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PROJECT COUNCIL

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INFORMATION MEETING (HEALTH)

J. J. Nickson

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January 16, 1945

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PROJECT COUNCIL MEETING

January 16, 1945

Present: A. H. Compton, R. S. Stone, R. L. Doan, H. J. Curtis, Prosser, J. L. Stearns, Watson, L. O. Jacobson, J. G. Hamilton. E. Miller, [illegible] Winn E. Fermi, A. J. Dempster, J. Simpson, E. H. Lakefield, J. J. Nickson, F. Foote, A. B. Groninger, L. Ohlinger, Simmons, Franck, H. Jesse, Szilard, M. Leverett, Cooper, Keller, Jones, J. T. Cantril

A. H. Compton turns meeting over to R. S. Stone.

R. S. Stone calls on J. G. Hamilton:

Soil Hanford results are presented. Results of data show that Hanford soil absorbs fission products very well if the soil is not completely wetted. If the volume of the fluid is many times the volume of the soil approximately 2% of the activities will pass through the soil. A determination of these elements is underway.

Data on exposure of animals to product smoke is presented. In 64 days, about one-half of the amount present in the lungs is eliminated. This is for the oxide smokes. The half-life of product chloride and product nitrate smokes is somewhat less. The discrepancy at present is not readily explainable.

Distribution of product in rats at 256 days -

	+3	+4	+6
Skeleton	45%	49%	44%
Elimination rate/day	0.11%	0.9%	0.9%

The elimination rate is expressed as fraction of the total amount present in the body.

In response to an inquiry by Dr. Cantril, it can be stated that in rats no effect of diet and age has been noted on product absorption.

Studies were recently completed on the intravenous administration of product. These were undertaken because of the lack of information about liver absorption by this means. It is desirable, if possible, to use intravenous routes for long-term experiments.

The following product compounds were used.

	Bicarbonate	Oxalate	Citrate	Tartrate	Serum
Liver	15.6 %	14 %	18.4 %	20 %	13 %
Skeleton	63 %	71 %	60 %	50 %	58 %

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It would appear that any one of these vehicles is a better carrier for product than is the +6 nitrate.

Dr. J. J. Nickson:

The usual plan of discussing briefly some of the activities of the section in general will be abandoned for this meeting. It has been decided that instead a rather detailed presentation of one phase of the Section's activity will be presented.

During the past month, a dog was injected intravenously with + 6 product nitrate. Approximately 2800 micrograms were given. The dog weighed 7.4 kilograms. This is a dose of 0.38 micrograms/gram of body weight. The dog was followed by members of all three Sections of the Health Division. The Medical Hazards Section was charged with excretion studies and determination of the amounts of product in the various tissues following the death of the animal. The animal lived 16 days. During the last four days the animal was acutely ill. On the 16th day, for reasons which will be discussed below, the animal was sacrificed.

For a detailed description of the results discussed below, the CH Report for the month ending January 15 should be consulted.

The excretion studies in the urine showed a total of 6.58 % of the amount injected excreted in the urine, 6.22 % was excreted in the first 6 hours following the injection of the material. The excretion curve dropped off very rapidly to a daily excretion rate of approximately .05 %/day during the 8th to the 16th day. The excretion rate/day tended to be a constant value, while the excretion amount/cc tended to fluctuate somewhat.

The stool excretion totaled 3.5% for the 16 days. Excretion on the first day was low and on succeeding days it increased until a specific activity per gram of stool approximated that of the urine. The volume of the stools varied somewhat from day to day. During the last few days the specific activity of the stool was somewhat higher than the specific activity of the urine.

The product analysis of the tissues will not be presented in detail here. The condensed list will be given. Spleen showed the highest activity with approximately 6 micrograms per gram being found. The liver was next in activity with approximately 3 micrograms/gram of tissue. The bronchial lymph nodes showed that next highest activity with approximately 1.2 micrograms/gram of tissue. The gall-bladder showed the next highest activity of approximately 0.9 micrograms/gram of tissue. It may be that this value is a falsely high one, inasmuch as the dissection of the gall-bladder from the liver may well have not been complete, with the result that small amounts of liver having a high value, noted above, might have contaminated the gall-bladder. The activity of the bile was extremely low - that is to say the activity was less than the sensitivity of the method we are using for detection of the material. Other tissues ranged below the levels given above. The activity of the blood during the last 5 days was 0.011% micrograms of product/milliliter of blood.

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The contents of the small intestines showed negligible amounts of activity while the contents of the large intestines showed considerable amounts of activity. It will be remembered that the bile showed little activity. Insofar as the data on this dog can be interpreted, it would appear that the excretion site in the intestine for product is from the large intestine.

The deposition of the material in bone was discussed. Evidence was presented which indicated that the material was deposited primarily beneath the endosteum in the bone marrow. The activity per gram of bone spicules in the bone marrow may well prove to be 15 to 20 micrograms per gram. It may well be that the selective deposition of product in bone may account for some of the lack of difference in toxicity between product and radium.

Activity of blood was discussed. It was shown that the activity from the 10th to the 16th day was 0.011$ micrograms of product/milliliter of blood. The activity is almost entirely found in the plasma fraction of the blood.

Dr. Stone:

Does the above data have any implications regarding the value of various types of tests which might be performed on humans?

Dr. Nickson:

The urine test will probably continue to be of considerable value as a survey of large numbers of people. In those individuals in which high values are found, it is planned to do both stool and blood determinations for product. It is questionable at the present time whether blood determinations will prove to be of value.

L. Prosser (for Biology Section):

The distribution of product in the plasma was investigated by means of the Tselius technique. It has been demonstrated that tuballoy is attached to the albumin fraction, and that product is attached to the alpha globulin fraction. There seems to be little doubt that the product is complexed.

The physical picture on the dogs was briefly discussed. The dog was clinically well until the 13th day, then showed a toxic reaction with elevation of temperature and heart rate, and a fall in blood pressure. The animal stopped eating and fluid intake continued essentially normal. The white count dropped markedly during the last week of life. On the 16th day the white count was 200. The white count presented the first sign of abnormality in the animal. There is similarity in the clinical picture of animals which have received x-ray in lethal doses.

Proteins were studied. The albumin and gamma globulin fractions remained

unchanged in total quantity. The alpha and beta globulins altered markedly. There was also an apparent increase in the fibrinogen. These phenomen of reversible coagulability with temperature drop and rise was described. It has been stated that this may be due to the increase in the alpha globulin.

The amino-nitrogen remained unchanged. Pigment metabolism, bilirubin levels and chloride balance were unchanged. These all suggest that there was an essentially normal liver function.

The above findings suggest that the animal died of mechanisms similar to those caused death in x-ray animals.

Comparison of radium and product. In mice the 100% lethal dose with intravenous injection of the chloride, in 30 days, is 1 microgram. 0.5 micrograms produces only 10% death in 30 days under the same conditions. In rats product injected at the level of 2 micrograms produces 100% lethal dose in 30 days, while 1.0 micrograms produces death in only 25% of the animals under the same conditions. Radium in mice has essentially the same toxic levels as does product.

Histological studies show no evidence of liver damage. Dr. Barron has found a decrease in the pyruvate metabolism of rat liver. The pyruvate metabolism in the kidney is not altered. The bone cells (osteocytes) are largely killed by product. This has not been seen after x-ray. It has been noted to a much smaller degree after injection of some of the fission products. The spleen and lymph nodes show marked damage to the lymphocytes. Bone marrow shows a marked disturbance in blood formation. The latter is true for fission products, such as strontium, localized in the bone. Damage to the liver and spleen has not been noted with fission products.

Intravenous injection of citrate was investigated. The figures of the uptake in the liver are essentially the same as those presented by Dr. Hamilton. The animals, however, are dying at the same level as produces death after the injection of the +6 nitrate.

On intramuscular injection in mice, 4.5 micrograms/gram was given. The animals did not die in one month. This difference between intravenous and intramuscular injection must be investigated further.

Radio-autograph of the spleen, liver and bones of rats injected with product are presented. The blood vessels show no activity. The spleen nodules show much activity. Decalcification of bone does not remove the product. A marked difference in distribution of radium and product in bone can be seen by studying the radio-autograph.

Dr. Cantril:

Evidence of spontaneous hemorrhage?

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Dr. Prosser:

There was slight evidence of hemorrhage in the kidney and a few of the cervical lymph nodes. Not nearly as much as in the x-ray animals.

Dr. Cantril:

Anemia?

Dr. Prosser:

No.

H. J. Curtis (for Clinton Laboratories, Biology):

Mice have been exposed to fast neutrons at the level of 1.15 n/day. A total of 150 n has been given. The animals are beginning to show changes. Weight level is below the controls and blood picture shows a fall in lymphocytes. The neutrophils are essentially normal. This picture is essentially similar to x-ray animals. One-half of the animals have died in the above experiment. Lethal dose, for one exposure, is approximately 90 n. This leads to the tentative conclusion that recovery processes are relatively ineffective. Comparable data for x-rays to be obtained. 40 curies of Tantalum have been made in the pile.

The lethal dose (50) for beta rays has been further investigated using phosphorus beta rays from P^{32}. For mice it is 4500 r; for rats it is 7500 r; for rabbits it is 19,000 r. The above figures are measured as dose to the skin. The mld 50 for x-ray for all of these animals is approximately 700 r. On basis of the energy absorbed for the two types of radiation, the difference is reduced to approximately a factor of 2. It is note-worthy that the death in the animals exposed to beta rays, if it is going to occur, occurs before the skin reaction develops.

There are differences in the weight curves in the animals exposed to x-ray and beta ray.

W. Jesse:

Measures of fast neutron concentration?

H. J. Curtis:

This was done with a Victoreen Condenser r Meter, 100 r chamber.

W. Jesse:

Availability of source for calibration?

H. J. Curtis:

Yes. Have means of comparison with Victoreen measurements.

R. S. Stone (for Clinton Laboratories):

A method of monitoring fast neutrons has been developed. It uses a fine grain film on which the number of tracks caused by protons are counted. Calibration of film by exposure to radium-beryllium neutrons, by putting the film in the pile. Tolerance has been established as nine ± 3 tracks per sq. mm per film. 95 films have been studied to date. No levels above tolerance have been found.