Radiation & Reproductive Health: Methodologic Issues

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Key Considerations

- Reproduction is a notably fallible process – vulnerable to exogenous influences
- Distinctive considerations for fetus, mother, and father
- Timing of exposure is critical, weeks or days rather than years
- Several key outcomes of interest are challenging to measure

Savitz DA, Hertz-Picciotto I, Poole C, Olshan AF. Epidemiologic measures of the course and outcome of pregnancy. Epidemiol Rev. 2002;24(2):91-101.

Available Research on Ionizing Radiation and Reproductive Health

- Limited in volume and quality
- Idiosyncratic sources of exposure
  - Occupation, medical treatment, nuclear disasters, proximity to nuclear power plants
- Sporadic suggestions of small increases in risk, RRs 1.1-1.3*
  - Miscarriage, stillbirth, reduced birthweight
  - 8-11 studies of each

*Frangione B, Hinton P, Villeneuve PJ. Low-dose ionizing radiation and adverse birth outcomes: a systematic review and meta-analysis. Int Arch Occup Environ Health. 2023 Jan;96(1):77-92.

Fertility

- Jointly determined by male and female factors, multiple pathways -- semen, ova, transport, implantation
- Infertility defined as 1 year or more of unprotected intercourse without conception (~10% of couples)
- Time to pregnancy is sensitive indicator of fecundability
- Ideally assessed prospectively among pregnancy planners
- Can be ascertained retrospectively through carefully constructed interviews
- Requires hundreds participants with informative experience to study subtle effects on fecundability

Pregnancy Complications

- Focus on common complications: hypertensive disorders, gestational diabetes
- Routinely screened and accurately identified in medical records
- In the range of 5-10% depending on age, parity, adiposity
- No established exogenous influences

Pregnancy Loss

- Includes miscarriage (<20 weeks) and stillbirth (20+ weeks)
- Stillbirth is medically documented, miscarriage is not
- Early losses most frequent and difficult to identify
  - Early pregnancy recognition leads to greater frequency of recognized loss
  - Biochemical monitoring -- ~30%
  - Pregnancy testing -- ~10%
- Feasible to assess based on recall but subject to errors in estimating gestational age at time of loss
- Limited evidence of exogenous determinants – probably affected by smoking

Birthweight and Gestational Age

- Routinely recorded accurately
- Continuous measures easily studied in relatively small populations (several hundred) but of little clinical consequence
- Preterm birth is clinically important, shorter gestation results in greater morbidity
- Small-for-gestational-age is marker of reduced growth, unclear importance except at extremes
- Established exogenous influences on birthweight

Birth Defects

- Common in the aggregate but individual defects are rare (<1 per 1000)
- Severe defects identifiable through medical records, not minor defects
- Narrow time windows when defects are caused
- Clearly established exogenous influences, primarily medications

Neurodevelopment

- Prenatal factors thought to affect risk of neurodevelopmental disorders
- Earlier onset more likely to have prenatal rather than postnatal determinants
- Range of severity for common conditions (ADHD, autism, cognitive deficits)
  - Risk dependent on intensity of screening
  - All in the range of ~2-10% prevalence
- Neurobehavioral testing identifies small variation in function including in the normal range
- Few exogenous influences established

Considerations in Designing Studies

- Source of available information
  - Medical records: pregnancy complications, stillbirth, birthweight, gestational age, birth defects
  - Self-report: time to pregnancy, miscarriage, neurobehavioral disorders
- Potential confounding by lifestyle factors
  - SES, tobacco, alcohol
- Focus on fetal exposure as most vulnerable to adverse effects

Particular Issues for Studies of Flight Crews

- Circadian rhythm disruption has hormonal effects that are plausibly related to reproductive health outcomes
- Physical and psychological work demands may affect course and outcome of pregnancy
- Potential for “unhealthy pregnant worker effect”
  - Greater fertility associated with declining participation in the workforce
  - Subfertility or pregnancy loss may lead to sustained employment
- Consider surveillance to monitor for signals rather than seeking conclusive etiologic research

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