In utero radionuclide exposures and risk of leukaemia

John Harrison
In utero radionuclide exposure and risk of leukaemia

- ICRP dose estimates for in utero radionuclide exposures
- In utero haemopoietic sensitivity to alpha and $^3$H beta irradiation
- Alpha emitters in human fetal tissues
The International Commission on Radiological Protection (ICRP)

- Dose coefficients for radionuclide intakes - Sv per Bq

- Ingestion, Inhalation

- Workers, Public
Selected radionuclides for 31 elements:

H, C, S, Ca, Fe, Co, Ni, Zn, Se, Sr, Zr, Nb, Mo, Tc, Ru, Ag, Sb, Te, I, Cs, Ba, Ce, Pb, Po, Ra, Th, U, Np, Pu, Am, Cm
Doses to the Embryo/Fetus following Intakes of Radionuclides by the Mother

- Acute and chronic intakes, before and during pregnancy
- Doses from radionuclides
  - retained in maternal tissues
  - transferred to fetus
  - retained in child after birth
Fetal model for alkaline earths

- Maternal blood
- Fetal soft tissue
- Fetal blood
- Fetal bone surface
- Fetal exchangeable bone volume
- Fetal non-exchangeable bone volume
Biokinetic model for calcium, strontium and related elements

- Rapid turnover (ST0)
- Intermediate turnover (ST1)
- Tenacious retention (ST2)

- Urinary bladder contents
- Urinary path
- GI Tract contents
- Faeces
- Kidneys: Other kidney tissue
- Cortical volume: Nonexch., Exch.
- Trabecular volume: Nonexch., Exch.
- Plasma
- Other soft tissues
- Skeleton

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Caesium-137 ingestion

-2.5y, -6 mo, conception, +5w, +10w, +15w, +25w, +35w, birth, birth+5, birth+10, birth+15, birth+20

- in utero
- post natal
- milk

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Haemopoietic tissues *in utero*

- Yolk sac
- Liver
- Bone marrow
ICRP assumptions for fetal bone dosimetry

• Alphas - homogenous mass
• Betas - trabecular structure
Doses following chronic ingestion of radionuclides throughout pregnancy

**Ratio of offspring to adult dose:**

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{32}$P</td>
<td>10</td>
</tr>
<tr>
<td>$^{45}$Ca</td>
<td>11</td>
</tr>
<tr>
<td>$^{90}$Sr</td>
<td>1.5</td>
</tr>
<tr>
<td>$^{131}$I</td>
<td>1.1</td>
</tr>
<tr>
<td>$^{137}$Cs</td>
<td>0.4</td>
</tr>
<tr>
<td>$^{210}$Po</td>
<td>0.1</td>
</tr>
<tr>
<td>$^{239}$Pu</td>
<td>0.04</td>
</tr>
</tbody>
</table>
Conclusions on ICRP fetal doses

• In general doses to offspring are less than adult doses
  - notable exceptions are isotopes of phosphorus and calcium

• NRPB to issue advice on occupational and public exposures
In utero haemopoietic sensitivity to $^{239}$Pu $\alpha$ and tritium $\beta$ irradiation

CBA/H mice exposed to:

- 0.5 Gy X-rays d7, d14 pregnancy
- $^{239}$Pu d6, d13
- $^3$H as HTO chronic

Stable chromosomal aberrations in direct marrow metaphase preparations from mothers and offspring 2 - 8 wks after birth

Kozlowski et al. IJRB 77, 805 (2001)
In utero haemopoietic radiosensitivity

Stable aberrations, break-points per cell

<table>
<thead>
<tr>
<th></th>
<th>Offspring</th>
<th>Mothers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>0.018</td>
<td>0.026</td>
</tr>
<tr>
<td>X-rays d 7</td>
<td>0.16</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>0.11</td>
<td>0.20</td>
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<tr>
<td>$^{239}$Pu d 6</td>
<td>0.09</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>0.06</td>
<td>0.09</td>
</tr>
<tr>
<td>HTO chronic</td>
<td>0.11</td>
<td>0.11</td>
</tr>
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## In utero haemopoietic radiosensitivity

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<thead>
<tr>
<th></th>
<th>Offspring</th>
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<tbody>
<tr>
<td>X-rays d 7</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>d 14</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>$^{239}\text{Pu}$ d 6</td>
<td>0.01</td>
<td>0.6 - 0.8</td>
</tr>
<tr>
<td>d 13</td>
<td>0.005</td>
<td>0.4 - 0.7</td>
</tr>
<tr>
<td>HTO chronic</td>
<td>0.7</td>
<td>0.7</td>
</tr>
</tbody>
</table>
In utero haemopoietic radiosensitivity

Relative biological effectiveness (RBE) of $^{239}$Pu $\alpha$ and $^3$H $\beta$ cf. X-rays

$^{239}$Pu $\alpha$ in mothers: 1 on average bone dose
2 - 3 on average marrow dose

$^{239}$Pu $\alpha$ in offspring: 50 - 100

$^3$H $\beta$ in mothers and offspring: 1 - 2
**In utero** haemopoietic radiosensitivity

- High RBE for $^{239}$Pu $\alpha$ induced stable chromosomal aberrations in CBA/H mice
- Not reflected in leukaemia induction in CBA mice: no AMLs in offspring after administration of $^{239}$Pu during pregnancy
  - d 4 or d 13 (*Humphreys*)
  - chronic (*Mountford-Lister*)
Alpha emitters in human fetal tissues

2nd trimester: v. low levels $^{239}\text{Pu}$
5 - 60 mBq kg$^{-1}$ $^{210}\text{Po}$

Fetal vertebrae 18 - 38 weeks:
- up to 180 mBq kg$^{-1}$ $^{210}\text{Po}$ Purnell et al. 1999
5 - 20 $\mu$Bq kg$^{-1}$ $^{239}\text{Pu}$ NRPB unpublished
Alpha emitters in human fetal tissues

Haemopoietic tissue doses:

30 $\mu$Sv natural alpha

$<< 1 \mu$Sv $^{239}$Pu
Alpha emitters in human fetal tissues

Haemopoietic tissue doses:

- $30 \mu$Sv natural alpha
- $<< 1 \mu$Sv $^{239}$Pu
- $500 - 600 \mu$Sv $^{40}$K, cosmic rays, external gamma
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Welcome to the International Scientific Conference for Childhood Leukaemia incidence causal mechanisms prevention