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A REPORT OF THE PAST, PRESENT, AND FUTURE RESEARCH  
ACTIVITIES FOR PROJECT 48-A-1.

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J. G. Hamilton, M. D.

The biological research program, which is identified as 48-A-1, was initiated in Crocker Radiation Laboratory at Berkeley on October 15, 1942. The objective of this program was primarily to investigate and evaluate the metabolism of the radio-elements produced by nuclear fission and a number of the fissionable elements, notably plutonium. A corollary phase of this program was the search for possible methods for the treatment of radioactive poisoning for both the longer lived fission products and plutonium. In addition to these two fields of effort, a significant fraction of the total program was devoted to the study of the behavior of certain of the fission products and plutonium in various types of soils and the metabolism of these radioactive substances in several representative plants of significance in the field of agriculture.

In summarizing the work accomplished since the inception of the program in October of 1942 to the end of the fiscal year 1946-47, it is convenient to summarize the work in the three major categories indicated below. The major portion of the program, which has averaged about 70% of the total effort, has been directed to the metabolic studies. Roughly 25% has been allocated to exploring in considerable detail the possible mechanisms responsible for the rather unique and dangerous predilection of plutonium and a number of the fission products for deposition and prolonged retention in the skeleton, together with the development of possible methods for the detection and treatment of radioactive poisoning by these agents. The remaining 5% of the total endeavor was devoted to the plant and soil studies.

The metabolic studies may be generally summarized as tracer experiments in that small amounts of the carrier-free radio-elements were employed at a dosage level below that which might be expected to produce radiation injury. With the exception of one human study using plutonium, all the studies reported here employed rats as the test subjects. The majority of the fission products selected for these tracer studies were those which possess relatively long half lives and are produced in high yields from nuclear fission. A major share of the effort devoted to the study of the fissionable elements centered about the studies made with plutonium. The fission products, as well as the fissionable elements, were administered orally and parenterally, the intramuscular route usually being employed for the parenteral studies, and the animals sacrificed at fixed intervals of time extending from 1 to 64 days in most instances and, in a few cases, as long as 256 days. The urine and feces were collected separately at daily intervals and from 12 to 15 organs and tissues removed from each animal and these samples individually assayed for their content of the radio-element under study. Thus it was possible to observe the absorption, distribution, retention and excretion for each of the radio-elements subjected to this type of investigation. In addition to these relatively straight-forward tracer studies, a detailed exploration was made of the character and degree of selective localization of the more important

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PROVENANCE

REPOSITORY: OFFICE OF HUMAN RADIATION  
EXPERIMENTS (OHRE)

COLLECTION: PLUTONIUM INJECTION INVESTIGATION  
FILES (OHRE 1)

BOX: 3

FOLDER: IRRELEVANT MATERIAL

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radio elements deposited in the skeleton. This was accomplished by means of the technique of radionautography which makes it possible to correlate the details of histological structure of tissues for the deposition of these radio-elements which accumulate in such structures.

The behavior of the fission products and fissionable elements in the body following their introduction into the lungs was subjected to careful study. The lung experiments were deemed of considerable importance since inhalation is one of the three principal routes through which entry of the radio-elements under study might gain access to the body. The initial lung experiments were done by the direct introduction of solutions of the individual fission products and plutonium into the lungs by intubation. These studies, which were somewhat qualitative in character, were extended by a series of aerosol experiments from which a number of successful procedures were developed and employed for the production of aerosol of carrier-free mixtures of the fission products and plutonium in both soluble and insoluble forms.

As was the case in the oral and parenteral tracer studies, the absorption, distribution, retention, and excretion were followed for varying intervals extending to nearly a year in these lung experiments. Radioautographic preparations were made of the pulmonary tissue in order that the sites of prolonged retention might be correlated with the detailed histological structure of the lungs.

The fission products and fissionable elements studied during the interval from October 1942 to 1947 included strontium, yttrium, zirconium, columbium, ruthenium, tellurium, iodine, xenon, cesium, barium, lanthanum, cerium, praseodymium, thorium, protoactinium, neptunium, and plutonium. In addition, studies during this interval were initiated, but not completed, with element 61, americium and curium.

The most significant aspects of the behavior of these substances in the body following oral and parenteral administration appears in the accompanying table. It is apparent that the majority of the longer lived fission products, as well as all of the fissionable elements studied to date, are not absorbed from the digestive tract and are accumulated to a high degree and tenaciously retained by the skeleton. The implications of this behavior are quite ominous in view of the unfortunate episodes of poisoning that have occurred in past years in the radium industry. It will be noted that in most instances with those of the fission products deposited in the skeleton, the rates of elimination proceed at a slower rate than these substances vanish by radioactive decay. In the case of plutonium in the rat, its rate of elimination from the skeleton is extraordinarily slow. The one human study done, using plutonium 239, indicated that at the end of nearly a year approximately 70% of the administered dose still remained in the skeleton and the combined rate of urinal and fecal excretion was less than .01% per day of the amount originally given to the subject.

During the interval that the tracer studies described above were made, a very satisfactory technique was developed for the preparation of

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this uncalcified bone sections. The procedure was eventually perfected to such a degree that it became possible to prepare intact longitudinal sections of the entire femur of the rat. These sections were made of nearly uniform thickness in the range of from 4 to 6 microns. As might be expected, this procedure was of incalculable value in the determination of the sites of localization of plutonium and a number of the fission products in the skeleton. By the use of these thin sections, it was possible to obtain microphotographs which showed in considerable detail the histological localization of these radio-elements which show a high degree of localization in the skeleton. The members of the fission product series subjected to study by this technique included strontium, yttrium, zirconium and cerium, and among the fissionable elements, thorium, plutonium and americium.

As might be expected, the deposition of strontium in bone was observed to be confined primarily to the mineralized portion of this organ. The other fission products and three fissionable elements listed above demonstrated a startling deviation from the pattern of distribution of carrier-free radio-strontium. With these radio-elements, accumulation is primarily in the periosteum, endosteum and region of trabecular bone. After careful study, it was apparent that certainly plutonium, and probably all of the others so deposited, were not incorporated in the mineralized portion of the bone but are accumulated in the osteoid matrix. Cerium and americium showed an additional variation which is of considerable interest in that a significant fraction of these two radio-elements appeared to be deposited in and about the small blood vessels of the cortical bone. Obviously, the predilection for all of these substances, and in particular plutonium, being laid down in the region of the inner and outer surfaces of the bone makes them relatively more dangerous than those radio-elements such as strontium and radium which accumulate primarily in the mineralized structure. As a result of this phenomena, radiation from substances like plutonium can enter the marrow cavity most effectively, as a large fraction laid down in the skeleton is held within a thin layer of tissue adjacent to the bone marrow. This situation is particularly serious for the material which emit alpha particles, for a large proportion of all of the disintegration will result in bombardment of the radio-sensitive bone marrow. Whereas with radium most of the alpha particles will be absorbed within the relatively more radio-resistant mineral portion of the bone due to the fact that the radium atoms are distributed throughout the inorganic bone salts.

The lung studies in the rat demonstrated that those fission products not absorbed from the digestive tract and plutonium which was unabsorbed from this route of administration, were retained by the pulmonary tissue for considerable periods of time after their direct introduction into the lungs by tracheal intubation as solutions of their soluble salts. The fission products found to be deposited and retained in pulmonary tissue under these conditions included yttrium, zirconium, cerium, lanthanum, ruthenium, cerium, and praseodymium. Plutonium also showed a high degree of retention in the lungs which was greatest for  $Pr^{IV}$  and least

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for  $Pu^{6+}$ . Radioautographs indicated that the retained radio-elements in all instances were distributed throughout the lungs in the alveoli. No significant accumulation in the bronchial tree, lymph nodes, or blood vessels was noted. A variable and significant amount of absorption took place through the lungs for all of the radio-elements retained in this organ, and with the exception of ruthenium most of the absorbed material was deposited in the skeleton, as was to be expected from the parenteral tracer studies. As might be expected, those fission products which are readily absorbed by way of the digestive tract, notably strontium, barium, tellurium, iodine and cesium were found to be almost completely absorbed through the lungs at a rapid rate.

These relatively qualitative pulmonary intubation studies were followed by a large series of aerosol experiments using airborne suspensions of the oxides of plutonium and carrier-free mixtures of the fission products. Most of the particles in these aerosols were estimated to range from .1 to .5 microns in size. Approximately 75% of the fission product and plutonium aerosols inhaled were retained and about equally divided between the lungs and upper respiratory tract. The fraction deposited in the upper respiratory tract were removed presumably by ciliary action and appeared in the feces. The portion remaining in the lungs was eliminated quite slowly and at an ever diminishing rate. There was very little absorption of plutonium through the lungs when the material inhaled was in the form of its oxides. However, aerosols of soluble compounds of plutonium, notably plutonyl nitrate, was followed by the prompt absorption of nearly 10% of the inhaled material and the subsequent deposition of this absorbed fraction in the skeleton. The remaining plutonium in the lungs was not absorbed and was slowly eliminated to appear in the feces at rates comparable to those observed in the studies using oxides of plutonium. The inhalation of aerosols containing the carrier-free fission product mixture was followed by the absorption of from 3 to 8% of the total radioactivity, of which a large fraction was found to be deposited in the skeleton.

The portion of the program devoted to attacking the problem of radioactive poisoning from fission products and plutonium attempted to approach this issue by three lines of investigation, namely the manner which these elements are deposited in the skeleton and possible factors which may influence this phenomena of deposition, fundamental studies of bone metabolism, and finally the direct exploration of different methods for both the removal and translocation of these materials once they have become deposited in the skeleton.

Since the studies in this sphere of effort are of necessity more laboriously detailed in many respects, most of the experiments were limited to four radio-elements, notably strontium, yttrium, cerium, and plutonium. The three fission products are fairly representative, on the basis of both their chemical and biological properties, of almost all of the more abundant and longer lived members of the fission product series. Since strontium is the only member of this group of four absorbed from the digestive tract, considerably more attention was given to the influence of possible agents in decreasing the uptake of this

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radio-element following its oral ingestion. Of the many factors studied, only two were found to possess any significant effect in altering the degree of absorption of this element from the digestive tract. These two factors were age, and level of calcium nutrition prior to the administration of radio-strontium. Young rats absorbed over five times as much strontium as did mature adult animals under conditions of normal calcium nutrition. An additional factor of increased absorption took place in both young and adult animals which had been maintained previously on a calcium deficient diet. The effect of the usual treatment in radium poisoning upon the chronic excretion of radio-strontium was found to produce a small but practically unimportant increase in the elimination of radio-strontium. Severe phosphorus deficiency by means of a low phosphate synthetic diet was observed to produce a marked increase in excretion of radio-strontium previously laid down in the skeleton. Further studies must be done to establish the therapeutic applicability of the rather promising results obtained in the animal studies represented here.

Various factors, which influence the degree of deposition, retention, and elimination of radio-strontium, and presumably the normal calcium of the bone, were found to have no demonstrable effect on the behavior of yttrium, cerium and plutonium. Comparisons have been made of the behavior of these four radio-elements under the following conditions. Age, level of calcium nutrition, prolonged lactation, healing bone fractures, severe phosphorus deficiency, rickets, and scurvy. In none of these instances was there found to be any appreciable alteration of the metabolic behavior of yttrium, cerium and plutonium from that observed with the normal controls. All of these factors showed appreciable, and in some instances large deviations in the metabolism of strontium from that observed in the normal adult animals. The deduction that may be made from these observations is that the mechanisms responsible for the accumulation of the two fission products and plutonium in the skeleton are apparently very different from those responsible for the laying down of strontium, and presumably calcium, barium, and radium in bone.

Because of the high degree of retention of plutonium by the skeleton and short range of the alpha particles emitted by this radio-element, it was felt that demineralization procedures such as phosphorus deficient diet followed by remineralization might overlay the plutonium deposits with new non-radioactive bone, thus shielding the bone marrow from the destructive action of the alpha particles whose range of penetration in bone is of the order of 30 microns. It has been demonstrated by the radioautographic technique that this overlaying process can be successfully accomplished to a very considerable degree. The evaluation of the therapeutic potentialities of this method must await actual toxicity experiments in which this procedure of layering has been employed. In addition, it must be determined whether there is any change in either direction of the incidence of bone tumors in animals subjected to this regime as compared to normal controls receiving the same quantities of plutonium.

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The absorption and fixation of yttrium, cerium, columbium, strontium, and plutonium by soils and plants reveal a number of very interesting phenomena. A very high degree of absorption and retention of these six radioactive materials was observed to take place in most common types of soils. Once these radio-elements in carrier-free state come in contact with soil, they cannot be removed by leaching, even with strong acid solutions. There was a very high degree of accumulation of all six of these radio-elements by the roots of plants grown in soils treated with these materials. A considerable fraction of the strontium accumulated by the plants was found to be translocated to the leaves and stems. From the known facts of plant physiology, it can be anticipated that barium and cesium will behave in a similar manner to strontium. Yttrium, zirconium, columbium, cerium, and plutonium showed a relatively small degree of accumulation in the leaves and stems but a measurable degree of translocation of these elements took place. On the basis of the studies made, it appears that soil activities of the order of 1 microcurie per gram in the region of contact with the roots will result in obvious injury to the plant. This arises from the fact that the roots possess the property of removing these materials from the surrounding soil and accumulate them to relatively high concentrations in their immediate vicinity.

Research Activities for the Present Fiscal Year 1947-48.

Tracer studies employed using plutonium, americium, and element 61 have been completed during the present year. As has been indicated in the table, these three radio-elements are not absorbed from the digestive tract to any significant degree and the skeleton is the principal organ of accumulation from which these radio-elements are released very slowly. New studies undertaken and in progress during the current year include investigation of the metabolism of carrier-free preparations of other members of the fission product series, notably arsenic, silver, indium, tin, cadmium, technetium, antimony, and rubidium. Uranium and actinium tracer studies have also been initiated, as well as experiments with carrier-free beryllium. In a number of instances, notably the experiments with beryllium, rubidium, tin, and actinium, the data in hand is not sufficiently complete to evaluate the salient factors concerning the metabolism of these substances. It is anticipated within the next few months that a fairly complete picture of the metabolic behavior will be available.

To briefly summarize the status of tracer studies now in progress, it can be stated that carrier-free radio-arsenic is very rapidly eliminated following its parenteral administration by intramuscular injection, with excretion occurring primarily by way of the feces. Approximately 50% is eliminated in the feces in 24 hours. Thereafter, elimination becomes relatively slow with a half-time of the order of 30 to 40 days. The accumulation was relatively low in all of the tissues with the exception of the red cells, where nearly all of the remaining arsenic in the body was concentrated. This curious effect was found to be specifically in the rat and did not occur with other animals studied,

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which included dog, cat, rabbit, guinea pig, chicken, and the mouse, the total uptake by the blood in 48 hours being from one eighth to one hundredth of the rat in a corresponding size limit. Carrier-free radio-antimony was found to be excreted following parenteral administration extremely rapidly, chiefly by way of the kidneys, eliminating approximately 95% of the total dose within 24 hours. It was of interest to observe that practically all of the antimony remaining after the 24 hour period was also retained in the red cells. Although the level of retention was only of the order of a few percent, that fraction retained was held almost as tenaciously by the blood as was found with arsenic. Oral absorption was observed to be relatively low and in the range of from 2% to 4% of the administered dose. Carrier-free radio-silver has been found to be eliminated very rapidly following parenteral administration, there being nearly 90% excreted in the first 24 hours by way of the feces. It was found that most of the excretion apparently was by way of the liver since ligation of the bile duct caused almost complete suppression of the excretion of silver. It was also noted that caloricorexia castroasis produces a temporary but striking decrease in the excretion of silver which suggests the possible application of this radio-element in the carrier-free state as a clinical test for liver function. Radio-silver in the carrier-free state is absorbed to a very limited degree by way of the digestive tract, the apparent level being less than 1% of the administered dose. Cadmium in the carrier-free state is eliminated by way of the feces following parenteral administration, but its excretion is slow and there is a high degree of retention by the liver, there being nearly 50% of the administered dose present two months after administration with radio-cadmium. Somewhat lower, but still relatively high levels of accumulation were noted in the adrenals and pancreas. Oral absorption was slow and was in the range of .2%. Radio-iodine resembles somewhat the metabolic behavior of cadmium except for a considerably slower accumulation in the liver and a more generalized distribution in the other tissues of the body, approximately 50% being eliminated at the end of 60 days. Oral absorption of iodine in carrier-free states was found to be less than .2%. Technetium was observed to be excreted with great rapidity following parenteral administration, there being 60% eliminated in the urine within 4 hours after administration. No significant retention or localization was noted in any of the tissues. Element 61 and actinium were found to behave in the rat in an almost indistinguishable manner to that of the other members of the rare earths, americium, and curium. Uranium, following parenteral administration, is accumulated primarily in the kidneys and skeleton. Initially the deposition in the kidneys is very high, but gradually falls to a level at the end of two months where its concentration in that organ is significantly less than the content in bone.

During the present year, radioautographic studies have been made of the distribution of columbium, element 61, actinium, and curium in the skeleton. Here it was of considerable interest to find that columbium presents a pattern of distribution essentially like that of yttrium, zirconium, thorium, and plutonium; namely, that deposition was primarily in the osteoid matrix with no apparent accumulation either in the

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mineralized structure of the bone or about the small blood vessels of the cortex. Radium, as might be expected from its close resemblance to americium in both chemical and biological properties, has a characteristic pattern of distribution in bone of almost identical character. Actinium, which metabolically as well as chemically closely resembles americium and curium as well as the rare earths, likewise showed a similar pattern of distribution in the bone. Similarly and by the same token, this situation was repeated with element 61.

The kinetics of the uptake of carrier-free radio-strontium by the skeleton and the excretion by the kidneys has been studied in young, rabbit and other adult rats. In the adult animals, the uptake of strontium by bone is slow and prolonged, and may be accounted for on the basis of a simple adsorption -- exchange with the calcium of the bone salts. In the young growing rats, both normal and rachitic, there is a very rapid and apparently labile combination of strontium in bone. This phenomenon, since it is present in both the young, normal, and rachitic rats, is felt to be associated with the osteoid matrix. The effect of prolonged fasting on the absorption of carrier-free radio-strontium in the rat has been to increase significantly the assimilation and produce a five-fold decrease in its excretion by the fasting animals.

The intraperitoneal injection of a massive dose of strontium citrate has been found to increase significantly the urine excretion of plutonium. The same observation was made several years ago in Chicago by Dr. Schubert and his colleagues. The investigation of this phenomenon has been made in considerable greater detail during the past year here at Berkeley. Factors such as the effects of valence states of the administered plutonium, routes of its administration, and time of treatment with massive doses of strontium citrate have been studied. In addition, a number of similar experiments have been carried out with carrier-free radio-yttrium. The most startling effect has been when either plutonium or yttrium were administered intravenously at the same time the massive doses of stable strontium were given. The treated animals excreted 10 to 15 times as much plutonium as the animals not receiving the strontium treatment. Fecal excretion was not significantly affected. Treatment with a massive quantity of stable strontium before or after administration of the plutonium and yttrium had relatively little effect. Since massive doses of strontium are rapidly excreted in the urine, these results suggest that strontium is acting as a carrier to facilitate the elimination of the carrier-free radio-yttrium and the plutonium. It is possible that an adaptation of this procedure might be of value when a laboratory worker receives a single and conceivably large amount of plutonium as the result of an explosion, contamination of cuts, etc. Obviously, there is much to be done before such a possible first aid procedure may be considered for human therapeutic application.

Projected Work for the Fiscal Year 1948-49.

It is planned to complete the tracer experiments now in progress which have been discussed briefly in the preceding section. An investiga-

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tion is to be made of the metabolism of those fission products not yet subjected to study, notably zinc, gallium, germanium, selenium, bromine, dysprosium, neodymium, samarium, and europium. This will complete the metabolic survey studies for the series of 34 elements that arise from the slow neutron fission of both uranium and plutonium. In addition to the investigation of the metabolic properties of these fission products, it is deemed highly desirable to study the behavior in the body of carrier-free radio-isotopes of a number of elements whose chemical and physical properties resemble closely some of the more important members of the fission product series. The purpose of such studies is to correlate the metabolic properties with the chemical properties of such substances so that the unique behavior of a number of the fission products in the body may be understood a little more clearly. Certain elements are of particular interest in this connection, notably the rare earths not normally occurring in fission, potassium, calcium, scandium, titanium, hafnium, tantalum, and tungsten.

Another phase of effort will be to explore in greater detail the behavior of those fission products whose metabolic characteristics are such that they may prove to be of clinical interest. An interesting example in this connection is the possible use of carrier-free radio-silver as a test for liver function, since it has been shown in animals that minimal and reversible liver damage is attended by a remarkable degree of retention of radio-silver by the liver. The relatively high uptake of carrier-free radio-cadmium and radio-iodine by the pancreas suggests further exploration to ascertain the possibility of the selective localization of these two radio-elements in the islet tissue of this organ.

The radioautographic studies are to be extended, in particular with reference to acquiring additional information as to the precise localization of a number of the fission products and fissionable elements within the various histological structures of the bone.

It is planned also, if time and facilities permit, to explore by means of the tracer technique the metabolism of a number of elements not produced directly by fission which are produced in very large radioactive quantities in the operation of the chain reacting pile. Such substances include the various components of structural units of the various types of piles, controlling devices, etc. Among such elements that should be subjected to study are vanadium, chromium, manganese, cobalt, and nickel.

Under appropriate and suitable circumstances, it is highly desirable to conduct human tracer studies with certain of the fission products and fissionable elements. Such work is to be done with two purposes in view. First, to establish the metabolic behavior of these substances in man, which may deviate both qualitatively and quantitatively from their properties in the rat. This can be readily and safely done in a number of instances using radio-isotopes of the elements in question with relatively short half-lives. A number of isotopes in this category,

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suitable for safe tracer experiments in man, can only be made by means of a cyclotron such as the 60" instrument in the Crocker Laboratory. Second, to investigate the potential diagnostic and therapeutic applications of these elements studied, as for example radio-silver, which possess metabolic properties that suggest they might be of clinical value. The human studies of this character will be undertaken in collaboration with Dr. H. S. Stone at the University of California Medical School.

The projected work for next year in the field of fundamental studies of bone metabolism and further exploration of the problems surrounding poisoning with the fissile products and fissionable elements will be essentially a continuation of present work. Several phases of the effort in this general program are to receive special attention and include the following. First, kinetic studies of the uptake of radio-yttrium, radio-cerium, and plutonium by the skeleton. This will be similar in nature to the work of this character now in progress with radio-strontium. Second, a detailed comparison, under comparable and carefully controlled circumstances, of the metabolism of calcium, strontium, barium and radium. This is to be done with particular reference to the mechanism of deposition of these substances.

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TABLE I

METABOLISM OF THE PRINCIPAL MEMBERS OF THE LONG-LIVED FISSION PRODUCTS AND CERTAIN OF THE HEAVIEST ELEMENTS IN MAN AND THE RAT FOLLOWING PARENTERAL AND ORAL ADMINISTRATION

Radio-Element	Half-Life(8)	Fission Yield (8)	Oral Absorption	Accumulation in Principal Organs of Retention	Rate of Elimination from Principal Organ of Retention (half-time in the body)
Strontium Sr <sup>89</sup> Sr <sup>90</sup>	53 D 25 Y	4.6% ...	5-60% 5-60%	65% Bone 65% Bone	Bone > 200 D Bone > 200 D
Barium Ba <sup>140</sup>	12.8 D	6.1%	5-60%	65% Bone	Bone > 50 D
Iodine I <sup>131</sup> ✓	8.0 D	2.8%	100%	30% Thyroid	Thyroid > 30 D
Cesium Cs <sup>135</sup>	33 Y	...	100%	45% Muscle	Muscle 15 D
Yttrium Y <sup>91</sup>	57 D	5.9%	< 0.05%	65% Bone 65% Liver 25% Bone	Bone > 500 D Liver 10 D Bone > 25 D
Lanthanum La <sup>140</sup>	40 H	6.1%	< 0.05%		Liver 10 D
Cerium Ce <sup>141</sup> Ce <sup>144</sup>	28 D 275 D	5.7% 5.3%	< 0.05% < 0.05%	55% Liver 25% Bone 30% Liver 40% Bone 50% Liver	Bone > 200 D Liver 10 D Bone > 100 D Liver 10 D
Praseodymium Pr <sup>143</sup>	13.8 D	5.4%	< 0.5%	30% Bone	Bone > 100 D
Erbium Er <sup>147</sup>	3.7 Y	2.6%	< 0.05%		Bone > 100 D
Zirconium Zr <sup>95</sup>	65 D	6.4%	< 0.05%	45% Bone 40% Bone 25% Blood	Bone > 100 D Bone 30 D Blood 1 D
Columbium Cb <sup>95</sup>	37 D	6.4%	< 0.5%		Kidney 20 D
Ruthenium Ru <sup>103</sup> Ru <sup>106</sup>	42 D 1 Y	3.7% 0.5%	< 0.05% < 0.05%	3.5% Kidney 3.5% Kidney	Kidney 20 D
Tellurium Te <sup>127</sup> Te <sup>129</sup>	90 D 32 D	0.033% 0.19%	25% 25%	15% Blood 6% Kidney	Blood 15 D Kidney 15 D
Thorium Th <sup>234</sup>	24.5 D	...	< 0.05%	50% Bone	Bone > 200 D
Protactinium Pa <sup>231</sup>	3 x 10 <sup>4</sup> Y	...	< 0.05%	40% Bone	Bone > 100 D
Neptunium Np <sup>239</sup>	2.2 D	...	< 0.05%	60% Bone	Bone 50 D
Plutonium Pu <sup>239</sup>	2.2 x 10 <sup>4</sup> Y	...	0.007%	65% Bone 70% Liver 25% Bone 70% Liver 25% Bone	Bone > 2 Y Liver 10 D Bone > 1 Y Liver 10 D Bone > 1 Y
Americium Am <sup>241</sup>	500 Y	...	< 0.05%		
Curium Cm <sup>242</sup>	150 D	...	< 0.05%		
Xenon Xe <sup>133</sup>	5.3 D	4.5%			

Distribution Proportional to fat content of body;  
half time + in the body two hours

Human studies (1)    Human studies (9)

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The following list of names includes those members of the group working on Project 48-A-I who have either received or are working towards their Bachelor's, Master's or Doctor's degree. All of these individuals have worked a minimum of half time to nearly full time in the laboratory. The average duration of their stay in the laboratory has been between two and one-half to three years, several having worked here for periods of time up to nearly five and one-half years. The training and experience received during this period has been primarily in the tracer applications of radioactivity to the biological sciences together with a considerable degree of contact in most instances with some of the more salient fundamentals of nuclear chemistry as they apply to biology.

## Received PhD

Louis Jacobson  
Henry Lanz, Jr.  
L. Van Middleworth  
K. G. Scott

## Working Toward PhD

Dorothy Axelrod  
Donald R. Bomberger  
H. R. Haymond  
Bergene Kavin  
Kernit Larson  
L. W. Tuttle

## Received M.A.

Marian J. Chace  
David C. Jones

## Working Toward M.A.

Josephine Crowley  
Freake V. N. Kohl  
C. W. Page, Jr.

## Received A.B.

Elizabeth Guthbertson  
Wilda Hammond  
Hope Hribal

## Working Toward A.B.

John C. Alley	Kathryn Kent
Ann Brookman	Mary McCarty
Jacqueline Bruning	John Post
Hugh Burleson	Wallace Shaw
Mahlon Connett	Edith Steinhuff
Mary Ann Delano	Patricia Wallace
Helen Goodwin	Bertha Webster

In addition to the training received by the group listed above, the teaching activities carried on by members of Project 48-A-I have included the presentation of a new course at Berkeley during the spring semester of 1947,

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Physics 126, which was an introduction to the biological applications of artificial radioactivity, and consisted of two lectures and one laboratory period each week for the entire semester. This course, which is being repeated this current spring semester, was given by three members of the group. Four members participated in a course presented at the University of California Medical School in San Francisco during the summer of 1947 which covered essentially the same material but was directed primarily in the medical applications of nuclear physics rather than the general biological applications.

In addition to the training activities already discussed, four officers from the Navy and two from the Army have received a year or more training at the Crocker Laboratory with the assistance and supervision of its staff.

Entirely apart from the general research program and the training activities of the group, a considerable amount of effort was devoted to certain phases of the Operation Crossroads from March 1946 to July 1947. Several members of the group participated in the exercises at Bikini, the work there being primarily in the field of radio-chemistry. After the tests, a procedure was developed in the laboratory at Berkeley for the decontamination of the Task Force vessels which had become radioactive. A successful method was developed which the Navy employed to satisfactorily remove this contamination from nearly fifty vessels. As a corollary to this particular effort, considerable assistance was rendered to the Navy in setting up its Radiation Laboratory at the Hunters' Point Navy Yard in San Francisco, California.

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## BIBLIOGRAPHY

Published research and papers in press, being prepared for publication, and pending declassification.

Axelrod, D. J.: An Improved Method for Cutting Unfossilified Bone Sections and Its Application to Radioautography - *Anat. Record*, Vol. 98, No. 1, May 1947 (EP-44)

Copp, D. H., Axelrod, D. J., and Hamilton, J. G.: The Deposition of Radioactive Material in Bone as a Potential Health Hazard - *Amer. Jour. Roent. and Rad. Therapy*, Vol. LVII, No. 1, July 1947 (EP-41)

Overstreet, R. and Jacobson, L.: On the Existence of a Calcium Isotope With an 8.9 Day Period - *Phys. Rev.* Vol. 72, No. 4, Pg. 349, August 13, 1947, (EP-44)

Hamilton, J. G.: The Metabolism of the Fission Products and the Heaviest Elements - *Radiol.* Vol. 49, No. 3, Pg. 325-343, Sept. 1947 (EP-90)

Hamilton, J. G.: The Medical Applications of Radioactive Tracers - Presented at the Symposium on the Use of Radioactive Isotopes, University of Wisconsin, Madison, Wisconsin, Sept. 1947 (EP-152)

Jacobson, L. and Overstreet R.: The Uptake by Plants of Plutonium and Some Products of Nuclear Fission Adsorbed on Soil Colloids - *Soil Sci.*, Vol. 65, Pg. 129-134, Feb. 1948 (EP-82)

Axelrod, D. J.: The Radioautographic Technique - Presented at the Meeting of the American Chemical Society, Sept. 1947 - To be published in U. S. Navy Med. Jour. (EP-111)

EP-48 Fissionable Elements and Their Products - J. G. Hamilton (Presented at the Radiological Society of North America Meeting, Dec. 1946)

EP-54 The Uptake of Plutonium, Yttrium, and Strontium by Callus Healing of Bone Fractures - L. Van Middlesworth, D. H. Copp, and J. G. Hamilton (Abstract for Meeting of Federated Societies - May 1947)

EP-69 Plutonium Metabolism in Bone - L. Van Middlesworth (Thesis) May 1947

EP-142 The Comparative Metabolism and Distribution of Carrier-free Radio-Arsenic ( $As^{74}$ ) - Henry Lans, Jr. - To be published (thesis)

UCRL-22 The Metabolism of Americium in the Rat - K. G. Scott, D. H. Copp, D. Axelrod, and J. G. Hamilton

UCRL-35 The Metabolism of Curium in the Rat - K. G. Scott, D. Axelrod, and J. G. Hamilton

UCRL-36 The Metabolism of Carrier-free Radioactive Silver in the Rat - K. G. Scott (Thesis) To be presented at the American Society for Clinical Investigation May 1948

**Bibliography (continued)**

OH-3588 Absorption and Fixation of Fission Products and Plutonium by Plants - Jacobson, L. and Overstreet, O. - June 1945

OH-3589 A Comparison of the Metabolism of Plutonium ( $Pu^{238}$ ) in Man and the Rat - J. Crowley, H. Lanz, K. G. Scott, and J. G. Hamilton. May 1946

OH-3590 Studies on the Inhalation of Fissionable Materials and Fission Products and Their Subsequent Fate in Rats and Man - K. G. Scott, D. J. Axelrod, J. Crowley, H. Lanz, and J. G. Hamilton (1945-1946)

OH-3606 The Metabolism of Thorium, Protactinium and Neptunium in the Rat - H. Lanz, K. G. Scott, J. Crowley, and J. G. Hamilton - Oct. 1945 - Apr. 1946

OH-3591 The Deposition of Plutonium and Certain Fission Products in Bone as a Decontamination Problem - D. H. Copp, D. M. Greenberg, J. G. Hamilton, M. Chace, L. Van Middleworth, E. H. Cuthbertson, and D. Axelrod - May 1946

**For Inclusion in National Nuclear Energy Series (Manhattan Project Technical Series)**

Columbium Isotopes from Zirconium and Niobium - L. Jacobson and R. Overstreet - Nov. 1944

The Metabolism of Carrier-free Fission Products in the Rat - K. G. Scott, R. Overstreet, L. Jacobson, J. G. Hamilton, H. Fisher, J. Crowley, I. L. Chaikoff, C. Entenman, H. Fischler, A. J. Barber and F. Loomis - June 1945 to June 1946

The Metabolism of Plutonium in Rats - K. G. Scott, H. Fisher, D. Axelrod, J. Crowley, and A. J. Barber - October 1944

The Isolation of Uranium without Carrier From Thorium Metal Bombarded with Deuterons - R. Overstreet and L. Jacobson - Jan. 1944

Scott, K. G., Axelrod, D. J., Crowley, J., and Hamilton, J. G. - The Elimination and Inhalation of Fissionable Materials from the Lungs of Rats and Man - To be submitted for publication in one of the Industrial Hygiene Periodicals.