



# **The Effects Of Environmental Factors On Reproduction**

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- **Reproduction** is one of the most important aspects of **human life** and is **influenced** by **different factors**.
- A **reproductive hazard** interferes with the ability of a couple to achieve a **successful birth**.
- **Environmental factors** and **reproductive hazards** affect **fertility, conception, pregnancy, and/or delivery, fetal and child health** .



- There has been **growing attention** to the potential reproductive effects of **preconception** and **prenatal exposures** to a variety of **toxic environmental agents**.
- **Lead,**
- **Mercury,**
- **Endocrine disruptors,**
- **Airborne pollutants,**
- **Inhalational anesthetics,**
- **Non-ionizing radiation,**
- **Anti-neoplastic drugs and**
- **Sterilizing agents**
- are among these **environmental agents**.



# TYPES OF REPRODUCTIVE HAZARDS

- The **three general categories** of reproductive hazards are:
- **Physical factors** (eg, radiation, exposure to electrical shock, excessive vibration or heat),
- **Biological factors** (eg, viruses, parasites), and
- **Toxic agents** (eg, toxicant exposure via **ingestion**, **inhalation**, or contact with **skin**).



# ENVIRONMENTAL EXPOSURES

- A **small proportion** of the **several thousand** occupational/environmental exposures has been **adequately assessed** for reproductive or developmental toxicity



# TYPES OF ADVERSE OUTCOMES

- Adverse reproductive and developmental outcomes from exposure to **toxic agents** include:
  - **Menstrual disorders** and other hormonal influences
    - ● **Infertility**
    - ● **Spontaneous abortion**
    - ● **Stillbirth or infant death**
  - ● **Low birth weight**
  - ● **Congenital malformations**
  - ● **Cognitive changes and reduced IQ**
  - ● **Developmental delays**
  - ● **Childhood cancer**



- **Air pollution** has been shown to have adverse effects on **different birth outcomes** and may lead to **preterm births** and **intrauterine growth retardation (IUGR)**.
- **Traffic** may affect **birth weight** through exposure to both **air pollution** and **noise** <sup>(1)</sup>.
- Using **mobile phones** can be linked to the early **spontaneous abortions** <sup>(2)</sup>.

- 1: BMJ. 2017; 359: j5299. Impact of London's road traffic air and noise pollution on birth weight: retrospective population based cohort study
- 2: Mahmoudabadiet al. Use of mobile phone during pregnancy and therisk of spontaneous abortion. J Environ Health Science & Engineering (2015) 13:34 DOI 10.1186/s40201-015-0193-z



- **Alcohol and tobacco** consumption have a negative effect on the process of **spermatogenesis**, and can affect the **sperm concentration, viability** and **motility**.
- A systematic review on 49 studies, have reported associations between occupational exposure to **chemicals** and **time to pregnancy (TTP)**<sup>(1)</sup>.
- 1: Occupational exposure to chemical substances and time to pregnancy: a systematic review. : Human Reproduction Update, Volume 18, Issue 3, May/June 2012, Pages 284–300,





- **Accurate data on baseline rates of specific adverse outcomes in the general population are difficult to assemble**



# ASSESSING RISK

- Studies in **humans** that assess the **causal relationship** between specific exposures and these outcomes frequently face **limitations and challenges**, including:
- Lack of accurate assessment of the **dose** of the **exposure to mother and/or fetus**;
- A need for **proper control** groups since a variety of other **genetic, physical** and **socioeconomic factors** affect reproductive toxicity;
- **Inadequate assessment** of the background **prevalence** of events;
- Difficulties with **reliable ascertainment** of the **outcome** or **endpoint** (eg, early abortion versus late heavy menses);
- And difficulties in accurate ascertainment of exposures and **multiplicity of exposures**



# PATHOGENESIS

- There are **multiple physiological events** that could be **affected** by environmental exposures:
- Interference with **oogenesis**
- Interference with the **menstrual cycle** and **fertility**
- Interference with **fetal development**
- **Effect of pregnancy**
- **Effect of maternal factors**
- **Effect of lactation**



# Effect of pregnancy

- The **physiological changes** of pregnancy may **alter** the amount of **toxin absorbed** and **delivered** to the **fetus**. As examples:
- **Delayed gastric emptying** and **reduced intestinal motility** increase **absorption** of ingested agents
- **Increased minute ventilation** and **tidal volume** increase **absorption** of **respiratory toxins**



# Effect of maternal factors

- The pregnant mother's **overall health** is also an important factor.
- If an exposure leads to **direct toxicity** to the mother, there may be **indirect** (as well as direct) adverse effects on the fetus.
- A mother with **carbon monoxide** poisoning or a **severe asthma attack**, as an example, may **not** adequately **perfuse the placenta** or **release oxygen** to the **fetus**.



# Effect of maternal factors

- Some substances, such as **mercury**, may cause **little** or **no clinical symptoms** in the mother, but cause **profound effects** on the fetus (**cerebral palsy**, limb deformities, **mental retardation**, blindness and **seizures**).
- In addition, job-related **physical** or **emotional stresses** could impact the **course of the pregnancy**.



# Lead

- lead exposure have been associated with an
  - **Increased risk of spontaneous abortion and still birth**
  - **Impaired cognitive development**
  - **Fetal neurotoxicity**
- **CDC Guideline on Lead and Pregnancy recommends that mothers living in developed countries with blood lead level (BLL) <40 mcg/dL should breastfeed** <sup>(1)</sup>.
- **Maternal calcium supplementation can reduce maternal blood lead levels** <sup>(2)</sup>
- 1: CDC Guidelines For The Identification And Management Of Lead Exposure In Pregnant And Lactating Women
- 2: Effect of Calcium Supplementation on Blood Lead Levels in Pregnancy: A Randomized Placebo-Controlled Trial. Environ Health Perspect. 2009 Jan; 117(1): 26–31.



# Bisphenol A(BPA) (plastics) and phthalates (salt or ester of phthalic acid)

- Fetal or **neonatal mortality, birth defects, or reduced birth weight**;
- **Little evidence** of associations of BPA or phthalate exposures with **fetal growth** <sup>(1)</sup>.
- "Negligible concern" for reproductive effects in **non-occupational exposed adults**;
- And "minimal concern" for **workers** exposed to **higher levels** in **occupational** settings

• 1: Exposure to Bisphenol A and Phthalates during Pregnancy and Ultrasound Measures of Fetal Growth in the INMA-Sabadell Cohort. Environ Health Perspect. 2016 Apr; 124(4): 521–528.





# Airborne pollutants

- **Numerous studies** have examined the links between **various airborne** pollutants and **adverse outcomes**, such as
  - Low birth weight (LBW),
  - Preterm birth,
  - And small for gestational age birth (SGA)
  -
- And have come to **different** conclusions
- Because of **difficulties** in **measuring exposures**, **timing of measurements**, and degree of adjustment for **confounding**.



# Airborne pollutants

- A systematic review of 41 studies of **air pollution** and **birth outcomes** found <sup>(1)</sup>.
- Exposure to **sulphur dioxide** was associated with **preterm birth**;
- Exposure to **fine particulate matter** was associated with **LBW, preterm birth, and SGA births**;
- And exposure to **particulate matter  $\leq 10 \mu\text{M}$**  was associated with **SGA births**.

• 1: Air pollution and birth outcomes: a systematic review. Environ Int. 2011 Feb;37(2):498-516.



# Airborne pollutants

- Recent epidemiological studies are showing an association between **fine particulate matter** (2.5microns) and **autism** (twice) <sup>(1)</sup>.

- 1: <https://www.hsph.harvard.edu/news/press-releases/fine-particulate-air-pollution-linked-with-increased-autism-risk/>



# Nonionizing radiation

- The reproductive risk of nonionizing radiation (eg, **electromagnetic fields** emitted from **computers, microwave communication systems and ovens, power lines, cellular phones, household appliances, heating pads and warming blankets, airport screening devices** for metal objects) has been studied **extensively**.
- The Oak Ridge Associated University panel and a committee of the National Academy of Sciences both concluded that the reproductive **risk of nonionizing radiation** is **minimal or nonexistent**
- Literature reviews have generally concluded that there **is a lack of evidence** for a **strong association** between a woman's use of a **video display terminal (VDT)** and **fetal loss or other adverse reproductive outcomes**



# PREVENTION

- When exposures cannot be controlled or eliminated, transfer the woman to a **different job without** the exposure.
- **Avoid exposure** to excessive **vibration**, **temperature extremes**, and **ionizing** and **non-ionizing radiation**.
- If **chemical contact** with the **skin** occurs, **wash** the **area** thoroughly **as soon as possible**.
- In general, work in **well-ventilated areas** and with **proper control of chemical** vapors or other toxicants.



# Chemicals and fetal growth (Claudia A. Snijder)

Human Reproduction, March 2012; Volume 27: 910-920

- In **4680** pregnant women (population-based prospective cohort study) from **early pregnancy** onwards in the Netherlands (2002-2006),
- **Results** suggest :
- Maternal occupational exposure to **several chemicals** during pregnancy is **associated** with
- **Impaired fetal growth (fetal weight, fetal head circumference, and fetal length)**
- And a **decreased placental weight.**



# Bisphenol A and fetal growth; Claudia A. Snijder

Environmental Health Perspectives, 2013 Mar; 121(3): 393–398.

- Women with BPACB  $> 4.22 \mu\text{g/g}$  VS  $< 1.54 \mu\text{g/g}$  had
  - lower growth rates for fetal weight and
  - Lower head circumference,
  - Resulting in a difference at birth of 3.9 cm in HC and 683 grams in birth weight.
- Higher concentrations of urinary BPA are inversely associated with fetal growth.



# Chemicals And **Hypertensive Disorders** During Pregnancy

Jaap Jan Nugteren; Plos One, June 2012; Volume 7: e39263 (prospective birth cohort study)

- **No consistent associations** between **any of the work-related risk factors**, such as
  - **long periods of standing** or walking,
  - **Heavy lifting**,
  - **Night shifts**, and
  - **Working hours**,
- Nor exposure to **chemicals**
- With **hypertensive disorders** during **pregnancy**.
  
- However, the **low prevalence of pregnancy** induced hypertension and preeclampsia, combined with the **low prevalence of occupational** risk factors **limit the power for inference** and **larger studies** are needed to corroborate or refute these findings





# Physically Demanding Work, **Fetal Growth**, And Adverse Birth Outcomes.

Claudia A. Snijder; Occupational and Environmental Medicine, August 2012; Volume 69: 543-550

- **No consistent significant associations** between physically demanding work **nor working hours** in relation to
- **Small-for-gestational-age,**
- **Low birth weight or**
- **Preterm delivery.**
- Women exposed to **long periods of standing** had **lower growth rates** for **fetal head circumference**, resulting in a reduction of approximately **1 cm (3%)** of the average **HC** at birth.



# Physically Demanding Work, **Fetal Growth**, And Adverse Birth Outcomes

- Compared with women working **<25 hours** per week, women working 25-39 hours per week, and **> 40 hours** per week had
  - **Lower growth rates** for both fetal **weight** and **head circumference**,
  - Resulting in a difference of approximately **1 cm in HC at birth** and a difference of **148-198 grams** in birth weight.
  - **Long periods of standing** and **long working hours** per week during pregnancy seem to **negatively influence** **intrauterine growth**.



# Díaz J. Effect of Environmental Factors on **Low Weight** in Non- Premature Births: A Time Series Analysis. PLoS One. 2016 Oct

27;11(10):e0164741.

- **Atmospheric particulate matter (PM)2.5** micrometers had influence on **LBW**.
- **Reducing the number of vehicles** would serve to **lower** pregnant women's exposure.
- In the case of **noise** should be limited the exposure to **high levels** during the **final weeks** of **pregnancy**.
- PM2.5 refers to **atmospheric particulate** matter (PM) that have a **diameter of less than 2.5 micrometers**, which is about **3% the diameter of a human hair**.



## Nuclear power plant and pregnancy

- Residence in the vicinity of a **nuclear power plant** is **not** a **significant factor** which will cause **abnormal health** situations during **pregnancy** <sup>(1)</sup>.
  - **Increasing odds** of **adverse birth outcomes** among infants born to pregnant women living closer to power plants <sup>(2)</sup>.
  - **More research** is warranted to better understand the causal relationship <sup>(2)</sup>.
- 1: Pregnancy outcome of women in the vicinity of nuclear power plants in Taiwan. Radiat Environ Biophys (2010) 49:57–65
  - 2: Associations Between Residential Proximity to Power Plants and Adverse Birth Outcomes. American Journal of Epidemiology, June 28, 2015, Vol. 182, No. 3



# Evidence of exposure to **chemicals** and **heavy metals** during pregnancy in Japanese women.

Reprod Med Biol. 2017;16:337–348.

- Exposure to **chemicals** and **heavy metals** ( High levels in the maternal blood and cord blood)
- Were **significantly** and **negatively** associated with **fetal growth**.



Adverse effects of **maternal lead levels** on birth outcomes in the ALSPAC study: a prospective birth cohort study. BJOG 2015;122:322–328.

- a **large cohort** of mother– child pairs in the UK (n = 4285).
- There was evidence for adverse effects of **maternal B-Pb** on the incidence of **preterm delivery, birth weight, HC** and **crown–heel length,**
- But **not** on the incidence **of low birth weight.**



## Low level **lead exposure** and pregnancy outcomes in an observational birth cohort study: dose–response relationships.

BMC Res Notes (2016) 9:291

- Effect of **maternal Pb levels** on birth outcomes
- An **increase** of **1  $\mu\text{g}/\text{dl}$**  was associated with changes in birth weight of  $-9.93$  (95 % CI  $-20.27, 0.41$ ) g, head circumference  $-0.03$  (95 % CI  $-0.06, 0.00$ ) cm and crown–heel length  $-0.05$  (95 % CI  $-0.10, 0.00$ ) cm.



**Association of adverse birth outcomes with prenatal exposure to vanadium: a population-based cohort study.** Lancet Planet Health 2017; Vol 1

September 2017

- **7297 women**
- **Urinary Ln-**vanadium** concentrations showed non-linear dose-response relationships with risk of **preterm delivery**.**





Ambient **air pollution** the risk of **stillbirth**: A prospective birth cohort study in Wuhan, China. *International Journal of Hygiene and Environmental Health* 221 (2018) 502–509

- **95,354 births** between June 10, 2011 and June 9, 2013.
- The exposure assessments were based on the **daily mean concentrations of air pollutants** obtained from the **exposure monitor** nearest to the pregnant women's residence.
- Exposure to **high levels of particulate matter 2.5, particulate matter 10, sulfur dioxide, nitrogen dioxide and carbon monoxide increases the risk of stillbirth** .
- The **most susceptible** gestational period to ambient **air pollution** exposure was in the **third trimester**.



## Prenatal **Heavy Metal Exposure** and Adverse Birth Outcomes in Myanmar: A Birth-Cohort Study Int. J. Environ. Res. Public Health 2017, 14, 1339

- Birth-cohort study on 419 pregnant women
- Maternal spot **urine samples** were collected at the **third trimester**.
- Prenatal maternal **cadmium exposure** was associated with an **occurrence of low birth weight**.



# conclusion

- Various occupational and environmental risk factors **may affect** various domains of human reproduction, including fecundity, **intrauterine growth**, **hypertensive disorders** during pregnancy, and **congenital malformations**.
- **Further studies** are needed to corroborate or refute these findings and to elucidate the **underlying mechanisms**.
- Effort should be put to **reduce the exposure** to occupational risk factors **during pregnancy** and to **increase awareness** among pregnant women.



Thank you for your attention