“Will that X-ray harm my unborn child”: A meta-analysis of fetal health effects indicates very low risk to fetus following occupational exposure of pregnant interventional physician.

J. Mihailovic¹, B. Schueler¹, J. Fiedler², G. Sturchio³, P. Best⁴, A. Cabalka⁴, M. Guerrero⁴, C. MacIntyre⁴, K. Fetterly⁴

¹Dept. of Radiology, Mayo Clinic, Rochester, MN
²Dept. of Radiation Safety, Mayo Clinic, Rochester, MN
³Dept. of Radiation Safety, Jacksonville, FL
⁴Dept. of Cardiovascular Diseases, Mayo Clinic, Rochester, MN
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Educational objectives

▸ Comprehensive literature review-collected and combined into one source.
  • Review of fetal risk levels
    - radiation dose (occupational radiation exposure)
    - maternal body mass index (BMI)
    - maternal age
    - hormonal therapy during the pregnancy

▸ Provide literature-based insight which cardiologists and radiologists can use to guide career decisions.
Take home message

- For our interventional cardiologists and radiologists with proper radiation safety practices, fetal radiation dose is predicted to be < 4 mGy per term.

- Compared with known risk of early childhood cancer from other causes, the predicted risk of cancer associated with estimated fetal radiation dose is very low.
Radiation dose defined

- International convention is to express dose to the human fetus in units milli-Gray (mGy), and this convention will be followed herein.
  - Radiation dose to human tissue is assigned units milli-Gray (mGy).
  - Whole body “effective dose” is assigned units milli-Sievert (mSv).
    - *In US regulations, the fetus dose limit is specified in units mrem, where 100 mrem = 1 mSv.*
Known fetal risks following high fetus radiation dose:

- Prenatal death
- Small head size
- Mental retardation
- Congenital malformation and
- Childhood risk of cancer

Summary of biological effects of prenatal radiation exposure taking into account time point of exposure related to conception as well as the threshold value of risk.

- No effect or fetal absorption >100 mGy at 0 weeks
- Microcephaly >50 mGy at 2 weeks
- Severe mental retardation >100 mGy at 8 weeks
decrease in IQ >100 mGy at 16 weeks
- Mild microcephaly >100 mGy at 25 weeks
- Organogenesis severe malformation >100 mGy at all stages
- Mild mental retardation >0 mGy at all stages

*adapted from Wagner, et al.*
Putting risks numbers into perspective...

- Exposure to high doses of radiation are known to be detrimental to the health of the fetus.

- Considering the necessary radiation exposure threshold for tissue effect to potentially occur is much higher that what an interventional cardiologists/radiologists would receive.

*ICRP 84 “Pregnancy and Medical Radiation”
* NCRP 54 “Medical radiation exposure of pregnant and potentially pregnant women”
As a rapidly evolving field, interventional cardiology has advanced remarkably since its inception ~50 years ago.

Yet, throughout the world, there is a major underrepresentation of women in interventional cardiology (IC).

Nonuniformity of the guidelines and often inconclusive data related with fetus health risk continues to be an important factor for women considering careers in IC.

3. Lewis SJ, J Am Coll Cardiol (2017)
4. Kurdi H, Br J Cardiol (2020)
Estimating fetus dose in our practice

- **Occupational exposure values (E, mGy) as measured at the left collar, outside the apron for working groups, radiologists and cardiologists, per year.**
  
  \[ E_{\text{collar, ave.}} = 18.5 \text{ mGy, (N = 191)} \]
  
  Range: 0.5 – 46.1 mGy

- **Multiply by 2 to estimate exposure at the abdomen, outside the apron.**

  \[ E_{\text{abd., outside}} = 36.9 \text{ mGy} \]

- **Estimate abdomen exposure inside a 0.5 mm Pb apron, assuming 3 % transmission.**

  \[ E_{\text{abd., inside}} = 1.1 \text{ mGy} \]

- **Assign exposure under the apron as conservatively high estimate of fetus dose (D).**

  \[ D_{\text{fetus}} \approx 3.9 \text{ mGy (mSv)} \]

*In dose estimations use of upper and lower body shield is assumed*
Material and methods

12,307 titles identified through database search (PubMed and Web of Science, Cochrane Library and Scopus)

1st screen (search by keywords)

729 titles selected for further evaluation

2nd screen

172 titles selected for abstracting

83 of titles were excluded

89 full text articles found eligible

50 additionally excluded

39 full text articles found eligible (studies dates range 1970-2019)
Results: Meta-analysis of maternal exposure to radiation and early childhood cancer risk

Pooled data using random effect model showed that risk of developing early childhood cancer increase with dose.
Results: Meta-analysis of maternal exposure to radiation and early childhood cancer risk

- This meta-analysis suggests that fetus dose greater than ~200 mGy may be associated with increased risk of adverse health effect.

- Other works have suggested that fetus dose >100 mGy may be associated with increased risk.

- Importantly, this meta-analysis demonstrates that HR for fetus dose < 5 mGy is not different than for dose of 0 mGy; HR = 1.001 [95% CI 0.8 to 1.09, p=0.967].
Results: Meta-analysis of maternal body mass index and risk of congenital heart defects in infants

Meta-analysis among the observational studies showed that maternal BMI is associated with increased risk of CHD in infants.

<table>
<thead>
<tr>
<th>Study</th>
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<tbody>
<tr>
<td>&lt;18 kg/m²</td>
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<tr>
<td>Persson et al (2019)</td>
<td>0.92 [0.85, 1.01]</td>
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<tr>
<td>Best et al (2012)</td>
<td>1.43 [0.86, 2.40]</td>
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<td>1.39 [0.62, 1.91]</td>
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<tr>
<td>Davey Smith et al (2009)</td>
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<tr>
<td>Asrani et al (2020)</td>
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Meta-analysis among the observational studies showed that maternal BMI is associated with increased risk of CHD in infants.
Results: Meta-analysis of maternal body mass index and risk of congenital heart defects in infants

Maternal BMI index and hazard risk for CHDs in infants have indicated a positive effect of:

- maternal overweight (BMI >30 kg/m²), HR 1.33 [95% CI 1.04, 1.63, p=0.03],
- underweight mothers (BMI <18 kg/m²), HR 1.18 [95% CI 0.78, 1.84, p=0.04].
Results: Meta-analysis of maternal age on preterm birth and low weight newborns

Meta-analysis showed an age gradient in the probability of giving preterm birth and a low-birth-weight child and was higher at maternal ages older or younger that at the reference category ages (25-35 yrs).
Results: Meta-analysis of maternal age on preterm birth and low weight newborns

Meta-analysis showed an age gradient in the probability of giving preterm birth and a low-birth-weight child and was higher at maternal ages older or younger than at the reference category ages (25-35 yrs).

- (age < 18 yrs HR 1.14 [95% CI 0.63, 1.66, p=0.06])
- (age > 45 yrs HR 1.27 [95% CI 0.81, 1.74, p=0.08])
Results: Meta-analysis of exposure to female hormone drugs during pregnancy and its effect on malformation in male children

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<td>Hemminski et al (1999)</td>
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Performed meta-analysis supports hypothesis that oestrogen/progestin drug therapy during pregnancy brings increased risk of malformations in children who were exposed in utero (HR 1.4 [95% CI 0.85, 1.75]). HRs were higher among exposed male children compared to control.
Summary

1. The meta-analysis demonstrates that HR for fetus dose < 5 mGy is not different than for dose of 0 mGy; HR = 1.001 [95% CI 0.8 to 1.09, p=0.967].

2. Maternal BMI > 30kg/m² was associated with HR 1.33 [95% CI 1.04, 1.63, p=0.03], increased risk in CHD in infants.
Summary

3. Maternal age > 45 years increases risk of preterm birth and underweight newborn with estimated HR 1.27 [95% CI 0.81, 1.74, p=0.08].

4. Hypothesis that oestrogen/progesterone drug therapy during pregnancy brings increased risk of malformation in male children who were exposed in-utero, HR 1.4 [95% CI 0.85, 1.75, p=0.08].
Conclusions

- This meta-analysis of 14 studies of childhood cancer incidence following in-utero radiation exposure indicates that even dose less than ~200 mGy is not associated with adverse health effect. This finding agrees with others that fetus dose less than 100 mGy is unlikely to be associated with adverse health effects.

- In our practice, dose to the fetus of interventional cardiologists and radiologists is expected to be less than 4 mGy.

- This work supports the position that radiation risk to the fetus of an interventional physician is exceptionally low.

- Factors that adversely affect the gestational and early postnatal environment such as maternal BMI, age and some disease treatments can significantly alter fetal development with persistent effects on health.
Suggested literature for cancer risk related to exposure to ionizing radiation:

8. Izumi S et al. (2003) Cancer incidence in children and young adults did not increase relative to parental exposure to atomic bombs.89(9):1709-1713.
Suggested literature on the impact of maternal BMI on fetal CHD:

References

Suggested literature on the impact of maternal age on preterm birth and low weight newborns:


Suggested literature on the impact of hormonal therapy during pregnancy on malformation of male children: