EFFECTS OF IONISING RADIATION ON PREGNANCY

by

S. Mondal, M.B.B.S., D.G.O.

S. Bhattacharya, B.Sc.

and

D. Sen, B.Sc.

Introduction

Throughout the whole evolutionary history all living organisms have been exposed to small but variable amounts of ionising radiations from their natural surroundings. To this it has now been added similar radiation from the inventions of man, i.e. nuclear weapon, x-rays and radioactive isotopes used in industry and medicines. In their biological action these differ little from each other and all must be taken into account while assessing the hazards of ionising radiations.

Pregnancy is an important stage of life through which all the females are supposed to pass some part of their lives and at that particular time they are also liable to get radiated from their natural surroundings, from their occupation if it was connected with any sort of ionising radiation and also when their physicians use this radiation for any diagnostic or therapeutic purposes. In this paper, efforts have been made to find out the effects of ionising radiation on the pregnant mice when they were subjected to whole body radiation at different dose levels with the aim of application of the experimental results to the particular problem encountered when humans are irradiated.

Department of Experimental Carcinology, Chittaranjan National Cancer Research Centre, Calcutta-26.

Received for publication on 28-1-63.

Material and Methods

Two strains of mice were used in this experiment — one was an in-bred strain ($C_{57}Bl$) and another was a hybrid strain ($C_{58}A$). In all 160 animals from each strain were taken and they were grouped in 8 batches of 20 each. The animals were approximately of the same age (5 — 6 months) and their body weight varied from 16 to 20 gms. The food and environment were same for all the animals. They were taken between 10th to 12th days of their gestation period and were given a whole body radiation ranging from 100 r to 800 r. The radiation was given from a 250 KV, 5 MA selfrectified x-ray unit, filtered through 0.75 mm. cu. 1 mm. Al (HVL 1.5 mm. cu.) and the target skin distance was 50 cm. The mothers were then left on observation for 30 days while the babies were examined from their birth up to the end of the weaning period (30 days). In case of any death of the mother in pregnant condition their abdomens

were dissected and the number and the condition of the embryos were noted. The characteristics which were studied after the birth of the embryos included their number, weight at birth and at weaning, external morphology, abdominal viscera etc.

Results

The observed results can be seen in the following Tables:

TABLE I

Effects on Mothers

Dose of radiation	$C_{57}BL$ 20 mice taken in each group		$C_{58}A$ 20 mice taken in each group	
	Death in case of normal female	Death in case of pregnant female	Death in case of normal female	Death in case of pregnant female
100r	x	x	x	x
200r	2	2	2	2
300r	2	2	2	2
400r	4	4	4	4
500r	4	4	4	4
600r	8	8	8	8
700r	12	12	10	12
800r	16	14	14	15

TABLE II

Effects on Pregnancy

Dose of radiation	$C_{57}BL$ 20 mice taken in each group			$C_{58}A$ 20 mice taken in each group		
	Death in pregnant condition	Abortion & premature delivery	Full-time delivery	Death in pregnant condition	Abortion & premature delivery	Full-time delivery
100r	x	10	10	x	8	12
200r	2	8	10	2	8	10
300r	2	10	8	2	10	8
400r	4	14	2	3	16	1
500r	2	18	x	3	17	x
600r	3	17	x	4	16	x
700r	3	17	x	5	15	x
800r	6	14	x	6	14	x

TABLE III

Incidence of Average Babies per Mother and That of Live Birth and Still-birth

Dose of radiation	No. of animals taken of each strain	Total No. of babies born		Average No. of babies per mother		Live birth		Still-birth	
		$C_{57}BL$	$C_{58}A$	$C_{57}BL$	$C_{58}A$	$C_{57}BL$	$C_{58}A$	$C_{57}BL$	$C_{58}A$
100r	20	132	142	6.6	7	132	140	nil	nil
200r	20	132	126	6.6	6.3	120	108	12	18
300r	20	100	120	5	6	84	90	14	30
400r	20	30	110	4.5	5.5	58	72	32	38
500r	20	80	100	4	5	46	60	34	40
600r	20	80	90	4	4.5	46	50	34	40
700r	20	74	90	3.7	4.5	40	45	34	45
800r	20	70	80	3.5	4	28	30	42	50

TABLE IV

Incidence of Prematurity and Deformity

Dose of radiation	Total No. of babies born		Premature and deformed		Normal	
	$C_{57}BL$	$C_{58}A$	$C_{57}BL$	$C_{58}A$	$C_{57}BL$	$C_{58}A$
100r	132	140	36	37	96	103
200r	132	126	57	60	75	66
300r	100	120	74	82	26	18
400r	90	110	83	105	7	5
500r	80	100	all	all	nil	nil
600r	80	90	all	all	nil	nil
700r	74	90	all	all	nil	nil
800r	70	80	all	all	nil	nil

TABLE V

Average Birth Weight, Average Weaning Weight and Total No. of Babies Covering the Weaning Period

Dose of radiation	Total babies		Birth weight (gm)		Weaning weight (gm)		No. of babies covering the weaning	
	$C_{57}BL$	$C_{58}A$	$C_{57}BL$	$C_{58}A$	$C_{57}BL$	$C_{58}A$	$C_{57}BL$	$C_{58}A$
100r	132	140	1.25	1.25	7.3	7.5	92	98
200r	132	126	1.25	1.25	7.0	7.5	60	60
300r	100	120	1.0	1.25	6.3	7.0	24	17
400r	90	110	1.0	1.0	5.6	6.5	6	5
500r	80	100	1.0	0.75	x	x	x	x
600r	80	90	0.75	0.75	x	x	x	x
700r	74	90	0.75	0.75	x	x	x	x
800r	70	80	0.50	0.50	x	x	x	x

Discussion

The well-known hazards of radiation are:

Superficial injuries, general effects on the body, particularly the blood and blood-forming organs, e.g. production of anaemia and leukaemia, induction of malignant tumours, genetic effects, other deleterious effect, e.g. cataract, obesity, impaired fertility and reduction of life span.

Influence of age, body weight and sex on susceptibility of mice to the lethal effects of x-radiation has already been studied elsewhere (1).

In this experiment we concentrated our attention on the span of the life of the mother, the pregnancy itself and the fate of the embryos. Table I shows that the LD_{50} (30 days) for normal mice and pregnant mice lies between 600 r — 700 r in these particular two strains of mice under this particular experimental condition. Thus we found that in this experiment of ours the pregnancy itself did not enhance the deliterious effect of radiation on the span of life of the mothers. Table II shows that the deliterious effect of the radiation on the pregnancy is directly proportional to the dose of radiation and we have seen that above 400 r there was no full-time delivery.

The first observation on the effect of ionising radiation on animal embryos was reported in 1904 by Gilman and Baetjer in the United States and by Tur in France (2). Opinion varies on the question of how much of the damages to the conceptus were direct and how much were caused indirectly through the damages to the mother; but in the neonatal life of the babies, mothers' health played an important part

i.e. if they were very sick due to the radiation they would not care for their babies properly which would ultimately die though they were otherwise normal. Thus it can be presumed that mothers' health had some bearing on the neonatal and postnatal health of their babies. It was further noted that the effects of ionising radiation on the embryos depended largely on the period of gestation. A survey of the entire gestation period of the mouse (4) gives us three broad phases as follows:— (1) period of preimplantation 0 — 5 days, (2) period of major organogenesis 6-13 days, (3) period of foetus i.e. period of growth and minor organogenesis, 14 days to term (19-20) days. In our study we irradiated the animals approximately on 10th to 12th days of the pregnancy i.e. in the period of major organogenesis and radiation was apt to cause disturbances in the process of major organogenesis. From Table III we find that with the increase of radiation the number of still-births were gradually increasing and the average number of babies born per mother were gradually decreasing. These two facts can be explained in this way that the radiation disturbed or arrested the major organogenesis resulting in the death of the babies in the uterus. Those babies were either born dead or were absorbed in the uterus leading to the reduction of the number of the babies. The abnormalities found on the babies born dead or alive were many e.g. microcephaly, vaulted cranium, narrow head, micropthalmia, snout and nostril abnormalities, cranial blister, spina bifida. hydronephrosis, overgrowth or absence of limb, digital reduction and reduction in tail length. In some of the babies no abnormalities were found on external examination except they were very small in size (less than 0.5 gm.) and pale in appearance. They were born dead or died within few minutes after birth. These were termed as premature in the Table IV which showed that prematurity and deformity increased as the dose of radiation was increased and from the dose above 400 r all the babies of both the strains were deformed and premature and none survived the weaning period (Table V). The birth weight of the normal mouse embryos varied from 1.50 gm. to 2 gm. and weaning weight varied from 8 to 10 gms. but in our series not a single embryo had these weights. Their average birth weight and weaning weight were far less and this reduction in weight was directly proportional to the dose of radiation and this may also be explained in the same way as the radiation either causing the disturbance or arrest of major organogenesis leading to the disturbance in the metabolism of the embryos in the uterus and thus adversely affecting their growth in the prenatal and postnatal life.

LD_{50} for human being lies between 400 r—450 r (5) i.e. much lower than that of the mouse. So the effects observed in cases of pregnant mice are expected at much lower doses in cases of human being.

This experiment indicated also that the potential radiation hazards in the period of major organogenesis were very great. In human pregnancy at least, part of this period is so early that pregnancy may still be unsus-

pected. It is, therefore, recommended that pelvic irradiation of women in childbearing age should be restricted to the first two weeks following the menses, when there is little chance of an unsuspected pregnancy.

Summary

Two different strains of mice (C_{57} BL and $C_{58}A$) were given whole body radiation, starting from 100 r—800 r, at 10th to 12th days of their gestation period. It was found that radiation at this period: (1) did not enhance the deliterious effect of radiation on the span of life of the mothers (2) affected the pregnancy directly (3) caused deformity and prematurity in the embryos and acted adversely on the number, size and span of embryonic and post-embryonic life. These effects were directly proportional to the dose of radiation.

References

1. Abrams, H. L.: Proc. Soc. Exptl. Biol. Med. **76:** 729, 1951.
2. Ellinger, F.: Medical Radiation Biology, U.S.A., 1957, Charles C. Thomas, p. 433.
3. Russell, L. B. and Russell, W. L.: Hazards to the Embryo and Fetus from Ionizing Radiations: Proceedings of the International Conference on the Peaceful Uses of Atomic Energy, 8th—20th Aug. 1955.
4. Russell, L. B.: J. Exptl. Zool., **114:** 545, 1950.
5. Schubert, J. and Lapp, R. E.: Radiation—What It Is and How It Affects You, London, Melborne, Toronto, 1957, Heinemann, p. 44.