Effects of radiation exposure on offspring and next generations

Effects consequent to intrauterine exposure to ionising radiation

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Richard WAKEFORD ICRP Committee 1

Intrauterine Exposure

• Considers exposure

- From the point of conception
- To the time of birth
- So, for humans, about 40 weeks

• Encompasses effects

- On the conceptus, embryo and through to
- The late fetus



Effects of Exposure in utero

• For antenatal exposure

- The risks of <u>cancer</u> and <u>hereditary effects</u> must be considered, as for postnatal exposure
- But the magnitude of these risks may well vary with gestational age

• But also

- <u>Teratogenic</u> (developmental) effects must be considered, such as congenital malformations
- The risk of teratogenic effects will vary with gestational age



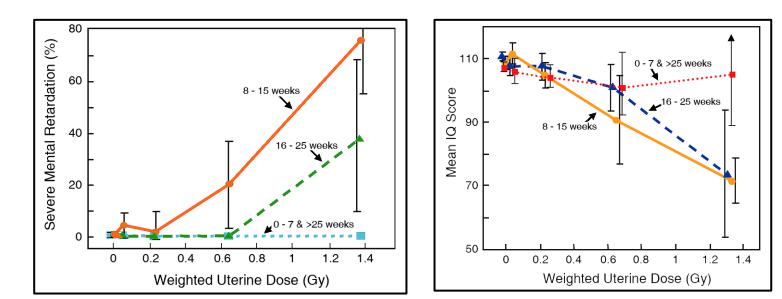
Teratogenic Effects

• Effects of exposure *in utero* include

- Lethality (spontaneous abortion, miscarriage, stillbirth), congenital malformations and growth retardation
- Level of effect varies with gestational age
- Mental retardation (Japanese atomic bomb survivors epidemiology)

Variation of <u>severe mental retardation</u> and <u>IQ score</u> with respect to uterine dose received during the bombings and weeks since conception at the time of exposure

ICRP Publication 90, 2003 NCRP Report No. 174, 2013





Cancer and Hereditary Disease

• Stochastic health effects

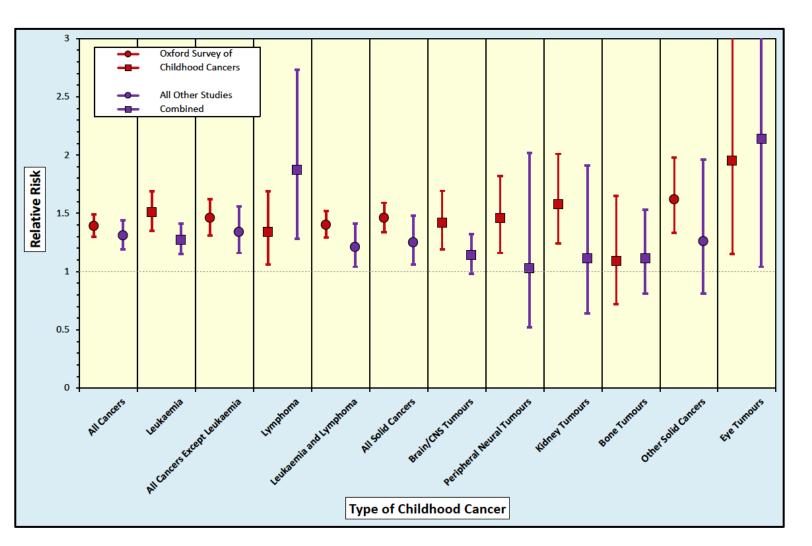
- Radiation exposure *in utero* is assumed to increase the risks of <u>cancer</u> and <u>hereditary disease</u>
- Degree of risk is likely to vary with gestational age
- Cancer risk
 - Human epidemiological findings available
 - Case-control studies of childhood cancer and antenatal X-rays
 - Cohort study of Japanese atomic bomb survivors exposed *in utero*
 - Oxford Survey of Childhood Cancers (OSCC) gives, for all childhood cancers combined (Doll & Wakeford, *Br J Radio*/1997; 70: 130-9)
 - ERR = 0.5 (95% CI: 0.3, 0.8) at 10 mGy (X-rays)
 - Little variation of ERR between the typical childhood cancer types



Childhood Cancer

Comparison of relative risks (RR = ERR + 1) of antenatal exposure to X-rays: Oxford Survey of Childhood Cancers and all other case-control studies appropriately combined in a meta-analysis

Wakeford & Bithell, Int J Radiat Biol 2021; **97**: 571-92





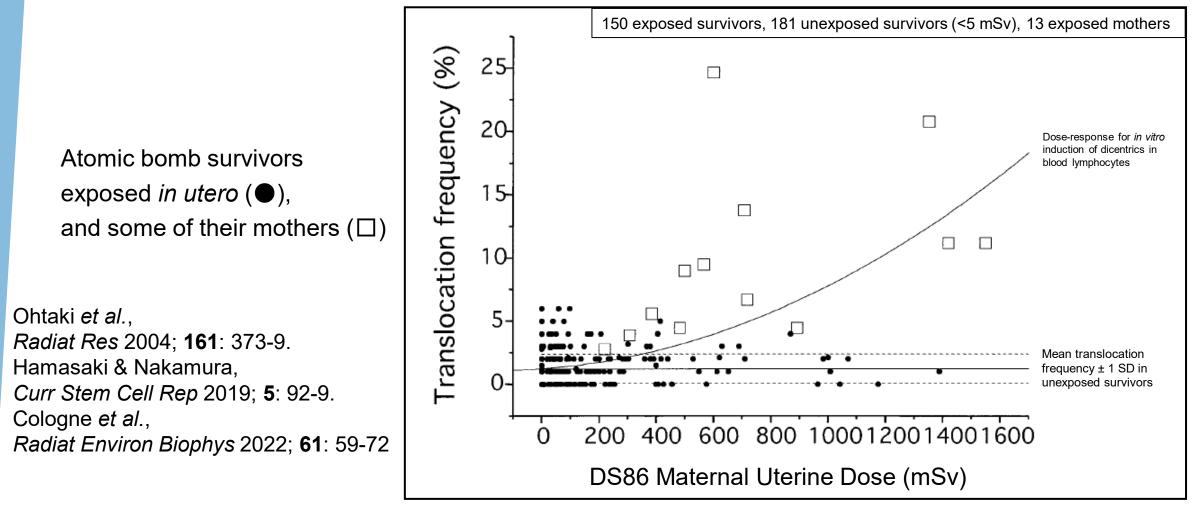
Bomb Survivors Exposed in utero

• Cohort study of survivors irradiated *in utero* (average dose, 0.25 Gy)

- <u>Solid cancer mortality</u> to end-2012 (66-67 years of age)
 - <u>Females</u>: ERR/Gy = 2.10 (95% CI: 0.26, 5.61) (21 deaths)
 - <u>Males</u>: ERR/Gy = -0.08 (95% CI: <-0.82, 1.36) (24 deaths)
- Sugiyama *et al., Eur J Epidemiol* 2021; **36**: 415-28
- Childhood cancers (Wakeford & Little, *Int J Radiat Biol* 2003; **79**: 293-309)
 - 2 cases of childhood cancer against 0.42 expected
 - O case of childhood leukaemia (but only 0.18 case expected)
 - Absence of childhood leukaemia surprising given the excess among those irradiated as young children



Chromosome Translocation Frequencies





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