# X-Ray Irradiation of Pregnant Rats: Attempts to Produce Congenital Cardiac Anomalies in Offspring. (22870)

ÅKE LILJESTRAND AND JESSE E. EDWARDS. (Introduced by Earl H. Wood)

*Sections of Physiology and Pathologic Anatomy, Mayo Clinic and Mayo Foundation,* Rochester, Minn.*

X-ray irradiation of pregnant animals has long been known to induce various malformations in the offspring of the animals thus treated. Certain types of deformities have been shown to result from single doses of x-rays given at specific stages of pregnancy (1,2). No changes in the heart, however, have been reported to follow this treatment. The lack of information on this point may be due to one of several reasons, among which may be the high resistance of this organ or the occurrence of cardiac lesions which cause intra-uterine death. Still another possibility is that the changes may have been overlooked, because of technical difficulties, in examination of the offspring. Our work was performed primarily with a view toward overcoming the last possibility and secondarily, because of the need for an experimental method of producing changes resembling the congenital cardiac anomalies in man.

*Methods.* Pregnant rats were treated with one irradiation each. Pregnancy was considered to prevail when spermatozoa were found in the vagina in the daily examination of the rats. The newborn rats were allowed to live for at least 10 days. Necropsy was done under a dissection microscope, with a magnification of 7 times. After the front portion of the thorax had been removed, the heart and the left lung were pushed to the animal's right. The aorta was inspected from the diaphragm to the ligamentum arteriosum, which was then cut, as was the left superior vena cava. The latter is a normal structure in the rat. The heart was then opened in the following order: 1. The right atrium from the inferior vena cava to the right superior vena cava. 2. The tricuspid valve and the right ventricle along its lateral border to the apex. From the apex the anterior wall of the right ventricle was opened ventrally through the outflow tract and the incision was carried into the pulmonary trunk. 3. The left atrium along the lateral border. 4. The left ventricle from the mitral valve to the apex along the lateral edge, and farther from this edge ventrally through the aortic valve. The fact that the rats had been allowed to reach a development of 10 days allowed a good view of the thoracic aorta, the ligamentum arteriosum, the atrial septum (from the right atrium), the ventricular septum (from the right ventricle and, especially below the aortic valve, from the left) and of each valve. After the left atrium had been opened, the orifices of the 4 pulmonary veins could be identified.

*Results.* The number of treated animals and of newborn rats, as well as the doses used, are shown in Table I. It is evident that a large number were treated with doses too high to permit survival of the young. Results were obtained from 46 young rats which lived for 10 days and which had been born to mature females irradiated on the sixth to the sixteenth day of pregnancy. The findings in the heart and great vessels in the thorax were consistently normal. This of course does not mean that cardiac lesions in viable rats cannot be obtained in this way, but the expected percentage of these instances is low among rats surviving 10 days. Some of those dying earlier may have had malformations but were not examined. The above results pertain particularly to radiation on the sixth and thirteenth days when adequate numbers of animals were used.

*Summary.* Pregnant rats were treated with single doses of x-ray irradiation. The heart and great vessels in thorax of offspring were investigated when the rats had reached at least 10 days of age. The method of dis-

* The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of University of Minnesota.

TABLE I. Doses, Number of Female Rats Irradiated and Resulting Offspring.

| Doses in r/rat | No. | Day after insemination 2 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 18 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 400 | R.t.* | 1 | 1 | | 2 | 3 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | | | |
| | N† | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| 300 | R.t. | | | | | | 1 | 1 | 2 | 1 | 1 | 3 | 1 | 1 | 1 | 1 |
| | N | | | | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2(0) | 0 | 10(0) |
| 250 | R.t. | | | | | | 1 | 1 | 1 | | | | | | | |
| | N | | | | | | 0 | 0 | 0 | | | | | | | |
| 200 | R.t. | | | | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 1 | | | |
| | N | | | | 5(3) | 0 | 1(0) | 0 | 1(0) | 0 | 0 | 0 | 0 | | | |
| 125 | R.t. | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | | | |
| | N | 0 | 0 | 0 | 11(9) | 0 | 2(0) | 0 | 1(0) | 0 | 0 | 2(0) | 0 | | | |
| 75 | R.t. | | | | | | 2 | 1 | 2 | 2 | 2 | 1 | 3 | | 1 | |
| | N | | | | | | 8(3) | 8(2) | 6(5) | 3(1) | 2(1) | 14(12) | 7(4) | | 8(6) | |
| Total No. newborn | | 0 | 0 | 0 | 16(12) | 0 | 11(3) | 8(2) | 8(5) | 3(1) | 2(1) | 16(12) | 7(4) | 2(0) | 8(6) | 10(0) |

* R.t. = Rats treated. † N = Newborn; stillborn not included.
Figures within parentheses give No. of newborn living 10 days or more.

section is described. In 46 young rats that survived 10 days no cardiac abnormalities were found. Examination of young rats that died before 10 days was not carried out.

1. Russell, L. B., *J. Exp. Zoöl.*, 1950, v114, 545.
2. Wilson, J. G., *Anat. Rec.*, 1949, v103, 520.

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## Oxygen Tension of Subcutaneous Gas Pockets in Cobalt-Treated Mice and Adrenalectomized Mice.* (22871)

HUGH D. VAN LIEW (Introduced by W. O. Fenn)
*Department of Physiology, University of Rochester School of Medicine and Dentistry, Rochester, N. Y.*

Cobalt (II) chloride† and adrenalectomy (2) have both been shown by Gerschman *et al.* to give protection against the toxicity of oxygen at high pressures in mice. The experiments described below were undertaken to see if these two treatments furnish their protection by causing a generalized decrease of tissue $pO_2$, such as might result from a circulatory or respiratory response to the treatment.

Campbell(3) was the main proponent of utilization of subcutaneous or intraperitoneal gas pocket containing nitrogen as index of tissue tension, and the method has been applied in studies of oxygen at high pressures by Campbell(4,5,6,7), Sibree(8), Taylor(9,10), Lambertsen *et al.*(11) and Bahnson and Matthews(12).

*Methods.* Subcutaneous gas pockets were formed in 20 g female mice of Carworth Farms Webster strain, by injecting 4 to 8 cc of air or a gas mixture (7% $CO_2$, 7% $O_2$ in $N_2$) under the skin of the back. No anesthetic was used. It was assumed that after a day, the oxygen tension in the pocket had come to a steady state level which was within 2 mm of the mean tension in the surrounding tissues. To sample, approximately 2 cc of

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† Unpublished observations of Gerschman, R., and Gilbert, D. L.