

## What are the Reproductive and Developmental Risks of Ionizing Radiation?

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Many pregnant women are concerned about the potential reproductive and developmental risks of radiation exposures. With the advent of the Internet, consulting has become more rapid and efficient. In 2008, the pregnancy website of the Health Physics Society (HPS), ATE (Ask the Expert), received approximately 2,400,000 hits. Over 700,000 prepared answers to questions were downloaded. Over 1,600 contacts were still anxious after reading the Website answers and requested a personal consultation. From this experience we have learned that many physicians and other counselors are not prepared to counsel patients concerning reproductive and developmental radiation risks. Approximately 8% of the contacts have provided inaccurate information that could have resulted in an unnecessary interruption of a wanted pregnancy.

Evaluating developmental risks requires attention to two important elements in order to provide scientifically and medically appropriate counseling. First, quality epidemiological studies are the foundation for determining human risks. It is rare that *in vitro* studies or animal studies can refute either negative or positive findings in epidemiological studies if an adequate and well-performed number of epidemiological studies are available. However, there have been instances when animal studies have been more reliable predictors of developmental effects. Secondly, biological plausibility is a powerful tool in evaluating alleged human risks; however, it is dependant on being knowledgeable in all the basic sciences and teratology principles.

There are five areas of radiation embryology with which counselors should be knowledgeable, as well as being familiar with the basic principles of teratology, in order to provide scientifically and medically appropriate counseling.

1. Can the fetus be harmed by ionizing radiation if it is not directly exposed? In other words if diagnostic radiological studies are performed on the head, neck, chest or extremities, is the embryo in the uterus at risk for an increase in adverse effects on development? The effects of radiation have been studied in animal models; these data indicate that radiation exposures in the diagnostic dose range (less than 0.1 Gy, or 10 rad) do not increase the risk of adverse developmental effects because the exposure to the embryo is very small.

Diagnostic radiological studies that do not expose the embryo will not increase the risk for birth defects or miscarriage above the background risk of 3% for birth defects and 15% for miscarriage.

2. Is mental retardation produced as a consequence of radiation during pregnancy a threshold phenomenon? There is no doubt that exposure of the developing human fetus to high doses (1–2 Gy) of ionizing radiation can result in mental retardation and microcephaly. The most vulnerable stage for the induction of mental retardation and severe microcephaly is reported to be from the 8th to 15th week of human gestation. During mid-gestation the brain can be depleted of neurons and when the neurons are killed at this stage they are not replaced, resulting in the induction of mental retardation and microcephaly. There is little disagreement about the vulnerability of the brain during organogenesis and fetogenesis. Although most radiation embryologists assumed that the exposures to diagnostic radiological studies were too small to produce mental retardation, there were few data in the human to confirm or refute this assumption. In 1984, Otake and Schull reanalyzed the data pertaining to the children who were irradiated *in utero* in Hiroshima and Nagasaki (RERF, Radiation Effects Research Foundation). They concluded that the most vulnerable period for the induction of mental retardation was from the 8th–15th week of gestation and that 40% of the fetuses who received 1 Gy were mentally retarded (I.Q. <70). They also concluded that mental retardation could be produced with exposures below 0.1 Gy and that radiation-induced mental retardation was a stochastic effect (non-threshold effect). Clinical analysis, the application of the concept of biological plausibility and animal studies did not support the concept that radiation induce mental retardation was a stochastic effect. Reanalysis of the A-bomb data indicated that the threshold for radiation induced mental retardation was approximately 50 rad (0.5 Gy). There was no increased risk of mental retardation or decrease in I.Q. from exposures of 10 rad (0.1 Gy) or below.
3. Does fractionation and protraction of radiation decrease the magnitude of the reproductive and developmental risks? Animal studies were very helpful

in evaluating whether fractionation decreased the teratogenic and growth retarding effects of ionizing radiation. Fractionation and protraction of the radiation exposure reduced the developmental effects of the radiation. Developmental risks were reduced when diagnostic x-ray studies occurred over a period of days, occupational exposures occurred over a period of weeks to years and when flying at high altitudes occurred over a period of hours.

4. Is there a period during pregnancy when radiation will result in an increased mortality but not an increase in malformations? The "all or none" phenomenon was described in the 1950s. Irradiation of rats and mice with up to 1.5 to 2.0 Gy during the pre-implantation and pre-organogenesis stages resulted in embryo lethality; however, malformation rates in the surviving fetuses at term were similar to the controls; at this early stage of pregnancy, high exposures induced cell loss or chromosome abnormalities that most likely resulted in zygote death or malformations that were lethal.
5. How vulnerable is the fetus to the oncogenic (cancer inducing) effects of radiation? This is the most controversial and difficult area to evaluate, because the epidemiological studies are not consistent. In 1999 Boice and Miller published their interpretation of the data pertaining to the oncogenic risks of low-level intrauterine radiation. They noted, "Evidence for a causal association derives almost exclusively from case-control studies, whereas practically all cohort studies find no association, most notably the series of atomic bomb survivors exposed *in utero*. Learned debate continues as to the causal nature of low-level intrauterine radiation exposure and subsequent cancer risk. The association is not questioned, but the etiologic significance is. Different scientists interpreting the same data have different opinions as to the causal nature of the association and the possible level of risk." The most recent publication based on the 60 year follow-up of the *in utero* population exposed to the A-bomb in Japan indicates that the embryo is actually less sensitive to the oncogenic effects of radiation than the child, with a suggested threshold at 20 rad (0.2 Gy). The population of *in utero* survivors numbers approximately 1,500, which is a small population for oncogenic studies and this population is only in their 60s, so we have to wait another 20 years to finalize the risk of cancer among those who were exposed to the A-bomb as embryos. In the mean time, parents of patients who

were exposed *in utero* to diagnostic radiation can be told that the oncogenic risk of those amounts of *in utero* radiation is very low.

We utilize the scientific information obtained from studies in these five areas to counsel patients concerning radiation risks during pregnancy. The willingness and persistence of scientists to debate the controversial aspects of this research and apply the best available scientific information to assist patients in turmoil about the risks of embryonic radiation to themselves and their offspring have saved thousands of lives and changed family histories.

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### Suggested Reading

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