but also of other elements. These two results have a common interpretation: the new nucleus produced during this transformation is not always formed right away in its ground state but is sometimes found in an excited state. In this case, the particle emitted during the reaction has correspondingly less energy, whereas the product nucleus changes into the ground state by emitting the stored energy in the form of gamma radiation. This change usually occurs within a time too small to be measured; therefore, it occurs practically at the same time as the emission of the new particle.

It is by no means trivial to prove the simultaneity of the two events, as one might think, because it may happen that the product nucleus is *always* produced in an excited state. This can be decided by coincidence measurements. In this case, even the particle group with the highest energy would have to be followed by gamma radiation. However, this is not the case if this group corresponds to the transition to the ground state of the product nucleus. (In case of "metastable" excited states, these considerations obviously have to be modified.) Such measurements were first performed in 1935 by H. J. von Baeyer, a Heidelberg student of mine, on the transformation of boron by alpha bombardment, which has already been mentioned. In the same manner, it is possible to decide whether two or more gamma quanta are produced in the same nucleus in one nuclear reaction, therefore produced at the same time, or whether they are alternatively emitted in the transformation of different nuclei. Such questions are of importance in energy balance considerations and, therefore, in the measurement of reaction energies and nuclear masses.

## Some Effects of Periodic X-radiation

Louis E. Moon, Harry F. Harlow, George P. Bogumill

Several studies have reported the effects of x-radiation on the physiology and behavior of animals, but generally they have employed a single, large dose of radiation. The present study (1) was undertaken to determine progressive behavioral and physiological changes occurring when animals are given repeated mild doses of x-radiation over a long period of time.

Twenty-three monkeys of the species *Macaca mulatta* were used in this investigation and were housed in pairs insofar as this was possible. Prior to radiation they were given extensive training on various tests that had been shown through previous experimentation to differentiate reliably between normal animals and those with various types of brain damage. Following this training, 12 of the 23 animals were randomly selected for radiation.

The weights of the experimental animals a week before radiation ranged from 5.19 to 9.44 pounds, with a mean of  $7.24 \pm 1.42$  pounds, and the control animals weighed from 5.00 to 10.17 pounds, with a mean of  $7.45 \pm 1.73$  pounds.

Radiation was accomplished by tying the animals in an adjustable, rotating plastic chair (Fig. 1) placed so that its axis of rotation, which was approximately the same as the long axis of the animal's body, was located 1 meter from the source of the x-rays. The whole body was irradiated, with the apex of the radiation cone located at the animal's midline slightly caudal to the heart. The x-ray machine used was a Westinghouse Quadrocondex, containing an XPT tube operating at 200-kilovolt peak and 10 milliamperes. The rays were filtered through 1 millimeter of aluminum and 0.5 millimeter of copper. The tube delivered from 6.0 to 6.2 roentgens per minute at a distance of 1 meter, and prior to each radiation the output was determined by means of a Victoreen roentgen-meter, and proper exposure times were calculated. The experimental animals were given 100 roentgens every 35 days until death.

Correlations in the directions of the different radiations emitted in a nuclear reaction and the angular distribution of the emitted radiation with respect to the direction of the bombarding radiation can also be determined and measured with coincidences. Experiments of this kind furnish valuable information concerning the structure of the atomic nucleus. Corresponding problems in the spontaneous transformations (natural and artificial radioactivity) can be attacked experimentally in the same way as was shown in the case of the decay of RaC (Bothe and Maier-Leibnitz in 1937).

The wide field of nuclear physics will offer in the future many possibilities for applications of the coincidence method. It can be stated without exaggeration that this method belongs to the necessary fundamental tools of the modern nuclear physicist.

The greatest number of roentgen units absorbed by any animal before death was 1900, in contrast with the results of Eldred and Trowbridge (2), who found that  $LD_{100}$  for rhesus monkeys weighing 5 to 7 pounds was 800 roentgens for a single dose. These results conform to the finding of other researchers (3) that divided doses are not as lethally effective as a single dose. Because of the small number of animals and the occurrence of illness in the early stages of the project, no estimate of  $LD_{50}$  is justified.

Radiation significantly affected animal weights. Eight experimental and eight control animals were paired on the basis of their mean weights for the 3-month period immediately preceding radiation. Between this period and the time of death of the experimental animal of each pair, the mean weight of the control subjects increased 9.6 percent, whereas that of experimental animals decreased by 4.7 percent. This difference is significant at the .01 level of confidence. A Pearson product-moment correlation of +.41 was obtained between mean weights of the experimentals for the 3 months prior to radiation and the cumulative number of roentgens administered before death. Although it is not statistically significant for the number of animals involved, the positive direction of this correlation suggests that weight before radiation may have some relationship to radiation resistance in monkeys.

The first two experimental animals succumbed after dosages of 300 and 500 roentgens, respectively, and were found at autopsy to have pulmonary tuberculosis. The examination was discontinued when the opened chest cavity revealed this condition. The third animal, which died after receiving a total of 900 roent-

The authors are members of the Departments of Psychology and Anatomy, University of Wisconsin, Madison.

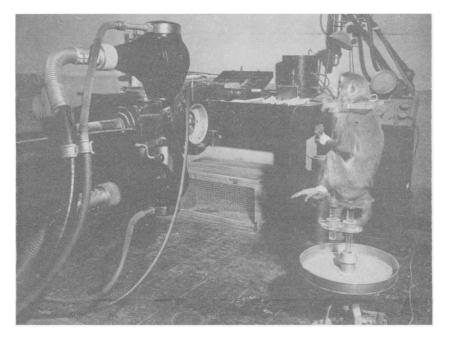


Fig. 1. One of the experimental monkeys in the chair in front of the x-ray apparatus. The chair is inserted into a motor-driven base that rotates the chair at 1 revolution per minute at constant speed.

gens over a period of 9 months, showed severe pathological heart changes consisting of widespread hemorrhages into all three layers of the cardiac wall, a partially healed infarction, and a recent mural thrombus attached to the medial cusp of the tricuspid valve. In addition the lungs showed pleural effusion, numerous petechial hemorrhages uniformly scattered over the lung surface, and filling of many of the alveolar air spaces with exudate. Gross examination of the cranial cavity revealed the presence of subarachnoid hemorrhages in the region of the cerebellar vermis, and there was subdural blood in the middle cranial fossae.

The autopsy findings on this third animal instigated a survey of the hematological condition of the remaining animals. Blood specimens from eight experimental and four control animals yielded decisive evidence of suppression of bone marrow function. The red cell count in each of the four animals that had received 900 roentgens was less than 2.5 million, an average of only 25 percent of that for the control animals. The four animals that had received 300 roentgens had a moderate anemia, their average count being 75 percent of that of the controls. The cases with severe anemia also showed extreme anisocytosis, poikilocytosis, hypochromia, nucleated red cells, and reticulocytes. Less severe changes in red cell morphology were seen in the moderate grades of anemia. White blood cell formation was also markedly depressed, to a point as low as 17 percent of the average count of the control group.

Every irradiated animal subjected to

autopsy showed severe pathological changes in at least one organ system, but in several cases two or more systems were severely involved. The organs most frequently damaged were the lungs, heart, kidneys, and large bowel. Marked congestion and interstitial hemorrhage occurred in the lung of one animal. Severe cardiac damage, with myocardial hemorrhage and infarction, was present in three monkeys. Tubular degeneration with glomerular and interstitial hemorrhage characterized the renal lesions that were present in four cases. Three monkeys exhibited damage to the large bowel, segments of which showed gross discoloration with thickening and induration.

Various tests of learning ability and measures of motivation were repeatedly administered to all monkeys throughout the course of the project. The ability of the animals to learn to discriminate between rewarded and unrewarded objects, to respond correctly after various intervals of delay up to 20 seconds to the one of two identical objects under which a reward had been concealed, and to learn other, more difficult tasks was measured.

Although no over-all significant differences were found between the performances of control and irradiated monkeys on any test, the irradiated animals were significantly superior to the controls on both oddity and delayed-response tests during the last 2 test-months. Irradiated monkeys showed no deterioration of their ability to solve even the most complex learning problems, and it was repeatedly observed that animals on the verge of death nevertheless maintained their high level of performance until they had be-

come so weak that response was no longer possible. The irradiated monkeys, however, did show significant decreases in general body activity and in appetite, with these decreases tending to become greater as the absorbed cumulative dose of roentgen units increased.

Locomotor activity was measured in a cage that was divided into quadrants by two intersecting photoelectric beams. Movement of the animal from one quadrant to another interrupted the beams, and the total number of such interruptions over five consecutive daily 20-minute test periods was recorded. No significant differences were found between irradiated and control monkeys on the first administration of the test, given after the experimental group had received an accumulative total of 300 roentgens. When the test was again administered to the control group and to the surviving irradiated monkeys that had absorbed a cumulative total of 900 roentgens, it was found that the locomotor activity level of the experimental monkeys was significantly lower than that of the controls.

Appetite was measured by presenting the animals with 45 raisins in food wells on a tray and counting the number of raisins secured by each animal within each of five consecutive 30-second trials per day on 4 successive days. This test was first given after the irradiated group had received a total of 300 roentgens, and again after a total of 900 roentgens. On both series experimental subjects satiated more rapidly than controls over the five daily trials, and their intake fell off progressively over the 4 days of the test, whereas control animals showed no substantial change in intake over the 4 days. These differences were significant beyond the .001 level of confidence.

The learning test results parallel those of Kaplan, Gentry, Melching, and Delit (4), who found that accuracy of performance and reaction times in a discrimination-retention problem were not significantly affected, even though the animals had received a dose of x-radiation that shortly proved to be lethal. They also found a rapid increase after irradiation in a failure to respond, which may be related to the activity and appetite decreases found in the present project.

## **References** and Notes

- 1. These researches were supported in part by a grant to the University of Wisconsin from the Atomic Energy Commission contract AT(11-1)-64 and in part by the Research Committee of the Graduate School from funds supplied by the Wisconsin Alumni Research Foundation. E. Eldred and W. V. Trowbridge, "Radiation sickness in the monkey," Radiology 62, 65
- 2. (1954).
- H. A. Blair. Recovery from Radiation Injury in Mice and Its Effect on LD<sub>50</sub> for Durations of Exposure up to Several Weeks, University of Rochester, Atomic Energy Proj. No. W-7401-eng-49, Rept., UR-312 (10 Feb. 1954).
- J. Kaplan et al., Some Effects of a Lethal Dose of X-radiation upon Retention in Mon-keys. USAF School of Aviation Medicine Proj. No. 21-3501-0003, Rept. No. 8 (August 1954).