
- Exposure to air pollution and particulate matter may be related to both low birth weight and preterm birth.
- A pregnant woman's exposure to lead and pesticides may cause preterm birth, low birth weight, and spontaneous fetal death or miscarriage.
- Environmental contaminants (e.g. lead) can affect menstruation, ovulation and sperm quality.
- Exposure to endocrine disruptors causes a decline in the sex ratio of males to females at birth.

Infant Mortality

- Over 22,000 infants died in the United States in 2017
- Five leading causes of infant death in 2017:
  1) Birth defects
  2) Preterm birth and low birth weight
  3) Maternal pregnancy complications
  4) Sudden infant death syndrome (SIDS)
  5) Injuries (e.g., suffocation)
Environmental Agents and Infant Mortality

- Elevates the risk of delivering a low birth weight (LBW), preterm, or small-for-gestational age (SGA) infant
- Exposure for at least 2 hours per day resulted in a mean birth weight reduction of 85 g and a twofold increased risk of LBW among infants of nonsmokers
- Dose-related effects of smoking resulting in a conception delay of approximately 2 months
Environmental Tobacco Smoke and Birth Outcomes

Air Pollution and Particulate Matter and Birth Outcomes

- Particulate matter is a complex mixture of extremely small particles and liquid droplets.

- Particle pollution is made up of a number of components, including acids (such as nitrates and sulfates), organic chemicals, metals, and soil or dust particles (http://www.epa.gov/pm/).

- Characterized according to size due to the variation of health effects associated with particles of different diameters.

- Decreased placental size and quality

  Animal studies suggested that volumes of placental compartments and calibers of maternal blood spaces were reduced.

- Fetal growth delay

  Studies using ultrasound measurements of fetal growth found strong associations between fetal growth delay and maternal exposure during mid-pregnancy.

- Small for Gestational Age (SGA)

  Associated with low birthweight, preterm birth, and SGA births.
Heavy Metals and Birth Outcomes

• Arsenic, cadmium and lead may compromise fetal health even at a low level through trans-placental circulation

• Prenatal cadmium exposure could impair steroidogenesis leading to suboptimal fetal growth and development

• Lead exposure may interfere with calcium deposition in the bone, resulting in decreased fetal bone growth

• Arsenic exposure during pregnancy may contribute to placental insufficiencies leading to intra-uterine growth retardation via oxidative stress
Phthalates and Birth Outcomes

- Associations have been reported between prenatal and early postnatal phthalate exposures and shorter anogenital distance as well as lower serum testosterone in newborns.
- Pre-natal exposure biomarkers have been associated with reduced gestational age.

Endocrine Disruptors and Birth Outcomes

- Chemicals that, at certain doses (high or low), may act on the endocrine system.
- Endocrine disruptors are found widely in contaminated water, air, food, and household products, like plastics.
- BPA binds to estrogen receptor and may disrupt estrogen function.

Endocrine Disruptors and Birth Outcomes

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Mode of Action</th>
<th>Effect</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPA</td>
<td>Direct binding to estrogen receptors</td>
<td>Disruptive</td>
<td>Reduced anogenital distance, lower serum testosterone</td>
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Potential Mechanisms – Barker Hypothesis

- Fetal origins of adult disease hypothesis.

- Fetal undernutrition in middle to late gestation leads to disproportionate fetal growth, programs later coronary heart disease.

- Not only coronary heart disease, but also diabetes, obesity, stroke and mental illness.

Potential Mechanisms – Fetoplacental Epigenome

- Epigenetic marks regulate development

- DNA methylation and histone modifications (acetylation, methylation, phosphorylation and ubiquitinization)

- Results in altered gene expression
Potential Mechanisms – Epigenetic Modification

Potential Mechanisms – Developmental Plasticity

The ability of a given genotype to produce different phenotypes in response to different environments.

Part of the organism’s “adaptability” to environmental cues.

The expressions of suites of genes, particularly during development or life history transitions, probably underlie the fundamental plasticity of an organism.

Provides the best chances of survival and reproductive success to organisms under changing environments.

Environmental conditions that are experienced in early life can profoundly influence human biology, child growth and maturation, and long-term health and longevity.
Potential Mechanisms – The Placenta

- Transient organ
- Functions in oxygen exchange, immunity, hormone secretion, nourishment and waste removal

- Exposure to environmental agents linked to reduced placental vascular density, efficiency, size, number
- Altered gene expression and vasoactive sensitivity
- Dual biomarker to assess maternal and fetal health

- Environmental agents may penetrate the placenta and disrupt function and efficiency
- Epigenetic markers in placenta may represent exposures from intrauterine and extrauterine environment
Potential Mechanisms – The Placenta

Summary

• Exposure to environmental agents affects birth outcomes

• Several mechanisms may be potentially involved and should be taken into consideration

• The placenta is a critical transient organ and is affected by environmental toxicants/toxins
Questions

- Ambient particulate matter is harmless and should therefore not be studied by toxicologists.
  - True
  - False
- It is important for clinicians to become knowledgeable about toxic environmental agents.
  - True
  - False
- Since the placenta is a transient organ it should not be a priority for clinicians.
  - True
  - False

Acknowledgments