THE PASSAGE OF STRONTIUM-90 THROUGH THE PLACENTA

T. V. Vorozheikina and Yu. D. Parfenov

Scientific Director – Professor D. I. Zakutinskii

(Presented by Active Member AMN SSSR A. V. Lebedev)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny,
Vol. 54, No. 8, pp. 96-100, August, 1962
Original article submitted February 25, 1961

Numerous investigations have confirmed that there is a risk of injury to the offspring from exposure of the mother to external ionizing radiation [4, 6, 7]. Meanwhile, the question of radiation injury to the embryo as a result of the entry of radioactive substances into the maternal organism, principally the long-lasting osteotropic isotope Sr^{90}, is one of considerable interest. It has been shown that Sr^{90}, if deposited in the mother's body, has a definite effect on the sexual function, the fertility, and the course of pregnancy of the animals [2,4]. It has further been established that some of the Sr^{90} entering the mother's body is passed to the fetus through the placenta [5,7-12]. The Sr^{90} accumulating in the embryo acts as a direct source of internal irradiation. There is no doubt that the radiation hazard to which the embryo is exposed depends on the quantity of Sr^{90} passing from the mother through the placenta.

We therefore considered that it would be of interest to study the quantitative aspects of the transfer of Sr^{90} from mother to embryos, and at the same time to determine the dose of internal irradiation received by the embryos during the period of intrauterine development.

EXPERIMENTAL METHOD

As experimental animals we used albino rats weighing 180-220 g and 5-6 months old. Females chosen for their reproductive powers were given a single intraperitoneal injection of Sr^{90} in equilibrium with its daughter product Y^{90} in the form of a solution of the salt $Sr^{90}Cl_2$. The dose injected was 0.4 μCi/g body weight. The rats were kept on a standard calcium diet throughout the experiment. On the third day after administration of Sr^{90} the females were mated with males for 24 h. Females of another group were mated on the seventh day after injection of the isotope, and at monthly intervals thereafter. The onset of pregnancy was determined by the vaginal smear method.

To determine the Sr^{90} content of the developing embryos, the experimental females were sacrificed at various times during pregnancy (starting from the seventh day of pregnancy*). The embryos were extracted from the uterine cornua and samples were prepared for radiometric analysis. Meanwhile, the Sr^{90} concentration was determined in the maternal tissues (femur, blood, placenta, soft tissues) and also in the cadaver of the rat as a whole. The Sr^{90} content was determined in control females, receiving Sr^{90} but not copulating, at the same times as in the pregnant rats.

Females of a third group received Sr^{90} by mouth once every three days in a dose of 0.0006 μCi/g body weight for a period of just over 15 months. The rats were mated at different intervals after administration of the isotope began, and the Sr^{90} content of the embryos and the maternal tissues was determined.

In order to restore radioactive equilibrium between Sr^{90} and Y^{90}, the activity of samples from the embryos and maternal tissues was measured 14 days after they were prepared.

The mean data for each time interval were determined from the results obtained in three animals. The numerical results were treated statistically.

The total Sr^{90} content in the embryos was expressed as a percentage of the quantity of Sr^{90} retained in the mother's body. The concentration of radioactivity in the embryos and in the maternal tissues was expressed in CDA (coefficient of differential accumulation) units, i.e., in fractions of the dose of Sr^{90} injected per 1 g body weight of the rat.

* The content of Sr^{90} in the embryos was technically difficult to measure before the seventh day of pregnancy.

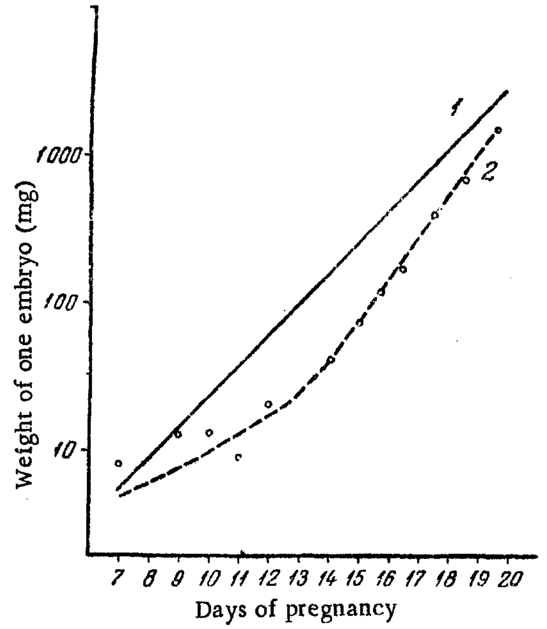

Fig. 1. Accumulation of strontium-90 in embryos after injection of a single dose of the isotope into the mother. The weight of the embryo is magnified. 1) Weight of embryo; 2) content of strontium-90.

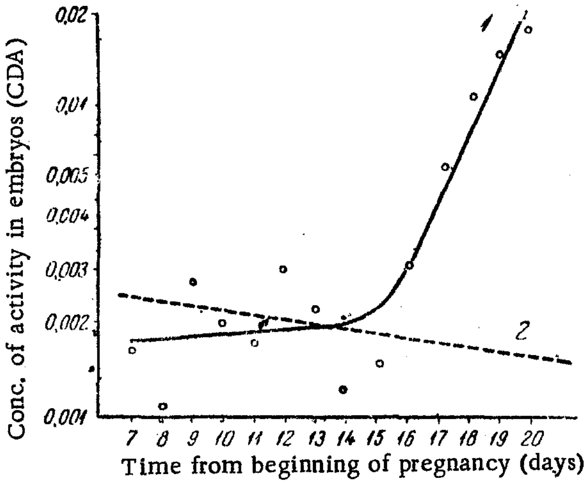

Fig. 2. Change in the mean concentration of radioactivity in the embryos (1) and the maternal soft tissues (2).

EXPERIMENTAL RESULTS

An idea of the changes taking place in the accumulation of Sr^{90} in the embryos in the period of intrauterine development after administration of the isotope to the mother in a dose of 0.4 μC/g can be obtained from Fig. 1. The total amount of Sr^{90} in all the embryos as a percentage of the activity retained by the mother is plotted along the ordinate on a logarithmic scale; the period of pregnancy is plotted along the abscissa on a linear scale. Each point plotted corresponds to the mean value for all the embryos of three rats.

It may be seen from Fig. 1 that with the development of the embryo the Sr^{90} content increased, to reach 0.2% of the amount retained by the mother on the last day of pregnancy. Hence, as the weight of the embryos increased, the quantity of accumulated activity rose. For purposes of comparison, in the same figure is shown the increase in weight of the embryos during pregnancy. The gain in weight is plotted on a logarithmic scale, and is represented by a straight line, i.e., it is dependent exponentially on the period of pregnancy. If we compare the gradient of the line reflecting the gain in weight with that of the curve of accumulation of Sr^{90} in the embryos, we may observe that in the initial period of pregnancy (approximately from the 7th to the 15th day) the accumulation of isotope lagged behind the gain in weight. Later, on the contrary, the accumulation of Sr^{90} was ahead of the increase in weight.

This feature of an intensified deposition of Sr^{90} regularly observed in the embryos toward the end of pregnancy was associated with the development of ossification [8, 11]. The beginning of organogenesis, and especially of the formation of the skeleton, undoubtedly played an important part in increasing the transfer of Sr^{90} through the placenta. Sr^{90} is a chemical analog of calcium and follows the same path in this physiological process. This was confirmed by the figures showing the change in the mean concentration of radioactivity in the embryos in the course of pregnancy (Fig. 2). Whereas, before the 15th day, the concentration of radioactivity in the embryo remained approximately constant and did not exceed the level of the Sr^{90} concentration in the maternal soft tissues, on the last day of pregnancy it was more than three times higher than this level, and in the newborn rat it was actually 5-10 times higher.

These results were in good agreement with those obtained from experiments on other species of animals [8,10,11]. Determination of the accumulation of Sr^{90} in the embryo revealed that the accumulated radioactivity was directly proportional to the weight of the embryo. On the basis of the figures showing the Sr^{90} content of the embryos on the 19th and 20th days of pregnancy, a linear equation of correlation between the weight of the embryo and the accumulated radioactivity was deduced: $y = 32 \cdot 10^{-5}(x - 1160)$.

The concentration of radioactivity found in the maternal organs during pregnancy in the experiment in which Sr^{90} was given during the three days before copulation, expressed in CDA units, was as follows: in the femur, 1.4 ± 0.2;

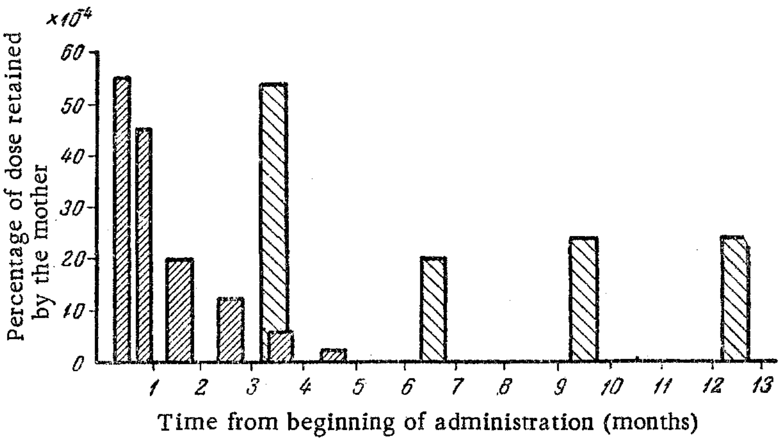

Fig. 3. Passage of Sr^{90} across the placenta on the 15th day of pregnancy, the latter commencing at different time intervals after a single (closely shaded columns) or after the first of a series of injections of isotope (widely shaded columns).

in the blood, 0.0019 ± 0.0005; in the muscles, 0.0020 ± 0.0004; in the placenta, 0.0014 ± 0.0003. The total Sr^{90} content of the mother was about 32 ± 8% of the amount administered. The effective half-elimination period of the isotope during this time was 200 days for the skeleton (femur) and 10-12 days for the soft tissues. When these results were compared with those obtained in the control females, the differences were not statistically significant.

We used our experimental results to calculate the mean potency of the absorbed dose of internal irradiation of the embryo in the period of intrauterine development as a result of the passage of Sr^{90} through the placenta. On the last day of pregnancy its value reached 0.4 rad/day. This figure was probably exceeded in the areas of ossification, where Sr^{90} was mainly deposited in the latter part of pregnancy. The tissue dose absorbed by the rat embryo during the whole period of intrauterine development, when the isotope was administered to the mother on the three days before copulation, was approximately 4 rad.

Data showing the placental transfer of Sr^{90} from mother to embryos at various time intervals after a single intraperitoneal injection of 0.4 μC/g of the isotope are given in Fig. 3. It is clear from this figure that the later pregnancy begins after administration of the isotope to the mother, the lower the percentage of Sr^{90} accumulating in the embryos in relation to that retained by the mother. This relationship, observed almost five months from the moment of administration, was exponential in form. This result differed to some extent from the findings of Holmberg and coworkers [6], who observed a decrease in the passage across the placenta in mice only when five months had elapsed after administration of the isotope.

The results of the accumulation of Sr^{90} in the embryos after repeated administration are also shown in Fig. 3. As a result of this continuous administration of Sr^{90} to the mother in small doses, the magnitude of the placental transfer when pregnancy began three months after administration of the isotope started was equal to that observed three days after a single injection. If pregnancy began after six months of administration of Sr^{90}, its accumulation in the embryos fell to the level of $(20\text{-}24) \cdot 10^{-4}$% of that retained by the mother at this time, and it stayed at this level even when pregnancy started 12 months after the start of administration of the isotope.

Hence, the transfer of Sr^{90} to the embryos after its continuous administration was almost independent of the time interval elapsing from the beginning of its administration. It remained at a relatively high level under these circumstances, and therefore it represented a greater hazard than in the case of a single injection.

As a result of the placental transfer of Sr^{90} to the embryo, a constant focus of internal irradiation was thus created. This focus persisted after birth of the young rat on account of the prolonged retention of Sr^{90}.

As regards the size of the tissue dose absorbed during the period of intrauterine development, attention should be drawn to the high radiosensitivity of the growing cells of the embryo. This has been studied in detail [3, 6, 7], but its limits have not yet been defined. According to P. G. Svetlov and G. F. Korsakova [4], external irradiation of pregnant rats with a dose of 30 r caused obvious and numerous disturbances of the normal development of the embryos.

The vulnerability of the embryos when irradiated on the 1st-11th day of development amounted to approximately 50%. These workers did not consider that this dose was the smallest that would cause injury. Russell [10] reported significant changes in the skeleton after irradiation of a fetus with roentgen rays in a dose of 25 r. Irradiation of the embryo in the period of organogenesis may lead to the formation of skeletal anomalies, possibly only appearing in later life. The accumulation of Sr^{90}, a continuous source of β-radiation, notwithstanding the smallness of the dose, may therefore lead to serious radiation injury, manifested primarily by its effect on the structure of the skeleton, development of the bones, and hemopoiesis.

When analyzing these results, we must not lose sight of the possibility of the genetic mutations which may arise in practice after irradiation with very small doses. Russell [9] reports that the possibility of such mutations is doubled in man by doses of 30-50 r. N. P. Dubinin [1] claims that they may appear after irradiation with a dose of only 3 r.

We cannot, therefore, disregard the amount of radioactive Sr^{90} passing from mother to fetus, despite the apparent smallness of its dose. The possibility of radiation injury to the developing embryo, and also of the appearance of late sequelae and genetic mutations must be taken into account when the risks of the entry of Sr^{90} into the human organism are being assessed.

SUMMARY

Strontium-90, entering the maternal body of rats, passes to the fetus through the placenta. This phenomenon intensifies with the development of ossification processes in the embryo and is in direct proportion to the embryo's weight. It decreases with the progress of time lapse following the isotope administration. Radiation doses received by the embryo during intrauterine development are sufficiently high to be fraught with the hazard of essential developmental disturbances.

LITERATURE CITED

1. N. P. Dubinin, Abstracts of Proceedings of a Scientific and Technical Conference on the Use of Radioactive and Stable Isotopes and Radiations in the National Economy and in Science [in Russian] (Moscow, 1957), p. 14.
2. A. P. Novikova and L. N. Burykina, In the book: The Late Sequelae of Injuries Caused by Ionizing Radiation [in Russian] (Moscow, 1959), p. 200.
3. A. A. Rubanovskaya and V. F. Ushakova, In the book: Data on the Toxicology of Radioactive Substances [in Russian] (Moscow, 1957), No. 1, p. 23.
4. P. G. Svetlov and G. F. Korsakova, In the book: The Effect of Ionizing Radiation on the Course of Pregnancy and the State of the Fetus and Newborn [in Russian] (Leningrad, 1960), p. 37.
5. J. N. Dent and E. L. Hung, J. Cell. Comp. Phys., 43, Suppl. 1, 77 (1954).
6. B. Holmberg, A. Nelson, and E. Wallgren, Radiat. Res., 12, 167 (1960).
7. B. Kidman, M. Tutt, and J. Vaughan, J. Path. Bact., 63, 253 (1951).
8. H. Kriegel, Strahlentherapie, 111, 273 (1960).
9. L. B. Russell, In the book: Radiobiology [Russian translation] (Moscow, 1960), p. 56.
10. W. Russell, In the book: Radiobiology [Russian translation] (Moscow, 1955), p. 436.
11. R. Wasserman, C. Comar, M. Nold et al., Fed. Proc., 16, 267 (1957).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. ***Some or all of this periodical literature may well be available in English translation.*** **A complete list of the cover-to-cover English translations appears at the back of this issue.**
