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Radiation and Pregnancy

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Radiation exposure during pregnancy often prompts many physicians and patients to contact the Illinois Teratogen Information Service. This RISK||NEWSLETTER is intended to provide a useful framework for evaluation of radiation exposure during pregnancy.

OF RAD AND REM

Ionizing radiation can be produced by electromagnetic waves consisting of uncharged photons such as x-rays and gamma rays. The terms x-ray and gamma rays refer to the origin of radiation; x-rays are generated by electrons whereas gamma-rays are emitted by nuclei involved in radioactive decay. Charged particles such as alpha and beta particles emitted by radionuclides can also produce ionization. All radiation is characterized by its energy, so no matter what the source, a radiation exposure can be expressed in the same units, either rad or rem.

The amount of radiation can be measured in two ways: ionizations produced in air by x-rays or gamma radiation from any source are measured in roentgens ®, and the radiation dose absorbed by the body tissue is measured in rad or Gray (Gy) (1 Gy = 100 rad, cGy = rad, mGy = 0.1 rad). Exposure of typical tissues to 1R yields approximately 1 rad of absorbed dose. Different types of ionizing radiation, however, can deposit the same total energy but produce different degrees of biological damage. The dose equivalent, expressed in Seivert (Sv) or rem (1 Sv = 100 rem, 1 mSv = 0.1 rem), reflects the differing biological effects of specific types of radiation. For those types of radiation typically used in hospitals, rem and rad are interchangeable. However, with alpha or neutron radiation (such as from plutonium or radium) the dose in rem would be a multiple of the rad. Radiation protection standards generally are expressed in rems; experimental studies often report radiation exposures only in R; dosimetry calculated for medical irradiation may be given in rad or rem (Jankowski 1986, Brent et al. 1993).

The following simplification of the relationship may be helpful: a dose of approximately 1 rem or an absorbed dose of approximately 1 rad is imparted to human tissue at a location where a survey instrument indicated an exposure of 1 roentgen.

NOT ALL “RADIATION” IS IONIZING

Radiation, the transmission of energy from one body or source to another, can be broadly classified into ionizing and non-ionizing radiation. Ionizing radiation is any form of radiation with sufficient energy to displace orbital electrons, resulting in the formation of electrically charged ions in matter. Examples of non-ionizing radiation are radar, microwaves, and magnetic resonance imaging.

The use of the term radiation to describe ultrasound is both confusing and erroneous. Ultrasound is a form of mechanical energy that produces oscillations in an elastic medium (water, tissue) at frequencies above the threshold for human hearing. Although there are still ongoing studies investigating the effects of ultrasound, this form of energy appears to be relatively safe (Brent 1989, 1993).

The biological effects of ionizing and non-ionizing radiation vary considerably. Exposure to non-ionizing radiation presents no measurable risk to the embryo or fetus (Brent et al. 1993). This RISK|| NEWSLETTER therefore will consider only the ionizing forms of radiation.

SOURCES OF INFORMATION ON RADIATION EFFECTS

Most information on the effects of acute exposure to ionizing radiation has come from epidemiological studies of children born to Japanese Atomic bomb survivors. One limitation of these studies is that they are examining the effects of a single, relatively high dose exposure and not of intermittent or continuous low dose exposures typically experienced in medical, occupational, or environmental situations (Boice 1990). In addition to animal studies, other sources of information have been patients treated with a radiotherapeutic procedure before or during pregnancy.

TIMING OF THE RADIATION EXPOSURE

As with any teratogen, the effects of prenatal exposure to radiation will differ depending upon the timing of the exposure. Preconceptional radiation effects on the germ cells, expressed by reduced fertility after radiation, has been well documented. The most critical target for ionizing radiation is DNA, so the possibility of radiation induced mutations in the parental germ cells exists. The most radiosensitive period is during rapid cell division in the testis. This occurs during spermatogenesis and may involve a period of up to six months prior to ejaculation. It has been suggested that the oocyte resting in suspended meiosis I is resistant to radiation induced mutations (Russell 1986). However, during the six or seven weeks prior to ovulation, when the first meiotic division starts, the oocyte becomes sensitive to damage by irradiation. But even during these periods of increased sensitivity, the magnitude of the genetic risk due to any kind of preconception radiation exposure appears to be insignificant (Brent et al. 1993, Russell 1986).

In order to assess the teratogenic risk of radiation exposure after conception, the stage of embryogenesis at the time of the exposure has to be considered. During the preimplantation period (approximately the first 14 days after conception), it is believed that radiation exposure will either be lethal or have no effect ("all or none") (Jankowski 1986). The period of organogenesis (from the end of the second week to the eighth week post-conception) is usually considered the most sensitive period for malformations. The central nervous system (CNS) is the most sensitive organ system as radiation induced malformations of other structures are uncommon (Mole 1991). The fetal period (from eight weeks until the end of gestation) is a time of decreasing sensitivity to most environmental agents; nevertheless, the CNS continues to develop throughout gestation, retaining sensitivity to radiation. Studies on Japanese A-bomb survivors who were exposed in utero have suggested the following critical periods for developing severe mental retardation (SMR) (Otake and Schull 1984). The probability for radiation related SMR is essentially zero with exposure before 8 weeks post-conception, is at a maximum with irradiation between 8 and 15 weeks, and decreases between 16 and 25 weeks. After 25 weeks gestation (and for exposures of less than 100 rad), no cases of SMR have been reported.

IS THERE A "SAFE" LEVEL OF RADIATION EXPOSURE?

There is general agreement that fetal exposure of less than 5 rads is not considered teratogenic (Bentur 1991, Brent et al. 1993). It cannot be stated that there are no risks associated with lower doses, however. It is important to stress that the risks are determined by the level of the fetal exposure, which is likely to be much less than the maternal exposure. On the other hand, it may be difficult to determine fetal dose accurately, especially for radioisotope exposure.

DIAGNOSTIC X-RAYS

One of the most frequent radiation exposures during pregnancy is a diagnostic x-ray from CT scan or fluoroscopy. To determine the fetal dose, factors such as patient size, equipment used, and technical considerations have to be taken into account. Russell (1986) stated that the gonad dose for similar examinations can vary between hospitals by two orders of magnitude. Nevertheless, there are few diagnostic studies, which result in a dose greater than 1 rem to the uterus. Certainly, diagnostic x-ray doses exceeding 5 rads to the fetus would be exceptional even when fluoroscopic diagnostic studies are involved.

The estimated fetal dose from a dental x-ray is 0.00001 rad and from a chest x-ray, 0.06 rad (Reprotox) or <0.01 rem (Jankowski 1986). Two diagnostic x-ray procedures, which may expose the fetus to higher levels, are a barium enema (0.8 rad; [Jankowski 1986, Reprotox 1993) and lumbosacral spine x-ray (0.64 rem [Jankowski 1986). A CT scan of the abdominal area may give an ovarian dose of 0.5 to 1.1 rems, depending on the circumference of the patient and technical factors.

RADIONUCLIDE EXPOSURE

Both the half-life of the isotope and the rate of biological elimination (if known) need to be considered. Risk assessment is frequently quite complicated, thereby requiring calculation by a radiologist or nuclear physicist. The nature of the isotope preparation may prevent its transfer across the placenta, so the dose will frequently be less than the maternal dose. In a majority of cases, the exposure will be too low to present a significant risk to the developing embryo or fetus (Brent et al. 1993).

RISKS OF IONIZING RADIATION

Radiation induced health effects are divided into two broad categories. Stochastic effects (phenomena involving chance or probability) refer to diseases such as cancer or genetic disease that can result from alterations produced in a point mutation. A risk for induction of stochastic effects is presumed to exist even at low exposures. Nonstochastic effects require multicellular injury and appear to have a threshold dose below which deleterious effects do not occur (Brent et al. 1993).

Individual risks are presented below:

CNS defects and Growth Retardation

Manifestations of in utero irradiation in humans are microcephaly, mental retardation and other CNS defects, and growth retardation (Mole 1991). Microcephaly is the most common malformation reported after exposure to a high dose of radiation during pregnancy. In one study, 25% of children exposed to more than 100 rads of radiation during gestation were microcephalic or hydrocephalic (Goldstein and Murphy 1929, 1930). Almost all microcephalic children irradiated in utero were mentally retarded and had short stature as well. The incidence of microcephaly rose with increasing exposure (Brent et al. 1993).

Mental Retardation (MR) and Seizures

A recent study of Japanese atomic bomb survivors exposed during gestation re-analyzed the absorbed dose to the mother’s uterus (Schull et al. 1990). As a consequence, four time periods were defined during gestation for which the developing brain has differing sensitivity to seizures and mental retardation following radiation. These periods, based on the number of weeks after conception, are: 0 to 7 weeks, 8 to 15 weeks, 16 to 25 weeks, and 26 or more weeks. There is no apparent increased risk of severe mental retardation associated with radiation exposure prior to the 8th week or after the 25th week of gestation.

The most sensitive period of the CNS is between 8 and 15 weeks of gestation whereas the period from 16 to 26 weeks showed reduced sensitivity. The frequency of severe mental retardation appears to be linearly related to the uterine dose and there is little evidence of a threshold below which no effect was seen. Analysis of IQ and school performance in the group exposed between 8 and 16 weeks also showed dose-related decreases, that is, an estimated loss of 0.2-0.3 IQ points per rad (Schull et al. 1990). Data for seizure activity showed the same time periods of sensitivity (Yamazaki and Schull 1990). Any dose of radiation between the 8 and 15 weeks of gestation could also increase the risk of microcephaly and mental retardation by 0.4% per rad and possibly decrease intellectual development and increase the subsequent development of seizures (Reprotox 1993). However, these effects were not detected at exposures of 5 rads or less.

Animal data support the contention that gross congenital anomalies will not be increased in a human pregnancy exposed to 20 rads or less. At an embryonic age of 18 to 28 days, exposure of 20 to 50 rads may be associated with an increased incidence of severe CNS malformations, mental retardation, and gross anatomic malformations. At this stage of development the incidence of severe CNS malformations occurs more commonly than mental retardation. The remainder of pregnancy requires exposure of 50 rads or more before any of these malformations or mental retardation are seen (Brent et al. 1993).

Congenital malformations

Studies have found no association of visceral, limb, or other malformations with in utero irradiation, unless the child exhibited growth retardation, microcephaly, or malformations of the eye (Brent et al. 1993).

Cancer

The association between in utero exposure to radiation and development of leukemia and other childhood cancers has been recognized for over 30 years. Whether or not the association is in fact causal remains unsolved (Mole 1991). There is evidence for a causal relationship (twin studies) and against a causal relationship (no excess cancer mortality in Japanese children irradiated in utero) (Mole 1991). A recent study did indicate that the incidence of adult cancers appeared to increase with increasing dose in the prenatally exposed Japanese atomic bomb survivors (Mole 1991).

Genetic Risk

Epidemiologic studies did not find an increase in genetic effects following radiation of parental germ cells (Brent 1993). The clinical risk of radiation induced mutations in parental germ cells is largely theoretical, since many induced mutations are likely lost before they appear in the offspring. It has become apparent that humans are less sensitive to genetic effects of radiation than previously thought (Boice 1990).

PUTTING RADIATION RISKS IN PERSPECTIVE

All unborn children are exposed to some radiation. Background radiation includes cosmic rays from outer space, terrestrial radiation from ground and building materials, and naturally occurring radioisotopes (ingested or inhaled). It has been estimated that background radiation contributes an exposure of approximately 0.075 to 0.1 rem during the period of gestation (Jankowski 1986). In addition, all pregnancies have spontaneous risks of malformations, abortion, or genetic disease. Estimates of the spontaneous risks are 15-20% for abortion, 2.7 to 3% for a major malformation, 4% for intrauterine growth retardation, and 8 to 10% for early or late-onset genetic disease. These risks are considerably greater than the risk attributed to an exposure of 1 rad during gestation. Brent)1989) calculates the risk of 1 rad to be approximately 0.003%! Thus, the present permissible fetal exposure levels of 0.5 rem in the workplace and 5 rem during medical procedures are considered appropriately conservative. The risks associated with these low-dose exposures are many thousands of times smaller than the spontaneous risks.

RECOMMENDATIONS

Unnecessary radiation exposure should always be avoided. If an exposure is unavoidable, three key concepts are:

1. Total exposure can be limited by minimizing the time of exposure;
2. The distance from the radiation source should be maximized; and
3. B>Shielding should be used whenever possible.

The patient should be counseled that the risk is extremely small for an exposure below 5 rads but that there is a significant possibility of damage for fetal exposure of more than 50 rads.

It may also be useful to emphasize that a single high-dose exposure appears to be more mutagenic than the same total exposure acquired in a series of low-dose exposures.