RELATIVE BIOLOGICAL EFFECTIVENESS OF FAST NEUTRONS COMPARED WITH X-RAYS: PRENATAL MORTALITY IN THE MOUSE

W. Friedberg, G. D. Hanneman, D. N. Faulkner

Civil Aeromedical Institute, Federal Aviation Administration
Oklahoma City, Oklahoma

and

E. B. Darden, Jr.
Biology Division, Oak Ridge National Laboratory
Oak Ridge, Tennessee

This report of work in progress is concerned with effects of fission neutrons and of x-rays on the mouse zygote.

METHODS.

Seven-week-old virgin mice were allowed a 12-hour mating opportunity beginning at 7:00 P.M. Between 1:30 and 4:00 P.M., except where indicated otherwise, the females which had mated (vaginal plug) during the night were either irradiated or sham-irradiated. At the time of irradiation the zygotes were in a pronuclear stage. Sixteen days later the mice were killed and the uteri dissected. We recorded the number of dead embryos, live embryos, and gross anomalies. Dead embryos were classified as to stage of development.

The neutron source was the Oak Ridge National Laboratory Health Physics Research Reactor, an unshielded fast reactor of the Godiva type. Neutron energies were those of a slightly moderated fission spectrum with an average energy of 1.2 MeV. The neutron-to-gamma ratio was approximately 8. Neutron absorbed doses ranged from 0.5 to 20 rads. The neutron dose rate was 2 rads/minute except for a group given a fractionated exposure at 0.05 rad/minute.

X-rays were from a General Electric Maxitron 300 operated under the following conditions: 300 kVp; 20 mA; added filtration 0.5 mm Cu plus 1 mm Al; h.v.l. 1.20 mm Cu; dose rate 66 to 68 rads/minute. X-ray absorbed doses ranged from 10 to 100 rads.

RESULTS AND DISCUSSION.

The survival curve which relates neutron absorbed dose and prenatal survival has an extrapolation number (n) of 1.3, a D_0 of 16 rads and an LD_{50} of 14 rads. For x-rays, n is 1.1, D_0 is 76 rads and the LD_{50} is 60 rads. The relative biological effectiveness of the neutrons compared with x-rays ranged from approximately 4.2 at 5 rads (neutrons) to 4.9 at D_0.

A survival curve with little or no shoulder ($n \tilde{=} 1$), as indicated by both the neutron and x-ray data, implies that prenatal death resulted primarily from a single lethal-injury event. In contrast, the presence of a shoulder ($n > 1$) would have indicated that sublethal damage to the zygote must accumulate for prenatal death to result. If our survival curves could be extended, it is possible that all the data already obtained would prove to be on a shoulder. The present curves extend down to approximately 0.3 survival; to investigate lower levels of survival would require an excessively large number of animals. Therefore, we are taking a different approach to the question of whether radiation causes sublethal damage to the zygote.

It has been observed with mammalian cells that where cell death requires an accumulation of sublethal damage (shoulder-type curve, $n > 1$), there is usually a repair mechanism. Evidence of repair is reduced lethality when the dose rate is lowered or the exposure fractionated. In a comparison of acute irradiation with a fractionated exposure at low dose rate, zygotes (in utero) were given a total neutron dose of 12 rads. One group was irradiated at 2 rads/minute from 12:43 to 12:49 P.M. and another group was exposed at 0.05 rad/minute from 10:00 to 12:00 A.M. and again from 1:30 to 3:30 P.M. Prenatal survival in the two groups was not significantly different: 60% for the acute and 57% for the fractionated low dose rate. The results suggest that embryo death after irradiation of the zygote with neutrons was a consequence of a single irreparable lethal-injury event. This is consistent with our interpretation of the neutron survival curve. A similar experiment with x-rays is planned.

More than 92% of the deaths in the irradiated (x-ray and neutron) mice occurred before day 11 in the 19-day gestation period. We calculated this from the number of resorption moles and the total number of dead embryos. A resorption mole is the amorphous remains of an embryo that died within 6 days after it implanted in the wall of the uterus. In the mouse implantation occurs about 4.5 days after fertilization of the ovum.

The number of preimplantation deaths at a specific radiation dose was estimated from the difference in number of implantation sites per pregnancy between the irradiated group and sham-irradiated controls. With neutrons the proportion of prenatal deaths that occurred preimplantation was 16% at 5 rads and 50% at 20 rads. At equivalent-lethality x-ray doses the percentages were similar. Thus, as neutron or x-ray dose was increased both preimplantation and postimplantation deaths also increased but there was a relatively greater increase in preimplantation deaths.