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Inhalation Group

Project Record. Work is proceeding on reports dealing with production and measurement of radioactive aerosols, toxicity of inhaled radio-cerium, inhalation of tracer amounts of radioactive aerosols. The report on effects of large doses of plutonium administered by intubation is complete. 4.5 man-months.

Plutonium Analysis. Analysis of tissues from rats exposed to plutonium by intubation and inhalation is nearing completion. 1.5 man-month.

Fission Product Analysis. Measurements of tissues from animals exposed to radio-yttrium and radio-cerium have been completed. 1.0 man-month.

Radiochemistry Group

Project Record. The radium, sodium, and rare earths reports are almost through the first-draft stage. The reports on methods of preparing fission products for animals and on analytical methods were started this month. 4.5 man-months.

Radium. Studies on the distribution and excretion of radium have been terminated during the past month. .5 man-month.

Plutonium. Experiments on the toxicity of plutonium will be completed in the next month. Slow injection appears to yield a significantly different distribution in the body from fast injection. A comparison of data by slow and by fast intravenous injection into rats will be reported later. 1.0 man-month.

Cerium¹⁴⁴. The distribution, excretion and toxicity of radio-cerium are being investigated in rats. These experiments will be continued for another month. 1.5 man-month.

Carbon¹⁴. A preparation of 7.5 mg. of radioactive acetic acid was made from Ba CO₃ through the Grignard Reaction in 67% yield. The final product emits about 150,000 counts/min. per milligram of acetic acid. 1.0 man-month.

Instruments. Maintenance of counting equipment. 0.5 man-month.

Hematology Group

Terminal Counts on Chronic Animals. The prediction of the chronic group of an anticipated increased peak of deaths in the long-range strontium series was borne out by the 355 terminal counts which were taken this month. This compares with 208 counts last month. 2.0 man-months.

Plutonium. The rough draft of the terminal report on the acute and chronic effects of plutonium was completed this month. Monthly counts are taken on six of the plutonium experiments currently in progress. 2.8 man-months.

Radium. Routine blood sampling was carried out on all five remaining radium experiments. The analysis of all radium results and the logarithmic smoothing of these data are now in progress in order that the terminal report on this subject can be written during the coming month. 2.0 man-months.

Strontium. Routine monthly blood samples were obtained on the four remaining strontium experiments. 0.8 man-month.

Yttrium. The routine counts on the yttrium series of rats which initially received daily doses by stomach tube over a three month period was taken for the last time at 224 days; complete recovery now seems to have occurred. 0.4 man-month.

The rough draft of the terminal report on the effects of enterally administered yttrium on the hematological constituents of the peripheral blood of rats has now been completed, and is in the hands of the Editors. A summary of these results follows:

Effects of Ingested Radio-Yttrium on the Peripheral Blood

In Experiment FN, radioactive yttrium (Y^{91}) was administered by stomach tube to Sprague-Dawley rats in single acute doses of 5, 10 and 20 $\mu\text{c}/\text{g}$ and in Exp. ED daily gavage (oral administration) of doses of 60 and 200 μg per rat was continued for 178 days and of 60, 200 and 400 μc per rat for 90 days. Using a hypothetical rat weight of 200 grams, this gives a concentration figure of 0.3, 1.0 and 2.0 $\mu\text{c}/\text{g}$, but it should be remembered that the rats were gaining steadily in weight throughout this treatment and also that unlike a soluble, absorbed β -emitter yttrium was but slightly absorbed from the intestinal tract so that it was exerting its effects on the walls of the gut and not over the body as a whole.

The administration of a single dose of 10 $\mu\text{c}/\text{g}$ or less of Y^{91} by stomach tube produced no detectable effects on the hemoglobin, erythrocyte values of the peripheral blood. A dose of 10 $\mu\text{c}/\text{g}$ produced a temporary lymphopenia and an erratic heterophilia. A single dose of 20 $\mu\text{c}/\text{g}$ produced an initial marked elevation in erythrocyte and hemoglobin values lasting 5 days, followed by severe anemia which reached its maximum at 20 days and recovered by 50 days. The same dose produced a lymphopenia which lasted 25 days. An erratic heterophilia occurred concomitantly with these changes. The local gastric changes with ulceration and hemorrhage were sufficient to account for the findings described.

The daily gavage of yttrium⁹¹ in amounts from 60 to 400 $\mu\text{c}/\text{rat}$ produced no anemia during the periods of administration (90 to 178 days) nor during 100 days after yttrium gavage was discontinued in the 90 days treatment group. In the experiment in which daily gavage of 60 $\mu\text{c}/\text{rat}$ and 200 $\mu\text{c}/\text{rat}$ was continued through 178 days a moderate lymphopenia was produced that reached its maximum at 60 days but which gradually recovered to normal values by 112 days. The group receiving 200 $\mu\text{c}/\text{rat}$ developed a moderate lymphopenia thereafter which persisted throughout the remaining period of observation.

In the second part of Exp. ED in which daily ingestion of 60, 200 and 400 $\mu\text{c}/\text{rat}$ was continued through 90 days, a lymphopenia developed in all three groups which reached its maximum at 90 days. Discontinuation of yttrium⁹¹ gavage at 90 days in these animals resulted in a prompt return of the lymphocyte values to normal limits where they were sustained during the remaining period of observation.

(to 224 days). It is suggested that the lymphopenia described above results from the local effect of β -radiation on the lymphatic tissue of the gastrointestinal tract.

No change of significance in the morphology of the nucleated cells of the peripheral blood occurred after the acute single dose of chronic yttrium ingestion. Particular attention to the erythrocytes in terms of cell size and hemoglobin content revealed no alteration when compared to the controls.

Histology Group

Section of Chronic Histology Mice. Mice from Clinton, N.C.I. and Chicago were serially sacrificed for chronic histogenesis studies of Pu, Sr, and slow n and External β . 4.5 man-months.

Autopsy and Embedding Animals. Moribund rats salvaged from experiments of other groups, on injected Pu and Ra, inhaled Y and Ce. 1.5 man-months.

Sr⁸⁹. A few young rats especially injected for changes in the bones, and followed by occasional roentgenograms, are being sectioned and studied. 0.5 man-month.

Project Record. Rough drafts of all the survey chapters have been completed, several are nearly ready for the editors. 7.0 man-months.

Distribution of Strontium⁸⁹, Yttrium⁹¹ and Plutonium²³⁹ in Laying and Non-laying Pigeons.

Three pigeons were injected intravenously with 0.15 $\mu\text{c/g}$ of strontium⁸⁹ or yttrium⁹¹, or 0.025 $\mu\text{c/g}$ of plutonium, during early calcification of an egg. Thirty minutes after injection, radioactivity was expressed as counts per mg. of calcium.

Strontium⁸⁹ deposition was heaviest in the shell gland and calcifying shell, slightly less in the femoral medullary bone, and about 10 times less in femoral cortex and humerus. Most of the yttrium⁹¹ was in femoral medullary bone, with about 1/8 as much in shell, femoral cortex and humerus. Plutonium deposition, negligible in the shell, in the shell gland exceeded five times that in femoral medullary bone and fifty times that in the femoral cortex and humerus. The percentage of injected dose in samples of shell containing 90 mg. of calcium was for strontium⁸⁹, 2.0%; yttrium⁹¹, 0.02%; and plutonium, 0.0005%.

The percentage of injected dose contained in long bones of male pigeons 30 minutes after receiving 0.01 to 10.0 $\mu\text{c/g}$ of strontium⁸⁹ did not vary with the dose; the percentage retained in these bones at three days was the same as at 30 minutes. From three days to four weeks activity was lost from long bones of males and non-laying females at roughly double the radioactive decay rate. The femur almost invariably showed more strontium⁸⁹ or yttrium⁹¹ activity than did the corresponding humerus.

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Physiology Group

Acute Toxicity of Sr⁸⁹ in Dogs and Goats. No new experiments were started last month, but excretion measurements were completed on previously treated animals. 1.0 man-month.

Chronic Toxicity of Sr⁸⁹ and Pu²³⁹ in Dogs. There were no new developments last month among the dogs which are being maintained for "chronic" effects. 2.0 man-months.

Effects of Single Doses of X-radiation. The terminal report on "The Clinical Physiology of Single Doses of Total-Body X-irradiation in Dogs" is nearly complete. This report includes all of the constants which have been collected by this group on non-irradiated dogs as well as the data on x-rayed ones. Several new dogs are being controlled in preparation for experiments to fill in points where existing data are incomplete. 3.0 man-months.

Tissue Breakdown after Irradiation

An analysis of weight loss and nitrogen excretion in dogs subjected to single lethal doses of total body X-irradiation indicates excess tissue destruction during the terminal period. Weight loss, nitrogen out-put and water balance closely reflected food and water intake during the first 10 days after irradiation. When irradiation was superposed on a background of starvation no immediate increase in nitrogen excretion occurred. However, in the period when food intake diminished to very low values and the dogs developed a fever, excess tissue breakdown occurred. An irradiated dog, for example, lost 16.3% of its weight in the last six days of life while a non-irradiated dog which was fed 75% of what the irradiated one ate lost only 4.2% of weight. Two dogs which were totally starved for 10 days lost an average of 1.9% of their weight per day whereas four dogs which ate very little during their terminal period lost an average of 2.8% in weight per day. The nitrogen excretion in irradiated dogs was maintained during the terminal period at about twice that of starved non-irradiated dogs. Correction for differences in body temperature failed to increase the weight loss or nitrogen excretion of normal dogs to levels found in irradiated dogs.

Chronic Radiobiology Group

Chronic Effects of Sr⁸⁹. Observations are being continued. Virtually all of the mice first treated 21 months ago (including their controls) are now dead. The major cause of death in the longest survivors, in both strains of mice used, appears to be lymphomatosis. This is apparently a strain characteristic and no relation of this to treatment can at present be established. Ninety-nine tumors arising in or near bone have now been observed in rats and mice treated with Sr⁸⁹; the great majority of these are osteogenic sarcomas. 4.0 man-months.

Chronic Effects of Plutonium. No qualitatively new findings have been made. Subcutaneous tumors at sites of injection, bone tumors, and the liver changes characteristic of plutonium are continually occurring in treated mice. There appear to be relatively more tumors of the spine and pelvis and relatively fewer of the long bones in plutonium - treated mice than in those receiving Sr⁸⁹. 4.5 man-months.

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Biochemical Studies. Work on the carbohydrate tolerance of rats receiving various doses of x-rays is nearly complete. It appears likely that the major factor in the "tolerance" changes is delay in absorption of glucose, and that this may largely be conditioned by delay in gastric emptying time. The increase in apparent "plasma volume" by the dye method, as observed on dogs, has been confirmed on rats; it is not yet certain whether this represents an increase in volume of plasma circulating through the cardiovascular system or is due to other factors, such as alterations in the permeability of capillaries to albumin. Further efforts have been made to determine whether reproducible changes in the "polypeptide" fraction of plasma of rats occur after radiation. Various data accumulated in the section make it appear that some rather marked variations occur in the nitrogen pattern of plasma in addition to the alterations in globulin reported by Dr. Barron's group, but present methods have not permitted identification of the substance or substances responsible for the changes. 2.5 man-months.

Metabolism of Sr⁸⁹. An investigation of the relation between age and retention of Sr⁸⁹ is nearly complete. 0.5 man-month.

Effects of Age upon Retention of Sr⁸⁹

Radio-strontium was administered to very young mice by (1) subcutaneous injection of known amounts of active material into 5, 15, and 25 day-old mice, (2) placental administration by intraperitoneal injection of pregnant females, and (3) ingestion by new-born mice nursed by injected foster-mothers.

Twenty-five days after treatment (25 days of age in the case of placental administration and 25 days after weaning in the case of ingestion) the retention of radio-strontium as compared to adult retention at 25 days was as follows:

Placental administration	230% (based on 0-day dose)
Injection at 5 days of age	205%
Injection at 15 days of age	180%
Injection at 25 days of age	170%

Statistics and Biometrics Group

Project Record. Time was allocated on reports as follows:

Mouse chronic survival.	1.25 man-month
Chronic effects on mice at N.C.I.	.5 man-month
Rat organ weights	.25 man-month
Rabbit X-ray survival	.25 man-month
Rabbit X/n ratio for blood effects	.50 man-month
The last three reports were completed during the last month	
<u>Statistics of Chronic Hematological Effects.</u>	<u>1.25 man-month</u>



Tissue Dosimetry. Details of an experimental method for the determination of the surface dosage of plutonium metal have been completed. The largest foil of plutonium available here is approximately 3 mm x 3 mm x .005 mm and is somewhat irregular. An accurate area determination of the foil is being made. A special electrode will hold the foil in the extrapolation chamber. Other determinations will be made with accurate apertures which are made from .001" aluminum foil.

The mechanical stage for the densitometer was completed by the shop.

Drawings for the two way plastic film stretcher are complete and are now in the shop.

Ryerson shop finished the upper electrode assembly for the precision extrapolation chamber.

A rather uniform distribution of plutonium dispersed in ethyl methacrylate was obtained by means of quick polymerization into a long rod. An attempt to make a thin plaque from pieces of the above rod failed. Considerable experience has been gained in the polymerization of styrene monomer.

Several preparations of tissue have been placed in contact with fine-particle film in order to determine the suitability of the film for radio-autography. 2.0 man-months.

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