Effect of Radiation on the Gonads

In general, the gonads are very radiosensitive but the biological effect of radiation varies considerably with the stage of development of the respective cells.

Testes

In the male, sperm production is continuous from puberty to death. The division of a spermatogonium (stem cell) to the development of a mature sperm takes about 10 weeks in man, and involves several different cell populations that vary in their sensitivity to radiation.

Since the spermatogonia are relatively radiosensitive and the mature spermatozoa are relatively radioresistant, the effect of radiation on fertility is not apparent immediately. After exposure to a moderate dose of radiation, the individual remains fertile as long as mature sperm cells are available, but decreased fertility or even temporary sterility follows when these are used up.

Most of the results regarding testicular irradiation have been obtained from radiation therapy experience. In humans, a dose above about 0.15 Gy may cause temporary sterility. A single dose of about 6.0 Gy or a fractionated dose of 15 Gy over 10 days will often induce permanent sterility. However, the induction of sterility in human males does not produce significant changes in hormone balance, libido, or physical capability.

Ovaries

The effects of radiation on the ovaries are quite different from those on the testes.

All oocyte production (about seven million) occurs in the embryo where the ovum, surrounded by a single cell layer, is known as a primordial follicle and after the foetal stage they no longer divide.

However, most of them soon degenerate so that less than two million are present in the two ovaries at birth, and only 300,000 at puberty. Then, during all the reproductive years of the female, only about 450 of these follicles develop enough to expel their ova; the remainder degenerate.

Effect of Radiation on the Gonads (cont)

Therefore, in the adult there are no stem cells but there are three types of follicles: immature, nearly mature, and mature.

Once again, from radiation therapy experience, it has been found that a dose of about 0.5 Gy may cause temporary sterility in some individuals, but a single dose of about 4 Gy or a fractionated dose of 15 Gy over 10 days will cause permanent sterility.

In contrast to the effect in males, though, pronounced hormonal changes comparable to those associated with the natural menopause accompany radiation-induced sterilisation in females.

Radiation-Produced Mutations

It is a common misconception of the lay population that exposure to radiation can produce bizarre and even horrific mutants in future generations. In reality, however, radiation does not result in genetic effects that are new or unique but rather increases the frequencies of the same mutations that already occur spontaneously or naturally.

Since radiation-produced mutations are identical in nature to those that occur spontaneously, you can appreciate that their study is particularly difficult and experimental sample sizes must be large in order to confidently detect those attributed to radiation as distinct from those that would otherwise appear.

Animal Studies

Estimation of hereditary risk is based almost entirely on the results of animal investigations. In an enormous biological experiment involving up to seven million mice (known as the ‘Megamouse project’), the development of hereditary effects from radiation were observed and evaluated.

Radiation-induced genetic changes, like mutations from any other agent, may be a consequence of a gene mutation or chromosomal changes. **Mutation incidence has no threshold and is a linear function of dose**; if the dose is doubled, the number of mutations is doubled.

Radiation-Produced Mutations (cont)

This has led to the concept of the **doubling dose**, which is the dose of radiation required to double the spontaneous mutation rate, that is, the dose of radiation that would produce a number of mutations equal to the spontaneous or background level. Results from the mouse data support an approximate doubling dose of 1 Gy.

Human Studies

Although many epidemiological investigations have been undertaken in humans, they have failed to demonstrate radiation-induced genetic effects. However, mutations of human cells have been identified in culture.

The largest population studied carefully for genetic effects is the survivors of the A-bomb attacks on Hiroshima and Nagasaki. Several genetic indicators have been studied for many decades in children born to the survivors. These include:

1. stillbirths, major congenital defects, early death;
2. childhood mortality; and
3. sex chromosome abnormalities.

Parents of children studied came from both cities and from low (0.01 to 0.09 Gy) and high (more than 1 Gy) dose groups. Individuals from outside the cities were studied as controls. Though no genetic indicator has been found to be statistically significant, the average doubling dose has been estimated to be 1.56 Sv.

In spite of this, numerical values of hereditary risk are currently based on a doubling dose of 1 Gy (equivalent dose of 1 Sv) and the ICRP estimate for radiation-induced hereditary disorders is 0.6×10^{-2} per sievert (that is, 0.6 percent per sievert). By way of comparison, it is estimated that the natural spontaneous mutation rate in humans is approximately 10 percent.

Effect of Radiation on the Embryo and Foetus

Although the increased risk of cancer-induction is of concern, the possibility of developmental effects is equally important.

Experiments in Animals

It is clear that moderate doses of radiation can have an enormous effect on the developing embryo.

The principal factors are the dose, dose rate and the stage of gestation. Most data have been obtained from experimental animals, predominantly mouse, where we have:

1. reproduction in quantity;
2. relatively short gestation periods;
3. accurate radiation doses; and
4. specific times of conception.

The in utero development period can be accurately divided into three stages; namely preimplantation, organogenesis and the foetal stage.

Preimplantation: he time from fertilisation to when the embryo attaches to the wall of the uterus.

It is the most sensitive stage for lethal effects of radiation.

However, during the first few divisions the cells are undifferentiated and lack predetermination for a particular organ system. If radiation were to kill some cells at this stage, the remaining cells could survive and continue the embryonic reproduction normally; the only effect would be a delay in development.

Consequently, there is either a radiation-induced spontaneous abortion (if all cells are killed) or the embryo survives and grows normally in utero and afterwards (if at least one cell survives). This is referred to as an all-or-nothing effect.

Organogenesis: period during which the major organs are developed.

The principal effect of radiation is the production of a variety of congenital abnormalities of a structural nature.

The Foetal Stage: the growth of the structures already formed takes place.

Effect of Radiation on the Embryo and Foetus (cont)

Functional changes have been observed on the haematopoietic system, liver, kidney and gonads following irradiation. Much higher doses of radiation are required to produce death during this period than at other stages of development.

Experience in Humans

Once again, our knowledge mainly comes from studies of bomb survivors and from early medical exposures which were mainly therapeutic irradiations.

At any given time, there will be a certain percentage of the female population who are pregnant. From a statistical point of view, the stage of these pregnancies should be distributed roughly uniformly throughout the typical nine-month gestation period.

Consequently, there ought to be approximately as many females who are only one day pregnant, or who are 100 days pregnant, or who are just one day from giving birth, etcetera.

In the bomb survivors who were irradiated in utero, too few persons have been identified who were younger than four weeks gestational age at the time the bomb was dropped. Additionally, no birth defects were found as a result of irradiation before 15 days of gestational age.

These results are consistent with animal experiments which demonstrated the ‘all-or-nothing effect’, that is, either death of the embryo or normal development.

In humans, the principal effects of irradiation in utero are small head size (microcephaly) and mental retardation.

These results are ultimately used to extrapolate to very low doses to give recommendations regarding dose limits for radiation workers (female) and the role of radiation tests in pregnancy.

Exposure to Medical Radiation

In humans, the relationship between microcephaly and x-irradiation of the pelvis was recognised from early radiation therapy experience. Additionally, several other defects were also reported and although the number of cases studied is small and the radiation doses not known with any certainty.

Cancer in childhood after irradiation in utero

An association between exposure to diagnostic irradiation in utero and the subsequent development of childhood cancer or leukaemia has been suggested.

Several investigations have demonstrated a very slight increase in cancer incidence in children exposed to radiation.

Of 7649 children who developed leukaemia or cancer, 1141 had been irradiated in utero, whereas in an identical number of control children (no cancer) only 774 had been irradiated in utero.

Although this suggests an association between irradiation and childhood cancer, you can see that this study also provides conflicting results. For example, many children (6508 in fact) who did develop cancer had not been irradiated in utero and 774 who had been irradiated did not develop cancer. Consequently, these results and others have stirred lengthy debate about whether or not the relationship is one of cause and effect, or simply a correlation dependent on other health-related issues.

Although, this debate is still ongoing it is obvious that careful consideration must be given to evaluate the possible benefits versus the potential risks involved in any radiological procedure involving foetal irradiation.

Factors Influencing Effects and Risks

Dose

The amount of dose delivered is also important in determining the likelihood and severity of effects. At doses under 0.1 Gy there is unlikely to be any significant effect on organogenesis or foetal development as the threshold for these problems is not reached.

Factors Influencing Effects and Risks (cont)

hen doses climb above this level in the organogenesis period, it is recommended that women be councilled over the potential for congenital abnormalities induced by radiation.

Depending on your religious or ethical viewpoints, it is also recommended that therapeutic abortion of the pregnancy be discussed with women who are irradiated in the organogenesis period.

The likelihood of stochastic effects is related to the exposed dose in a linear fashion.

Limits of data on humans

There is no evidence in humans that radiation increases the rate of death during the implantation period. This data must be interpreted from animal studies.

There is no compelling evidence that exposure during organogenesis leads to significant abnormalities from human studies. Data is interpreted from animal studies.

Data on exposures after embryogenesis is limited to survivors of the atomic bombs; and is limited to evidence of microcephaly and mental retardation.

Gestational Age

The gestational age is the most important factor in determining what kind of effect will occur.

Before implantation has occurred, the most likely effects are loss of the embryo (dose dependent) or no effect. It seems that the cells at the preimplantation stage are capable of differentiating into any of the required cells for development to occur, and the loss of a significant number of these cells leads to demise of the embryo.

Organogenesis occurs between implantation and the commencement of the foetal stage. During this period the precursors of all major organs are formed. Damage to these prognenitor cells may lead to severe development abnormalities (such as failure of organ formation or structural defects).

Factors Influencing Effects and Risks (cont)

The foetal stage (from about 6 weeks after conception) is more resistant to serious abnormalities or prenatal death. Animal studies suggest a high rate of growth retardation. Human evidence suggests microcephaly, growth retardation and mental retardation are more common, particularly in the early foetal period.

Irradiation in all periods can increase the rate of childhood cancer, which is more dose dependent.

Pregnancy and the Radiation Worker

Once pregnancy has been declared, the conceptus should be protected by applying a supplementary equivalent-dose limit to the surface of the worker's abdomen of 2 mSv for the remainder of the pregnancy.

This will ensure that the foetus does not receive a dose in excess of the 1 mSv limit applicable to members of the general public.

Typically, the annual occupational radiation dose received by radiation therapy technologists is of the order of 200 µSv. Consequently, there is usually no reason from a radiation safety point of view that should restrict such a person from working until the full term of the pregnancy

However, it is appropriate that the pregnant worker be excluded from any employment activity that carries a significant probability of high accidental doses.

For example, radiation workers would routinely be excluded from high-dose brachytherapy applications, fluoroscopy and radiopharmaceuticals work.

In terms of radiation protection, a second badge dosimeter for the abdomen needs to be issued, and the two badges need to be checked on a monthly basis (instead of once every 3 months) throughout the term of pregnancy. Lead abdomen shielding is also available for a pregnant radiation worker.