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THE METABOLIC PROPERTIES OF THE FISSION
PRODUCTS AND ACTINIDE ELEMENTS

by

J. G. Hamilton, M.D.

March 1948

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Information Division
University of California
Radiation Laboratory
Berkeley, California

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ABSTRACT

THE METABOLIC PROPERTIES OF THE FISSION
PRODUCTS AND ACTINIDE ELEMENTS *

Joseph G. Hamilton, M. D.

An investigation of the assimilation, distribution, retention, and excretion of the fission products and actinide elements in the rat has been conducted at the Crocker Radiation Laboratory, University of California, Berkeley, California. These studies were initiated October 15, 1942, and are continuing at the present time. An extensive survey has been made of the metabolism of twenty-two different radio-elements in the rat.

This entire project has been carried forward by Dorothy Axelrod, M.A., Ass't. Professor D. H. Copp, M.D., Ph.D., Josephine Crowley, A.B., Henry Lenz, Jr. Ph.D., Kenneth G. Scott, Ph.D., eight technicians, and the author. During the early phases of the project, we were fortunate in having the advice and aid of Professors I. L. Chaikoff and D. M. Greenberg, who assisted the program materially, particularly in the studies with strontium, barium, and cesium. Also with the group during the war were Assoc. Professor Roy Overstreet and Ass't. Professor Louis Jacobson, whose work included a large share of the radio-chemical isolation as well as the studies with soils and plants. We acknowledge with gratitude the facilities that were extended to us to do this work in the Radiation Laboratory by Professor Ernest O. Lawrence, the constant advice and encouragement given to us by Doctor Robert S. Stone and Dean Stafford L. Warren, the operating crew of the 60" Cyclotron for the preparation of most of the radio-elements used in these studies, and to Professor G. T. Seaborg, Dean W. M. Latimer and

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their associates for providing us with certain key radio-elements for these studies, notably neptunium, plutonium, americium, and curium.

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These radioactive materials were administered by mouth and by injection. The fission products studied included the carrier-free radioactive isotopes of strontium, yttrium, zirconium, columbium, ruthenium, tellurium, iodine, xenon, cesium, barium, lanthanum, cerium, praseodymium, and element 61. In addition, the eight members of the actinide series which were subjected to metabolic experiments included actinium, thorium, protactinium, uranium, neptunium, plutonium, americium, and curium. The results of these studies indicated that most of the fission products and all of the heaviest elements are absorbed to a very small degree by way of the digestive tract, deposited primarily in the skeleton following parenteral administration, and eliminated very slowly from that organ. The fission products studied which are accumulated in the skeleton include strontium, barium, yttrium, lanthanum, cerium, praseodymium, element 61, zirconium, and columbium. From 25% to 70% of the material absorbed following parenteral injection is laid down in the skeleton and is eliminated from that organ at rates less than the rates of radioactive decay, with the exception of Cb^{95} , Ce^{144} , 61^{147} , and possibly Sr^{90} . The remaining five long-lived radio-elements, ruthenium, tellurium, xenon, iodine, and cesium, do not show any significant degree of localization in the skeleton and, in addition, there is no remarkable deposition in any of the other tissues with the exception of the accumulation of iodine in the thyroid gland. The rate of elimination for all of these five radio-elements is much greater than their rate of radioactive decay with the exception of iodine deposited in the thyroid. In this particular case, the release of the accumulated iodine in the thyroid

is much slower than its rate of radioactive decay. The members of the long lived fission product group which are absorbed by way of the digestive tract include strontium, barium, tellurium, iodine, and cesium. The uptake by the skeleton of the eight members of the actinide group is very similar to that observed with the members of the fission product series studied which are deposited in this structure. With the exception of uranium, elimination from bone occurred very slowly.

Radioautographic studies indicated that strontium, and presumably barium, are deposited primarily in the mineral structure of the bone. The other fission products deposited in this organ are laid down in the region of the inner and outer coverings of the bone and about the trabeculae, but do not apparently enter in to the mineral structure of this organ to a degree comparable to strontium. In the case of the actinide elements, a similar accumulation in the region of the non-mineralized portion of the bone has been observed with actinium, thorium, plutonium, americium, and curium. The curious property of the members of the fission products and the majority of the actinide elements to be laid down in this portion of the skeleton and to be retained there for prolonged intervals, renders them of considerable concern from the point of view of the possible medical hazards to be encountered should these materials be accidentally introduced into the body.

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THE METABOLIC PROPERTIES OF THE FISSION PRODUCTS AND ACTINIDE ELEMENTS

J. G. Hamilton, M.D.

The discovery and development of the chain reacting pile brought with it a series of medical problems of considerable magnitude. The production of plutonium on the kilogram scale is associated with the formation of a comparable mass of fission products whose radioactivity is at the level of hundreds of megacuries. Thus those working in the atomic energy program had to be protected from the radio-elements created in the pile as well as the neutrons and gamma rays which arise directly from nuclear fission.

Radioactive substances can produce injury either by external or internal radiation of the body. Of the two, the potentialities for injury are greater if the radioactive substance is within the body. The history of the radium industry is illustrative of this point. Up to the time of World War II there had been isolated about one kilogram of radium. A large number of cases of radium poisoning have been reported, notably in the luminous dial industry, a large proportion of which terminated fatally.

The medical program of the plutonium project, under the direction of Dr. R. S. Stone, was faced with the responsibility of protecting the personnel against quantities of radioactivity which were of the order of a millionfold greater than had been encountered by the radium industry over a period of nearly half a century. Here the problems had to be met quickly in the haste of wartime urgency for the thousands of scientists and technicians working on the Atomic Energy Project. One of the many research programs that arose from these needs was a survey of the metabolism of the various radio-elements created by the release of nuclear energy. A review of part of this work has been presented recently (1).

It is appropriate to mention a few of the salient factors involved in the problem of radioactive poisoning, because it was these considerations that shaped the pattern of the research to be described in this article. In order to evaluate the potential hazard of a given radio-element or

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compound it is necessary to consider the half-life, radiation characteristics, route of entry into the body, assimilation, distribution, retention, excretion, and the relative susceptibility of the different organs and tissues to the radiations emitted by the deposited material.

Radiation injury, both acute and chronic, is a function of the intensity of the radiation and the duration of exposure to the radiation. A radioactive substance, either as an element or a compound, may enter the body by one or more of four routes, namely, the lungs, digestive tract, the intact skin, and through cuts or abrasions. Once the material has been absorbed, regardless of the portal of entry, it will be distributed to the many tissues of the body and will be taken up in widely varying concentrations and be retained for different intervals of time in these tissues. The degree of injury will vary with the character of the radiation and the radio-sensitivity of the irradiated organ or tissue. For example, alpha particles are relatively more destructive to most living organisms than beta and gamma rays, when the biological effects are compared on the basis of equivalent amounts of total ionization in the tissue. With regard to variations of vulnerability to radiation, the bone marrow, which is the center of hemopoiesis, is very sensitive, while structures such as liver, brain, and muscle are relatively radio-resistant.

If the assimilation, distribution, retention, and excretion of a given radio-element is determined, it is possible to make an estimate of the amount of exposure to such a substance which might be expected to produce either acute or chronic injury. If the tracer or metabolic studies are done with laboratory animals, as they were in these experiments, there is a variable error introduced in extrapolating from the experimental animals to man. However, in many instances this error is probably not much greater than the individual variations between different humans in

their response to a novel biological experience such as is offered to the body by these elements.

The metabolism of the 22 different elements listed in Table I has been investigated in considerable detail. With the exception of strontium and iodine and uranium, little or nothing was known about the metabolic properties of these substances prior to 1944, most of which are not presumed to be normal constituents of living organisms.

Radioactive isotopes of each of the 22 elements were prepared in the carrier-free state as far as it was chemically feasible and individually administered to rats (2) (3) (4) (5) (6) (7) (8). Three of the four possible routes of entry into the body were simulated by administering the radio-isotopes orally, by injection, and introducing them directly into the lungs. The fourth possible route of entry, namely through the intact skin, was not investigated. Each radioelement was prepared and used in the carrier-free state for two reasons. First, all of the fission products and several of the heaviest elements would only be encountered in this situation. Second, it is possible that the quantitative metabolic pattern might be altered if inert material isotopic with the radio-element were present. An excellent example of this second consideration may be found in comparing the metabolism of carrier-free radio-iodine with radio-iodine diluted with stable iodine (9). Here, there are large quantitative variations in the distribution of the labelled iodine when different amounts of inert iodine are added to the radio-iodine. In addition to the quantitative variations encountered under these conditions, there is a very striking qualitative difference observed in the behavior of carrier-containing and carrier-free radio-iodine in the thyroids of patients suffering from hyperthyroidism. A similar phenomena has been recently demonstrated with carrier-free and carrier-containing radio-silver (10).

The fission products selected for the studies reviewed in this report were chosen on the basis of two major considerations: First, that they are produced in relatively high yields from fission, and second, that they have half-lives in the range of days to months. Such a selection includes most of the fission products that might be considered as the major hazards insofar as internal radioactive poisoning is concerned. All eight of the heaviest elements, recently classified as the actinide rare earths by Seaborg (2), were also subjected to metabolic study. These studies were initiated in 1942. In a number of instances, the radio-isotopes were prepared by cyclotron bombardment. This was done for a number of different reasons, notably greater ease of radio-chemical isolation, unavailability of pile-produced radioactivities at the time the experiments were undertaken, and more desirable radioactive properties of the cyclotron-produced radio-isotopes for the type of tracer studies to be done. The radio-isotopes employed, together with their radioactive properties and methods of production, are listed in Table I.

Each radio-element, whether produced by cyclotron bombardment, pile irradiation, or from the decay of a radioactive parent, was isolated in the carrier-free state and free from measurable amounts of radioactive contaminants. With the exception of xenon, each radio-element was prepared and administered in an isotonic solution of sodium chloride. The solution was given by intraperitoneal injection, intramuscular injection, or by stomach tube. The rats were sacrificed at various time intervals extending from 1 to 64 days. In several of the experiments, the time intervals extended to 256 days, and in a number of instances, the studies had to be concluded before 64 days due to the limiting half-life of the radio-element being investigated. The excreta, and from 12 to 18 organs were removed and individually assayed for their content of radioactivity. Frequently the

assays were very laborious and time consuming. This was particularly true for plutonium, americium, and curium, which emit alpha particles, as well as for element 61 whose beta rays are very soft, having a maximum energy of .2 Mev. In such instances, for each individual radioactive assay it was necessary to free the radio-element from the ashed tissue by chemical means. A discussion of the more detailed aspects of the techniques employed in handling the biological materials and their assay is reported elsewhere (6). Likewise, the behavior of the fission products and of plutonium, following their entry into the lungs, has been described elsewhere (11).

In addition to the tracer experiments described above, a considerable amount of effort was directed to a study of the sites of localization of a number of the fission products and the actinide elements in bone by means of the radioautographic technique (12). This is an issue of importance because nine of the fourteen fission products studied and all eight of the actinide elements are accumulated and tenaciously retained by the skeleton. Longitudinal sections of the femur were prepared from the undecalcified bone. These sections were of uniform thickness in the range of from 4 to 6 microns. The technique of cutting thin sections of undecalcified bone was developed by Axelrod (13) and McLean and Bloom (14). The necessity for using this difficult procedure instead of using decalcified specimens arises from the fact that the agents employed to remove the mineral elements from bone are very likely to either leach out or translocate the radio-element deposited in the bone.

RESULTS

The most important metabolic characteristics of the fission products and the actinide elements studied are listed in Table II. It will be noted that most of the fission products and all of the actinide series are not absorbed to any significant degree by way of the digestive tract. Following parenteral administration, these substances are accumulated by the skeleton

and eliminated from this organ very slowly. Only five of the listed fission products are absorbed from the digestive tract to a significant degree, notably strontium, barium, tellurium, iodine, and cesium. Xenon is readily and rapidly absorbed through the lungs following inhalation and is an readily eliminated from the lungs. Strontium and barium are deposited and retained to a high degree by the skeleton. Iodine is accumulated and retained by the thyroid. Tellurium shows some accumulation in the kidneys and blood, with a rather rapid rate of release from these tissues. Cesium is distributed quite uniformly throughout all of the tissues, the greatest accumulation occurring in the muscle, and it is quite promptly excreted. The pattern of distribution of strontium, barium, tellurium, iodine, and cesium, following oral absorption, is indistinguishable from their metabolism after parenteral administration. With the exception of ruthenium, the remainder of the fission product series and all of the actinide elements listed in Table II show a high degree of accumulation and prolonged retention by the skeleton as shown in Figures 1 and 2. In the case of lanthanum, cerium, praseodymium, element 61, americium, and curium, there is an initially high degree of accumulation by the liver, but they are quite rapidly excreted from this organ, presumably by way of the bile (Figs. 3 and 4). Uranium is unique among the actinide group in that there is a very high initial accumulation in the kidney. With the exception of the liver and kidney, the content in the other soft tissues is relatively small following the parenteral administration of the fission products and actinide elements. After two months the spleen and kidney usually had the highest concentration per gram wet weight of the soft tissues and ranged from one-tenth to one-quarter that of bone.

It will be noted in Table II that, with the exception of Cb^{95} and possibly Sr^{90} , Ce^{144} , and 61^{147} , the rates of elimination of the different fission products that are accumulated in the skeleton are less than their

rates of radioactive decay. The long-lived fission products that fall into this category include Sr⁸⁹, Y⁹¹, Zr⁹⁵, Ba¹⁴⁰, La¹⁴⁰, Ce¹⁴¹, and Pr¹⁴³. With the exception of iodine in the thyroid, the remainder of the fission products listed in Table II, namely Ru¹⁰³, Ru¹⁰⁶, Te¹²⁷, Te¹²⁹, Xe¹³³, and Cs¹³⁵, are rapidly excreted and at rates greater than their half-lives.

The rates of elimination from the skeleton of the actinide elements listed in Table II are very slow and in the case of plutonium, the excretion in the rat falls to 0.01% per day of the amount remaining in the body within a year following the intramuscular administration of this radioactive element. The excretion of uranium differs both qualitatively and quantitatively from the other members of the actinide series in that the urine is the principal channel of elimination and the loss from the skeleton, while quite slow, is relatively much more rapid than the other seven members of this group of elements. The metabolism of plutonium following intramuscular injection is the same after the administration of this element as Pu³⁺, Pu⁴⁺, and Pu⁶⁺. This indicates that plutonium is converted by the body to one valence state regardless of the valence of this element when administered. Considerable evidence has been accumulated to indicate that plutonium in the body is tetravalent (see Fig. 2).

Radioautographic studies were made of the distribution of Sr⁸⁹, Y⁸⁸, Zr⁹⁵, Cb⁹⁵, Ce¹⁴⁴, Gd¹⁴⁷, Ac²²⁷, Th²²⁸, Pu²³⁹, Am²⁴¹, and Cm²⁴² in 5-micron sections of undecalcified rat femurs. The metabolism of strontium in the skeleton is very similar to that of calcium and, as might be expected, the radioautographs revealed that the accumulated radio-strontium in the femur was quite evenly distributed throughout the mineral structure of the bone in young rats (Fig. 5). The other radio-elements studied by this technique showed a startling deviation from the pattern of distribution of the radio-strontium. Plutonium exhibits this phenomenon to a marked degree, and in Figure 6 it can be seen that most of this element is deposited in the

periosteum, endosteum, and in the region of the trabecular bone. These results suggest that the plutonium in the trabecular structure is not incorporated in the bone but rather, is deposited in the covering of the trabeculae.

Radioautographs of yttrium, zirconium, columbium, and thorium are shown in Figures 7, 8, 9, 10. It will be noted that these four radioelements are apparently distributed in bone in a pattern very similar to that noted with plutonium. The radioautographs of cerium, element 61, actinium, americium, and curium, shown in Figures 11, 12, 13, 14, 15, indicate concentration of radioactive material about the surfaces of the bone and trabeculae as has been indicated with the previous group. In addition, there is an appreciable amount of activity laid down in a spotty manner throughout the calcified shaft of the bone. The deposited radioelements are apparently accumulated in the region of the small blood vessels present in the mineralized cortical bone. In order to establish this point, a number of bone sections containing element 61, americium and curium and their corresponding radioautographs were studied at high magnification and indicated that the accumulation of radioactivity was in the region of the small blood vessels. However, the resolution was not sufficiently great to establish whether the material was actually in the walls of the blood vessels or had penetrated 20 to 50 microns beyond the vessels into the adjacent mineral structure of the bone. A representative example of this is shown for americium in Figure 16. The pattern observed with curium and element 61 appear to be essentially identical in character.

The results obtained by radioautographic experiments with both fission products and the actinide series of elements suggest that accumulation in the skeleton occurs to a considerable degree in the superficial layers of the bone structure and very possibly is bound to proteins rather than being directly incorporated into the inorganic bone salts. It is note-

worthy that the distribution patterns for these elements does not change significantly with time. Radioautographs from adult female rats which have received plutonium nearly a year before they were sacrificed showed no fundamental differences in distribution in the bone as compared to studies in which the animals were sacrificed a few days after the administration of this radio-element.

DISCUSSION

Two aspects of the metabolic characteristics of the fission products and actinide elements are of importance to consider. First there is the evaluation of their relative hazards as radioactive poisons. Second, and possibly of greater interest, is the apparent correlation in a number of instances of their chemical properties with their fate in the body.

The outstanding characteristic of nine of the fission products described in this report and all eight of the actinide elements accumulated and tenaciously retained by the skeleton has a most ominous significance. Justification for this opinion is borne out by the tragic situation which has surrounded the radium industry. There is evidence to show that prolonged retention over a period of many years of about 1 microgram of radium may result in the appearance of bone tumors with a fatal outcome. Somewhat large quantities of radium, in the range of 10 micrograms, deposited in the skeleton are frequently associated with a profound anemia and occasionally the victim develops leukemia, which is fatal. Both of these disorders are presumably the result of the bombardment of the very radio-sensitive bone marrow. The gloomy picture of radium poisoning is darkened further by the fact that to date no successful method has been developed for removing significant quantities of the radium once it has been locked in the mineral structure of the bone.

The fission products which localize in the skeleton are similar to radium in that they also tend to be tenaciously held in that tissue. A number of considerations reduce the relative menace of these substances as radioactive poisons in comparison to radium. First, they give up much less energy per disintegration and the amount of ionization is relatively much less since they emit only beta and gamma rays. Added to this is the fact that on the basis of an equal amount of ionization per unit volume of tissue, alpha particles are from 5 to 10 times more destructive than beta and gamma radiation. Second, with the exception of Sr^{90} and 61^{147} , the more abundant fission products that are accumulated in the skeleton have a half-life of less than one year, whereas the half-life of radium is approximately 1600 years. Most of these fission products have half-lives in the range of from two weeks to two months. Third, with the exception of strontium and barium, a negligible degree of absorption of the fission products takes place through the digestive tract.

Yttrium, zirconium, columbium, and the lanthanide rare earths are deposited to a high degree in the immediate vicinity of the bone marrow as contrasted to the more diffuse distribution of strontium, and presumably barium, throughout the mineral structure of the bone. This behavior tends to enhance the radio-toxicity of this group of fission products both on the basis of geometrical considerations and a minimal amount of self absorption of the beta radiation, which is quite soft for several of the fission products under discussion.

The actinide series of elements in general share the dangerous characteristics of radium, namely long half-lives, alpha particle emission, and selective deposition with prolonged retention in the skeleton. Their tendency to deposit themselves adjacent to the bone marrow potentially gives them a relatively great degree of radio-toxicity than radium. The

only important metabolic property of the actinide elements that tends to reduce their hazardous quality is the fact that absorption from the digestive tract is negligible as compared to radium.

The second aspect of the studies described in this report is the apparent correlation of the chemical properties of a number of the different elements with their metabolic behavior. It can be seen from Table I that of the fission products described in this report there are two members of the alkaline earths, strontium and barium, four members of the lanthanide series of rare earths, lanthanum, cerium, praseodymium, and element 61, and yttrium whose chemical properties are similar to the lanthanide group of elements. The behavior of strontium and barium are essentially indistinguishable insofar as their assimilation, distribution, retention, and excretion are concerned, as determined by following their fate in the body using carrier-free radio-isotopes of these two elements. The outstanding metabolic characteristics shared by both are their ease of absorption from the digestive tract, selective deposition and prolonged retention in bone, relatively minute accumulation in any of the soft tissues, and slow rates of elimination. The radioautographic studies of bone indicate that strontium is deposited primarily in the mineral structure. It is presumed likely that a similar pattern of distribution in the bone would be observed with barium. A number of factors which are known to affect the calcium metabolism of bone, such as age, calcium deficient diet, pregnancy, prolonged lactation, phosphorus deficient diet, rickets, fracture, a number of drugs such as ammonium chloride, and the parathyroid hormone influence the metabolism of carrier-free radio-strontium in the same direction and to a comparable degree (15) (16) (17) (18). Similar studies with barium are now in progress and preliminary results indicate a close resemblance in the behavior of this element to strontium in all of the circumstances listed above that have been

subjected to study at the present time (19).

The four rare earths and yttrium share the common properties of (1) negligible absorption from the digestive tract, (2) a high degree of deposition and prolonged retention by the skeleton, (3) excretion primarily via the digestive tract, and (4) an appreciable accumulation in several of the soft tissues, notably liver, kidney, and spleen. The metabolism of zirconium and columbium is similar in many respects to the five elements listed above although columbium is apparently eliminated more rapidly from the skeleton than the others. The four lanthanide rare earths share in common the phenomena of the very high transient uptake by the liver. The fact that this does not take place with yttrium is noteworthy in view of the fact that this element is quite similar chemically to the lanthanide rare earths.

When the histological structure of bone is compared with the regions of deposition of these different fission products in bone, a number of different interesting points arise. The fact that strontium and barium are laid down in the calcium-containing mineral portion of the bone is reasonable in view of the similar chemical properties of the alkaline earths. That none of the other fission products behaved in this manner in bone was not predictable, and as has been mentioned before, yttrium, zirconium, columbium, and the rare earths are apparently laid down primarily in the non-mineralized areas. As yet it has not been definitely established that some of the material combines with the superficial surfaces of the mineralized structure of the bone. An interesting variation occurs which is peculiar to the rare earths only, namely the deposition of some activity in the regions of the small blood vessels within the heavy mineralized shaft of the bone. The radioautographic data that demonstrates this point is only available for cerium and element 61 due to the relatively shorter half-lives of La^{140} and Pr^{143} . However, it appears almost certain that

lanthanum, praseodymium, and neodymium would give the same pattern of distribution in the bone, It will be noted that this effect is correlated with the high but transient uptake of the four rare earths by the liver. The uptake by the liver of yttrium, zirconium and columbium is relatively small, as compared to the lanthanide series, and no appreciable activity appears in the region of the small blood vessels of cortical bone.

If the effects of the various agents which alter calcium and strontium metabolism of the skeleton are tried with representative members of the fission product series, notably yttrium, zirconium and cerium, the results indicate that their deposition, retention and distribution in bone remain essentially unchanged (15) (16) (17). Presumably the same indifference to these agents would apply to other members of the lanthanide rare earths. In the case of columbium it is not as completely predictable but a similar lack of effect would be likely.

The metabolic behavior of the actinide series of rare earths brings forth a number of interesting apparent correlations. The most impressive is the fact that actinium, americium, and curium behave in an almost indistinguishable manner from the lanthanide rare earths. This quality of apparent metabolic identity includes the phenomena of high liver uptake and the accumulation of material about the small blood vessels of cortical bone. Presumably this situation arises from the fact that these three members of the actinide series and the four lanthanide rare earths studied are all trivalent with chemical properties of great similarity. These observations tie in closely with the prediction and subsequent demonstration by Seaborg and his colleagues (20) that the chemical properties of americium and curium should resemble closely those of lanthanide rare earths and actinium. While uranium, neptunium, and plutonium all possess the trivalent state, they are treated in the animal body quite differently from these

other two groups of bivalent elements. Neptunium and plutonium are much alike in their metabolic characteristics and in turn resemble thorium, which normally only exists in the plus four valence state. Since plutonium follows the same metabolic pattern, whether administered as Pu^{+3} , Pu^{+4} , or Pu^{+6} , it appears that the body converts it to one valence state. The tracer studies and bone radioautographs show no significant differences between the metabolic characteristics of thorium and plutonium which suggests that plutonium in the body is in the tetravalent state, regardless of the valency of the administered material. The same situation is likely with neptunium, but sufficient data is not yet available to establish this point.

This view has added evidence from the behavior of uranium which is rather different than the other seven members of the actinide series in that the uptake and retention by the skeleton is less, excretion is primarily by way of the urine, and there is a very high and fairly prolonged accumulation in the kidney. It would appear likely that U^{+3} would behave like the lanthanide rare earths, actinium, americium and curium. On the same basis U^{+4} should resemble metabolically thorium and plutonium, which it doesn't. Since U^{+5} is very unstable under most conditions, it seems plausible, but not certain, that uranium in the body exists as U^{+6} in the form of UO_2^{++} or may be complexed with the carbonates present in the body.

The effects of agents which alter calcium and strontium metabolism has only been investigated with one of the actinide group, namely plutonium (15) (16) (17). As in the case of the comparable studies with yttrium, zirconium, and cerium these agents did not disturb the normal metabolism of plutonium.

TABLE I

PART I

FISSION PRODUCTS

<u>Isotope</u>	<u>Half-Life</u>	<u>Type of Radiation</u>	<u>Method of Production</u>
Sr ⁸⁵	65 D	K, gamma, e ⁻	Rb-d-2n
Y ⁸⁸	87 D	K, gamma	Sr-d-2n
Zr ⁸⁹	78 hr	Positron	Y-d-2n
Zr ⁹⁵	65 D	B ⁻ , gamma	U-n
Cb ⁹⁵	37 D	B ⁻ , gamma	Zr ⁹⁵ B ⁻ decay
Ru ¹⁰³	42 D	B ⁻ , gamma	U-n
Ru ¹⁰⁶	1.0 Y	B ⁻	U-n
Te ¹²⁷	90 D	I.T., e ⁻ , x-ray	U-n
Te ¹²⁹	32 D	I.T., e ⁻	U-n
I ¹³¹	8.0 D	B ⁻ , gamma	Te ¹³⁰ -d-p, Te ¹³¹ B ⁻ decay
Xe ¹²⁷	34 D	K, gamma, e ⁻	I-d-2n
Cs ¹³⁷	33 Y	B ⁻ , gamma	U-n
Ba ¹³³	38.8 hr	I.T., gamma, e ⁻	Cs-d-2n
Ba ¹⁴⁰	12.8 D	B ⁻ , gamma, e ⁻	U-n
La ¹⁴⁰	40.0 hr	B ⁻ , gamma	Ba ¹⁴⁰ B ⁻ decay
Ce ¹⁴¹	28 D	B ⁻ , gamma	U-n
Ce ¹⁴⁴	275 D	B ⁻	U-n
Pr ¹⁴³	13.8 D	B ⁻	U-n
Pr ¹⁴⁷	3.7 Y	B ⁻	U-n

PART II

ACTINIDE ELEMENTS

Ac ²²⁷	13.5 Y	B ⁻ (99%) alpha (1%)	Ra ²²⁶ -n-gamma, Ra ²²⁷ B ⁻ decay
Th ²³⁴	24.5 D	B ⁻ , gamma	U ²³⁸ Alpha decay
Pa ²³³	27.4 D	B ⁻ , gamma, e ⁻	Th ²³² -d-p, Th ²³³ B ⁻ decay
U ²³³	10 ⁵ Y	Alpha	Pa ²³³ B ⁻ decay
Np ²³⁹	2.2 D	B ⁻ , gamma	U ²³⁸ -d-p, U ²³⁹ B ⁻ decay
Pu ²³⁹	2.2 X 10 ⁴ Y	Alpha	Np ²³⁹ B ⁻ decay
Am ²⁴¹	500 Y	Alpha	Pu-alpha-p,n
Cm ²⁴²	150 D	Alpha	Pu-alpha-n

SUMMARY OF THE METABOLISM OF THE PRINCIPAL MEMBERS OF THE
LONG-LIVED FISSION PRODUCTS AND CERTAIN OF THE FISSIONABLE
ELEMENTS IN THE RAT FOLLOWING PARENTERAL AND ORAL ADMINIS-
TRATION

<u>RADIO ELEMENT</u>	<u>HALF LIFE</u>	<u>FISSION YIELD</u>	<u>% ORAL ABSORB-TION</u>	<u>% ACCUMULATION IN PRINCIPAL ORGAN OF RETENTION</u>	<u>RATE OF ELIMINATION FROM PRINCIPAL ORGANS OF RETEN.</u>
Strontium					
Sr ⁸⁹	53 D	4.6%	5-60%	65% Bone	Bone > 200 D
Sr ⁹⁰	25 Y		5-60%	65% Bone	Bone > 200 D
Barium					
Ba ¹⁴⁰	12.8 D	6.1%	5-60%	65% Bone	Bone > 50 D
Iodine					
I ¹³¹	8.0 D	2.8%	100%	30% Thyroid	Thyroid > 30 D
Cesium					
Cs ¹³⁵	33 Y		100%	45% Muscle	Muscle 15 D
Yttrium					
Y ⁹¹	57 D	5.9%	< 0.05%	65% Bone	Bone > 500 D
Lanthanum					
La ¹⁴⁰	40 H	6.1%	< 0.05%	{ 65% Liver 25% Bone	{ Liver 10 D Bone > 25 D
Cerium					
Ce ¹⁴¹	28 D	5.7%	< 0.05%	55% Liver	Liver 10 D
Ce ¹⁴⁴	275 D	5.3%	< 0.05%	25% Bone	Bone > 200 D
Praseodymium					
Pr ¹⁴³	13.8 D	5.4%	< 0.5%	{ 30% Liver 40% bone	{ Liver 10 D Bone > 100 D
Element 61					
61 ¹⁴⁷	3.7 Y	2.6%	< 0.05%	{ 50% Liver 30% bone	{ Liver 10 D Bone > 100 D
Zirconium					
Zr ⁹⁵	65 D	6.4%	< 0.05%	45% Bone	Bone > 100 D
Columbium					
Cb ⁹⁵	37 D	6.4%	< 0.5%	{ 40% Bone 25% Blood	{ Bone 30 D Blood 1 D
Ruthenium					
Ru ¹⁰³	42 D	3.7%	< 0.05%	3.5% Kidney	Kidney 20 D
Ru ¹⁰⁶	1 Y	0.5%	< 0.05%	3.5% Kidney	Kidney 20 D
Tellurium					
Te ¹²⁷	90 D	0.033%	25%	15% Blood	Blood 15 D
Te ¹²⁹	32 D	0.19%	25%	6% Kidney	Kidney 15 D
Thorium					
Th ²³⁴	24.5 D		< 0.05%	50% Bone	Bone > 200 D
Protoactinium					
Pa ²³¹	3 X 10 ⁴ Y		< 0.05%	40% Bone	Bone > 100 D
Neptunium					
Np ²³⁹	2.2 D		< 0.05%	60% Bone	Bone > 50 D
Plutonium					
Pu ²³⁹	2.2 X 10 ⁴ Y		0.007%	65% Bone	Bone > 2 Y
Americium					
Am ²⁴¹	500 Y		< 0.05%	{ 70% Liver 25% Bone	{ Liver 10 D Bone > 1 Y
Curium					
Cm ²⁴²	150 D		< 0.05%	{ 70% Liver 25% Bone	{ Liver 10 D Bone > 1 Y
Xenon					
Xe ¹³³	5.3 D	4.5%		Distribution proportional to fat content of body; half-time* in the body two hours	
Actinium					
Ac ²²⁷	13.5 Y		< 0.05%	{ 45% Liver 30% Bone	{ Liver > 4 D Bone > 4 D
Uranium					
U ²³³	1.6 X 10 ⁵ Y		< 0.05%	{ 40% Kidney 40% Bone	{ Kidney 4 D Bone 60 D

* Human studies

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FIG. I: DEPOSITION OF CARRIER FREE FISSION PRODUCTS IN THE SKELETON OF THE RAT FOLLOWING THEIR PARENTERAL ADMINISTRATION

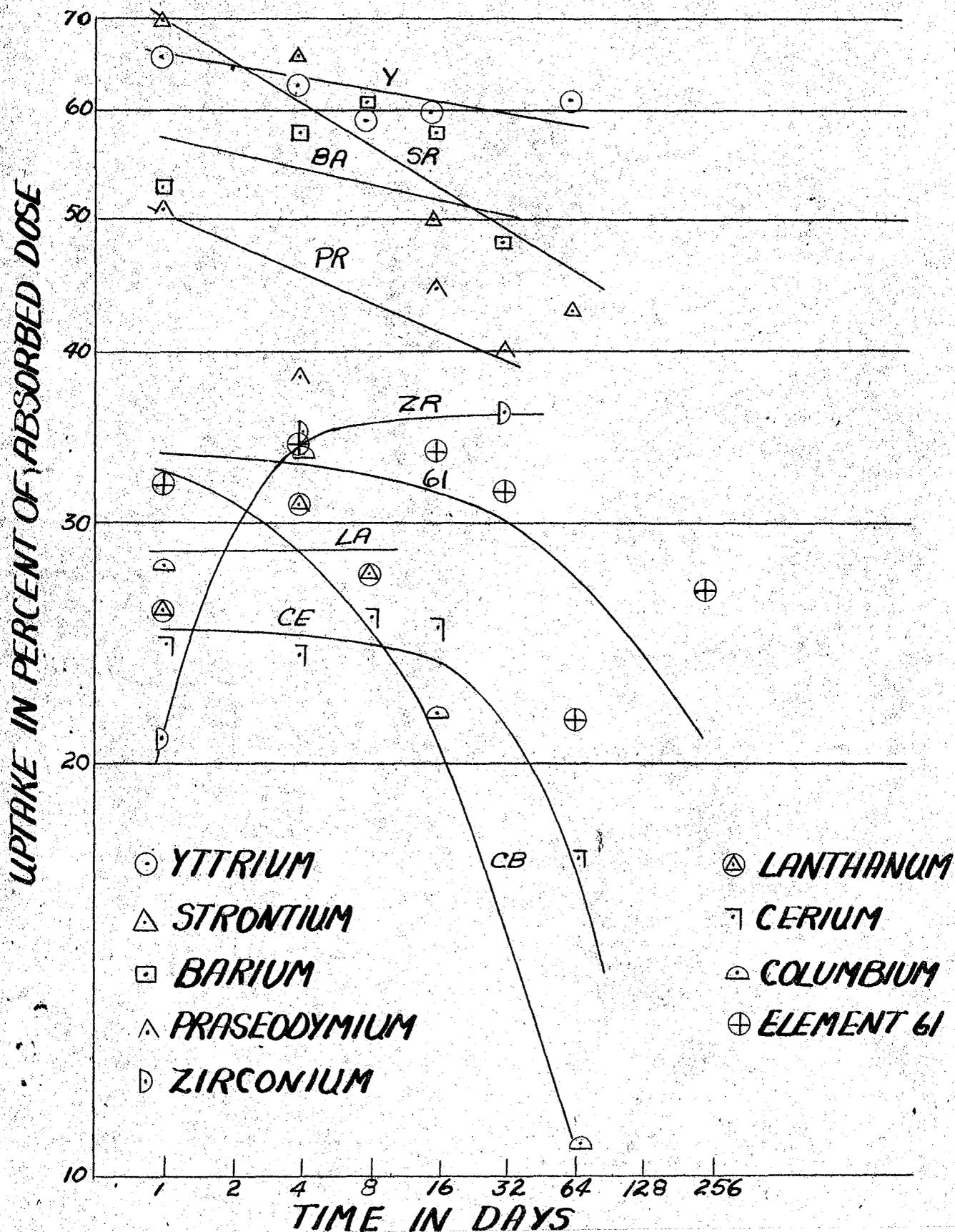


FIG. II: DEPOSITION OF ACTINIUM, THORIUM, PROTOACTINIUM, URANIUM, NEPTUNIUM, PLUTONIUM, AMERICIUM AND CURIUM IN THE SKELETON OF THE RAT FOLLOWING THEIR PARENTERAL ADMINISTRATION

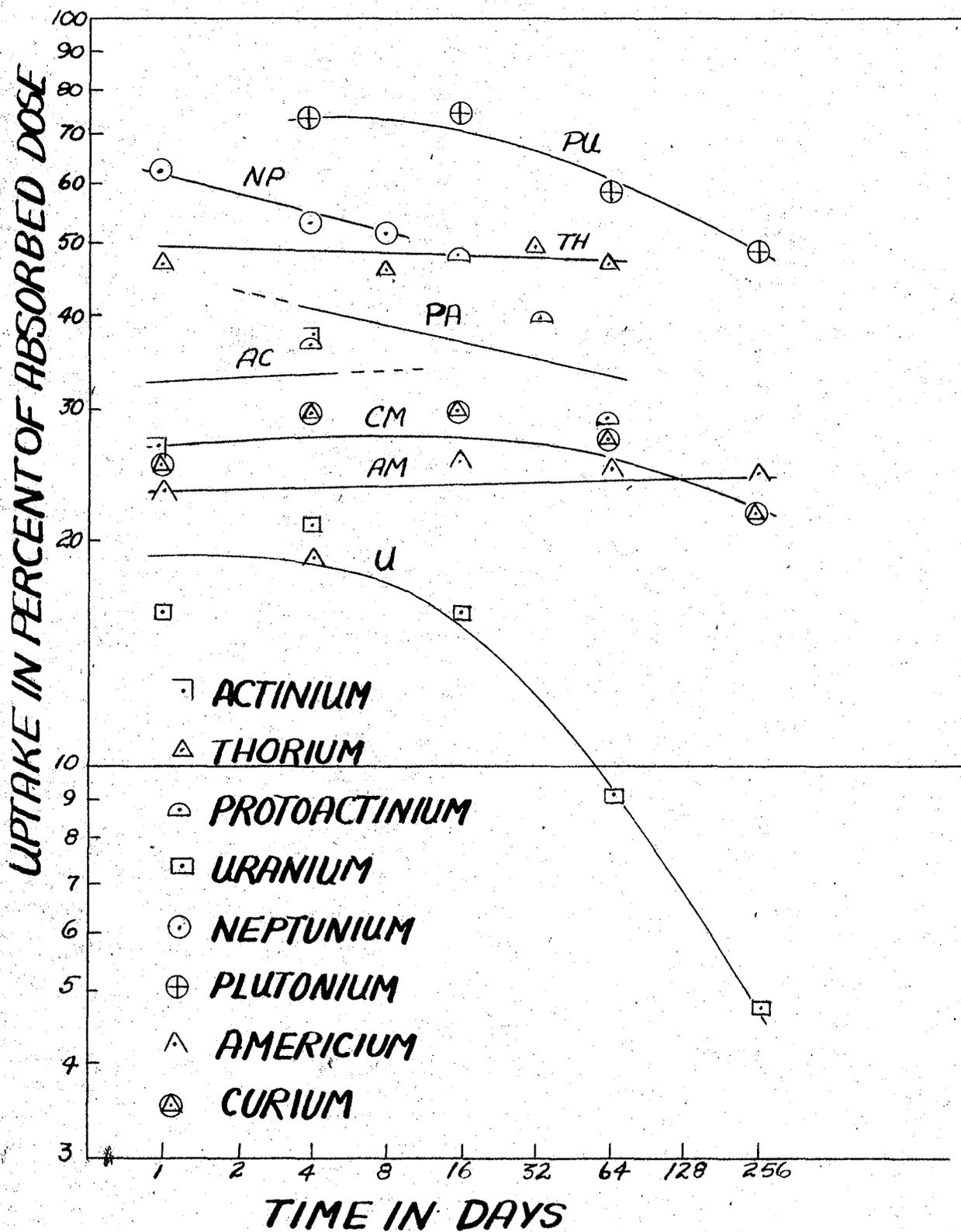


FIG. III : DEPOSITION OF CARRIER FREE FISSION PRODUCTS IN THE LIVER OF THE RAT FOLLOWING THEIR PARENTERAL ADMINISTRATION

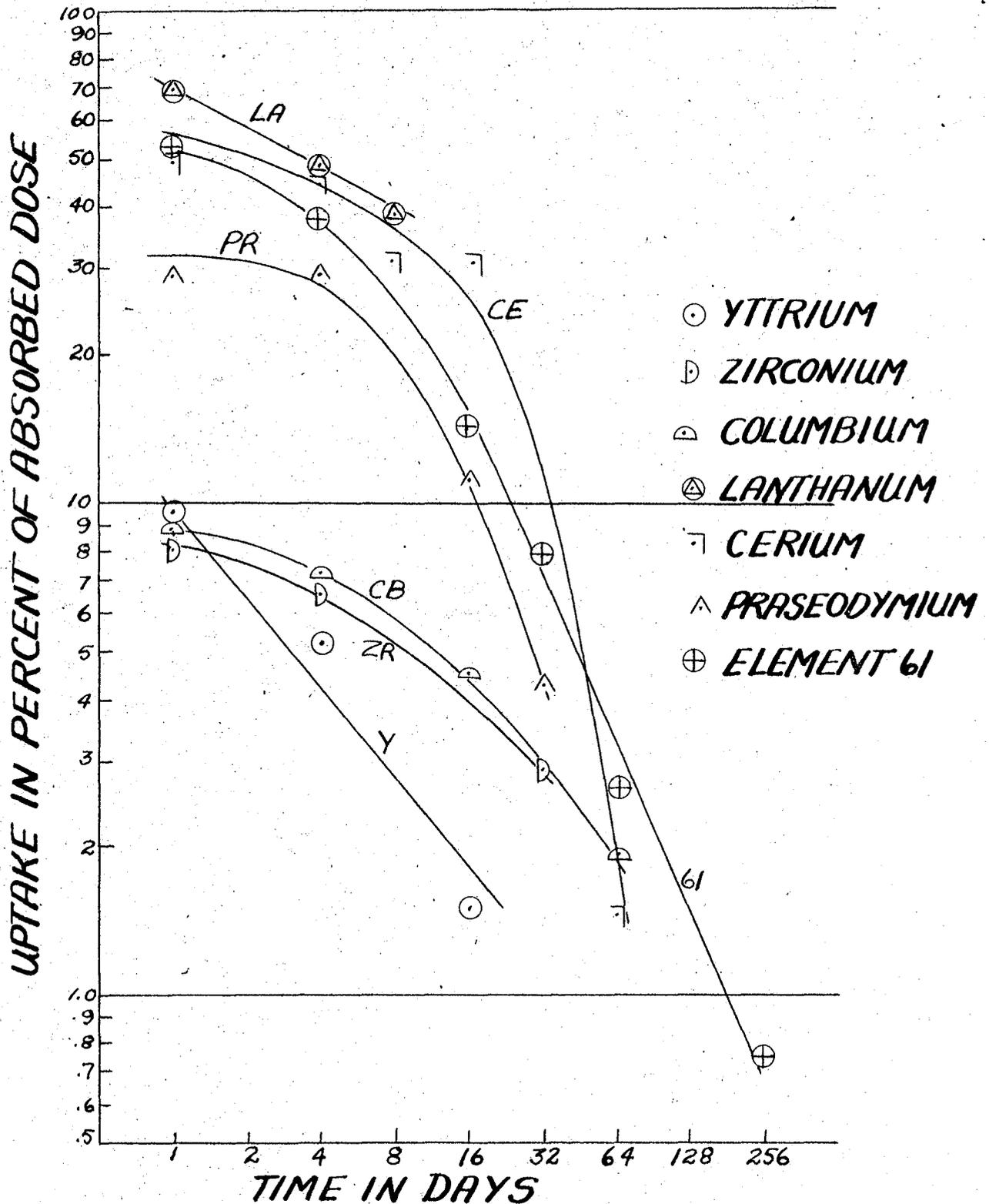


FIGURE 5

Femur from young rat injected with radio-strontium
and sacrificed at 1 week. Note strontium deposition
in shaft and calcified areas below epiphysis. (X $6\frac{1}{2}$)

X-5

AP-12



X-5

AP-12



FIGURE 6

Femur from adult rat injected with plutonium and sacrificed at 8 weeks. Note superficial plutonium deposition in area of trabecular bone, periosteum, and endosteum. A comparable pattern is found after 7 days and 256 days. (X 10)

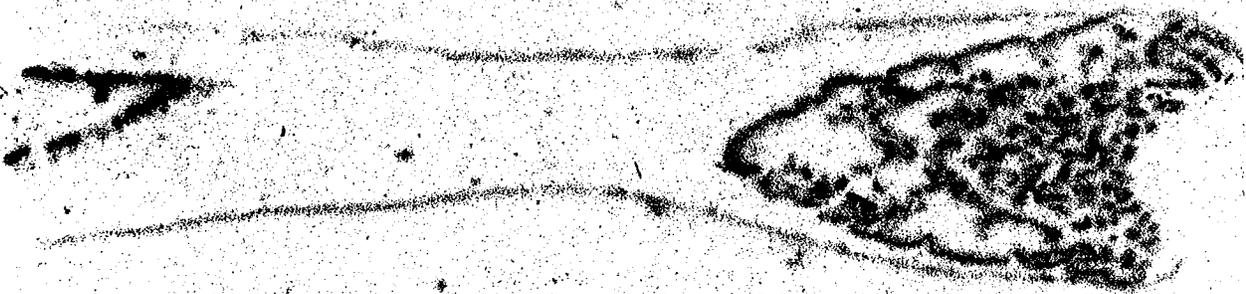
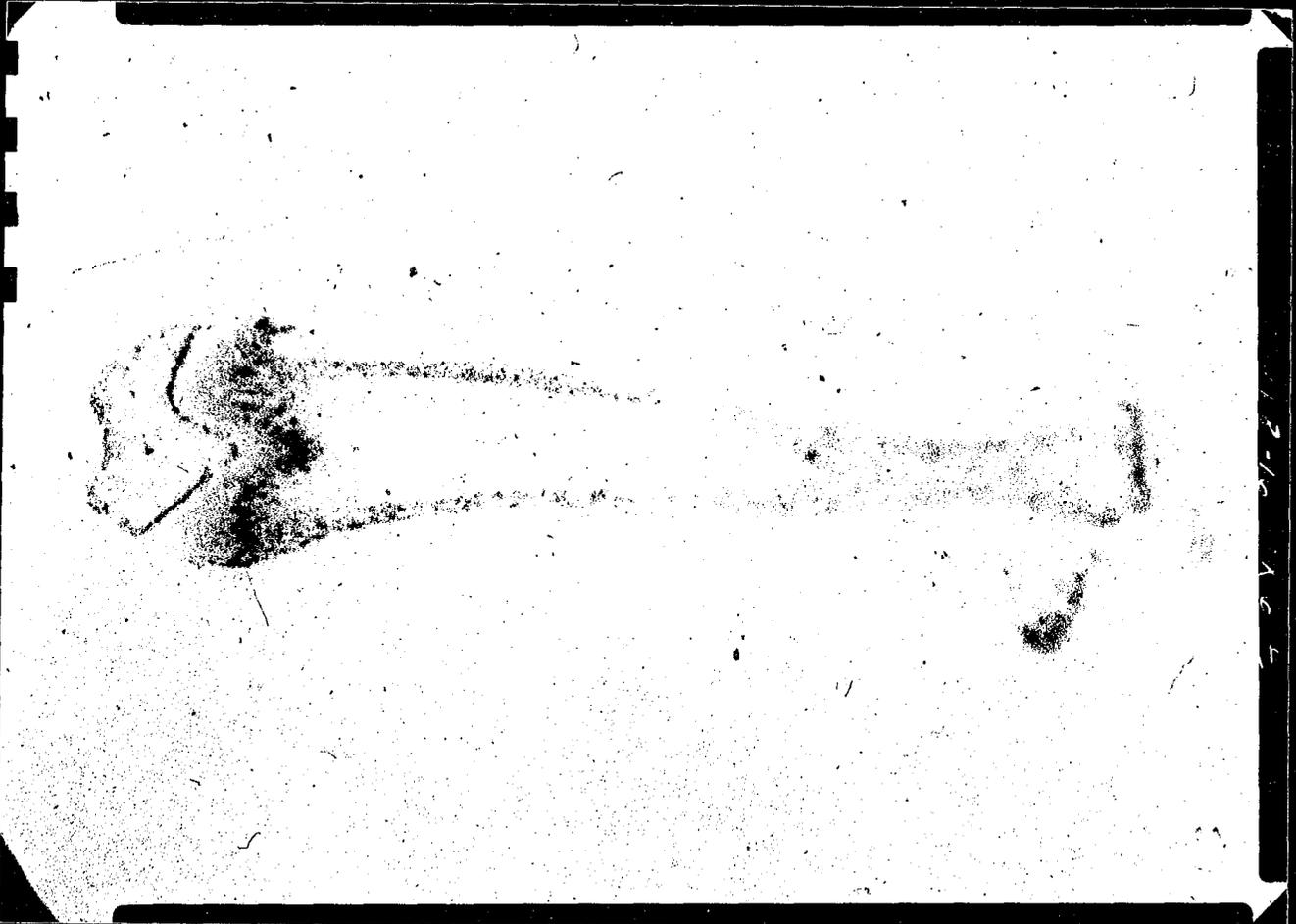
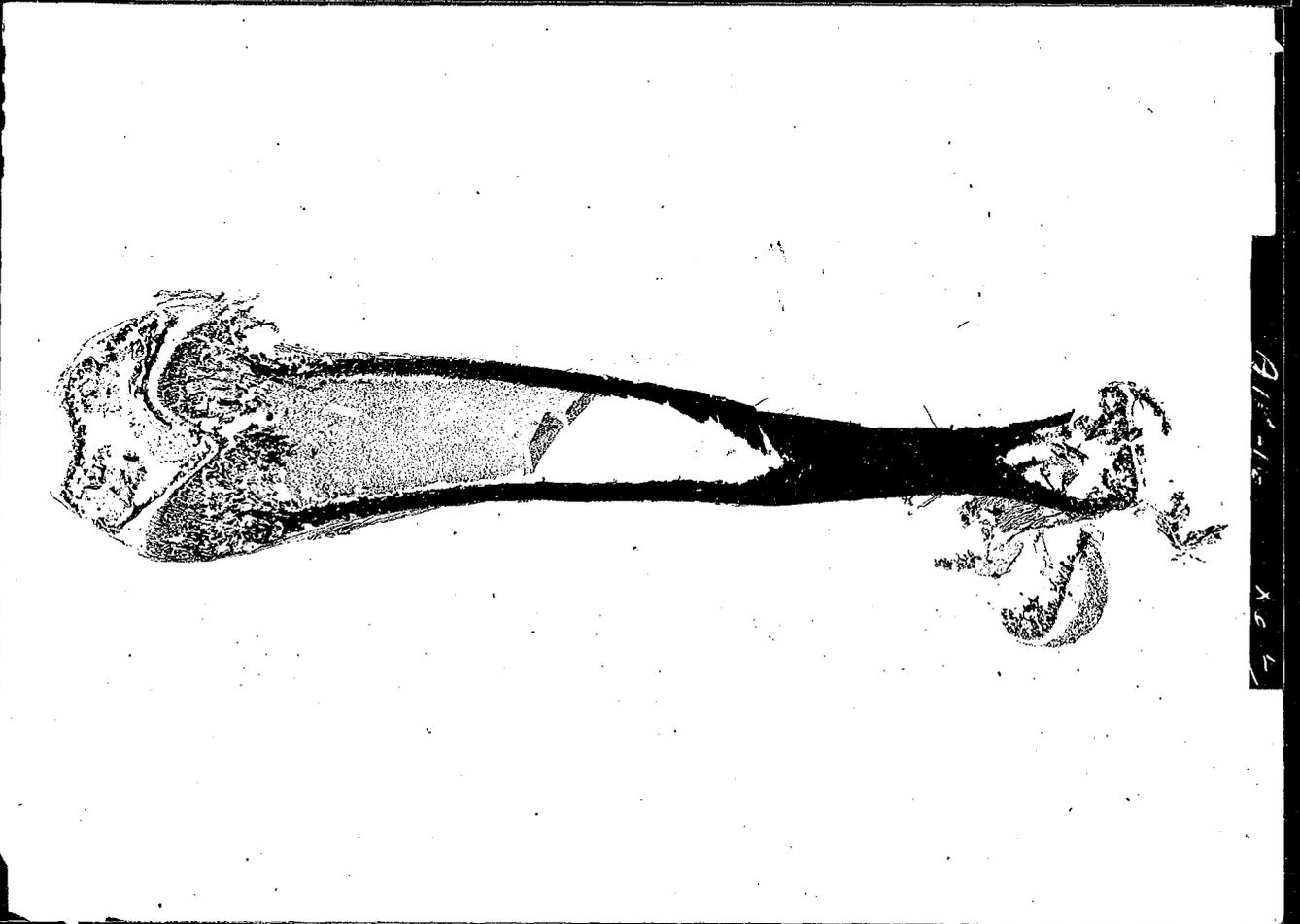


FIGURE 7

Femur from adult rat injected with yttrium and sacrificed at 2 weeks. Note deposition in compact bone shaft and the high concentration in bone trabeculae. (X $6\frac{1}{2}$)



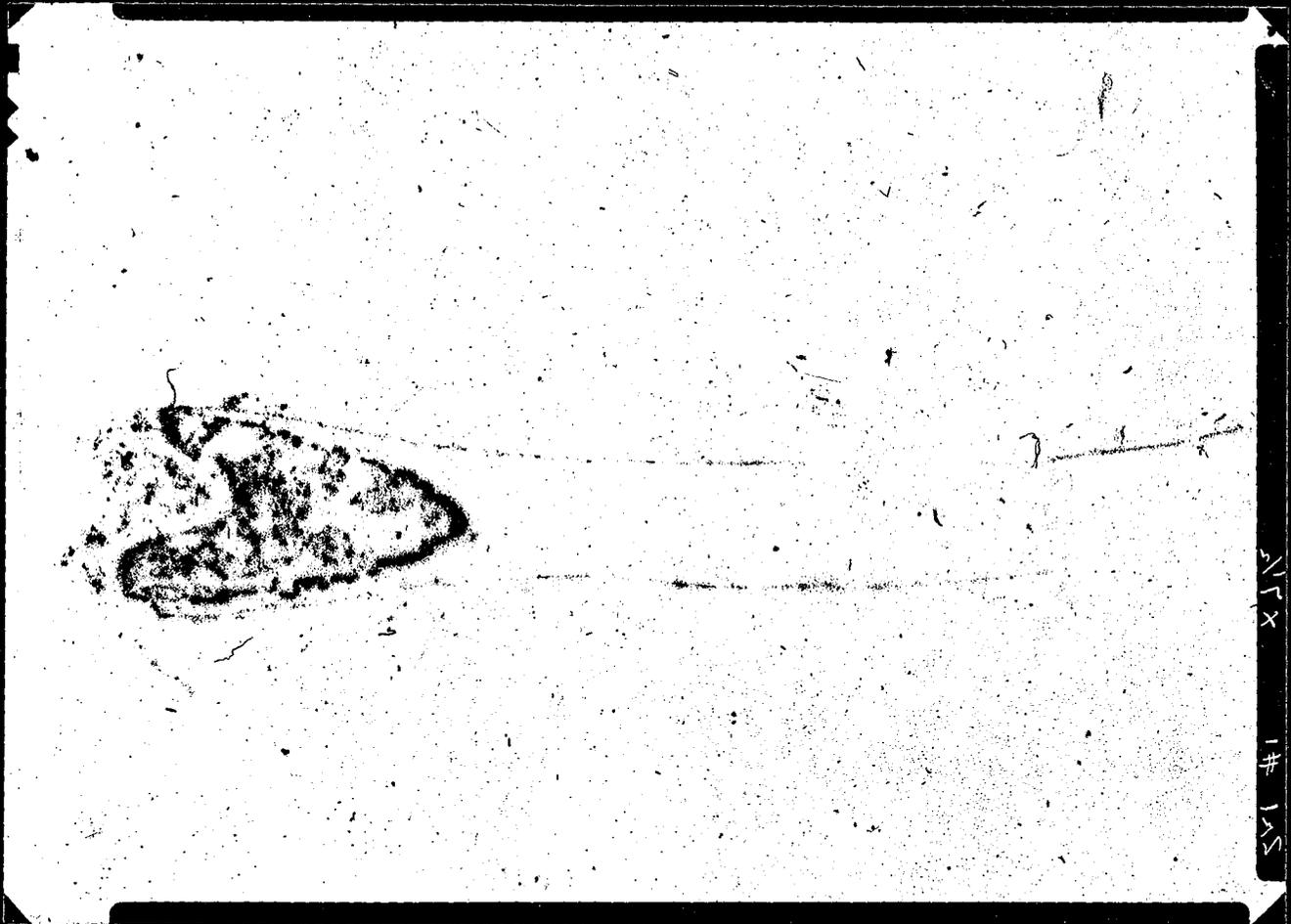
17-10 X 5 L



21-10 X 5 L

FIGURE 8

Femur from adult rat injected with zirconium and sacrificed at 2 weeks. Note similarity to plutonium deposition in Figure 6. (X $7\frac{1}{2}$)



155
#



156
#

FIGURE 9

Femur from adult rat injected with columbium and sacrificed at 8 days. Superficial deposition appears to be similar to that of plutonium and zirconium.

(X 14)

CP (A) #5 X (H)



CP (A) #5 X (H)



FIGURE 10

Femur from adult rat injected with thorium and sacrificed at 8 days. Superficial deposition resembles zirconium, columbium, and plutonium bone deposition. (X 8)

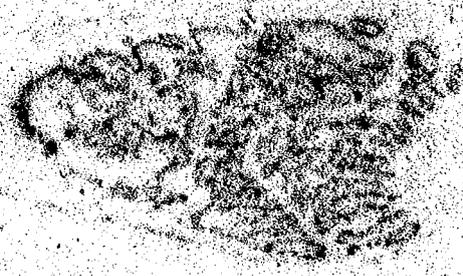
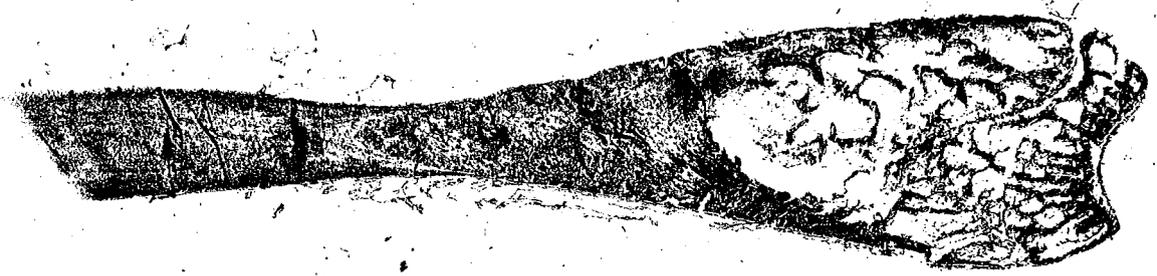
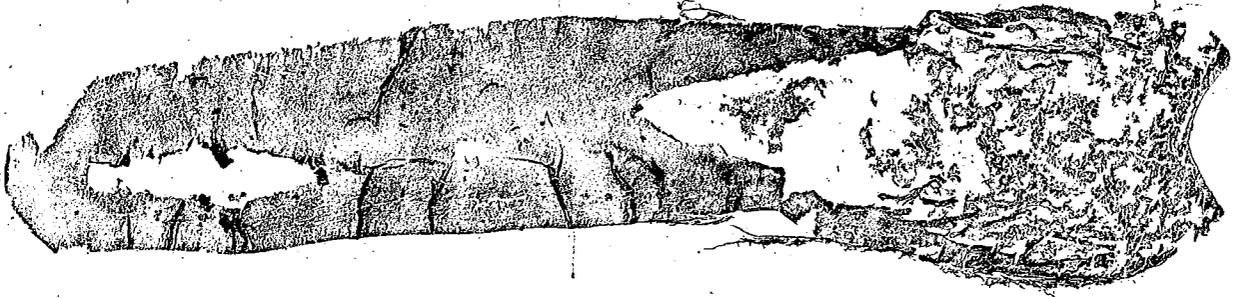


FIGURE 11

Femur from adult rat injected with cerium and sacrificed at 64 days. Note cerium deposition on surface of bone and the spotty distribution in the shaft. (X 8)

8X 1# 25



8X 1# 1 X 8

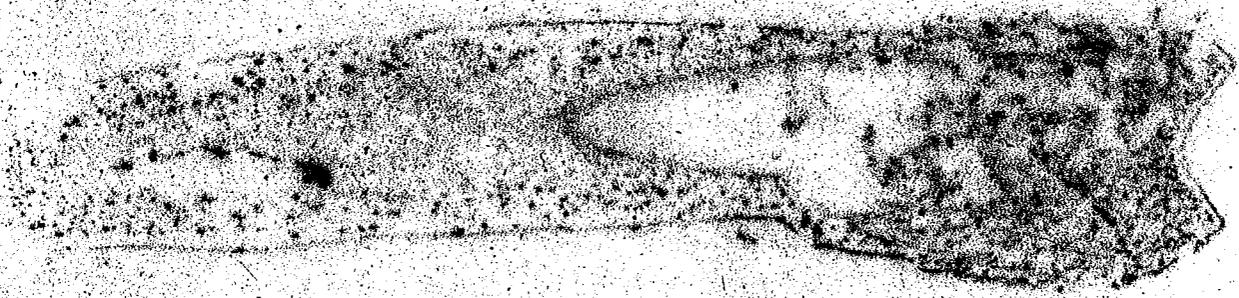


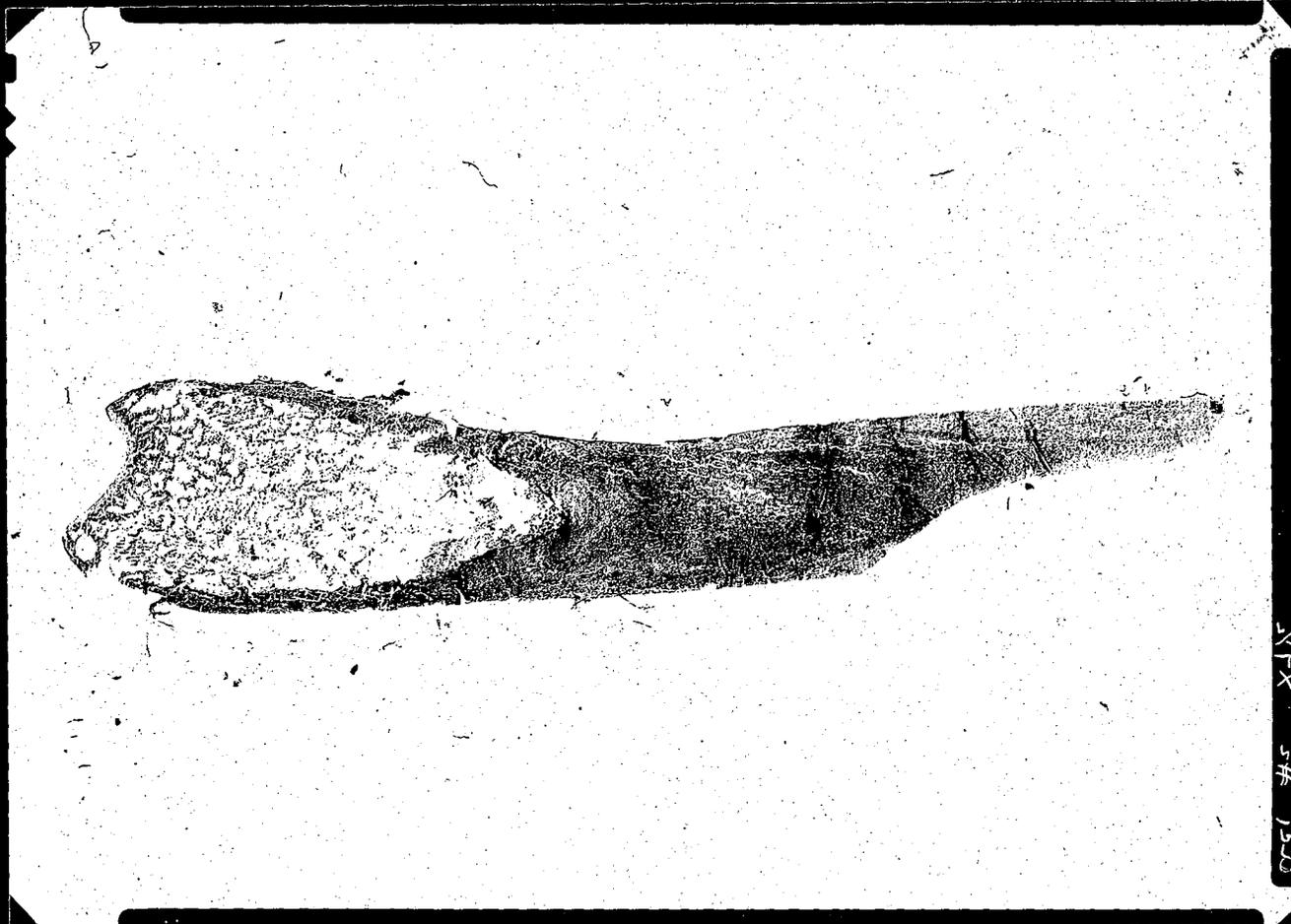
FIGURE 12

Femur from adult rat injected with element 61 and sacrificed at 4 days. Note resemblance to cerium (Fig. 11), i.e. superficial deposition and spotty distribution throughout calcified shaft. Note surface deposition on trabecular bone. (X 7)

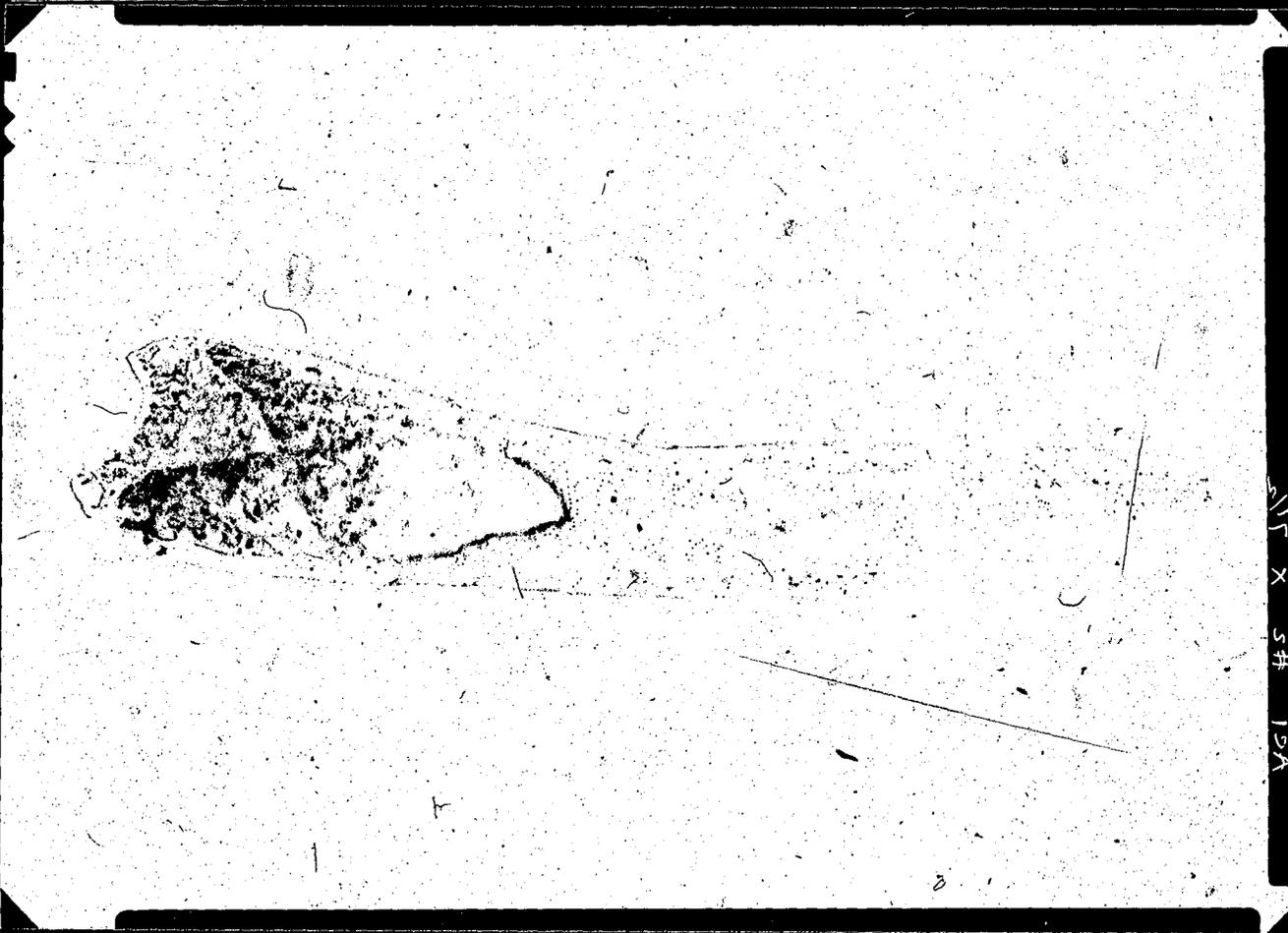


FIGURE 13

Femur from adult rat injected with actinium and sacrificed at 17 days. Note resemblance to cerium and element 61. The specimen was allowed to age for 100 days before making the autograph to permit equilibrium of the radioactive daughter to be attained. (X $7\frac{1}{2}$)



SIX #4 153



SIX #4 154

FIGURE 14

Femur from adult rat injected with americium
and sacrificed at 16 days. Note similarity to cerium,
element 61, and actinium. (X 8)

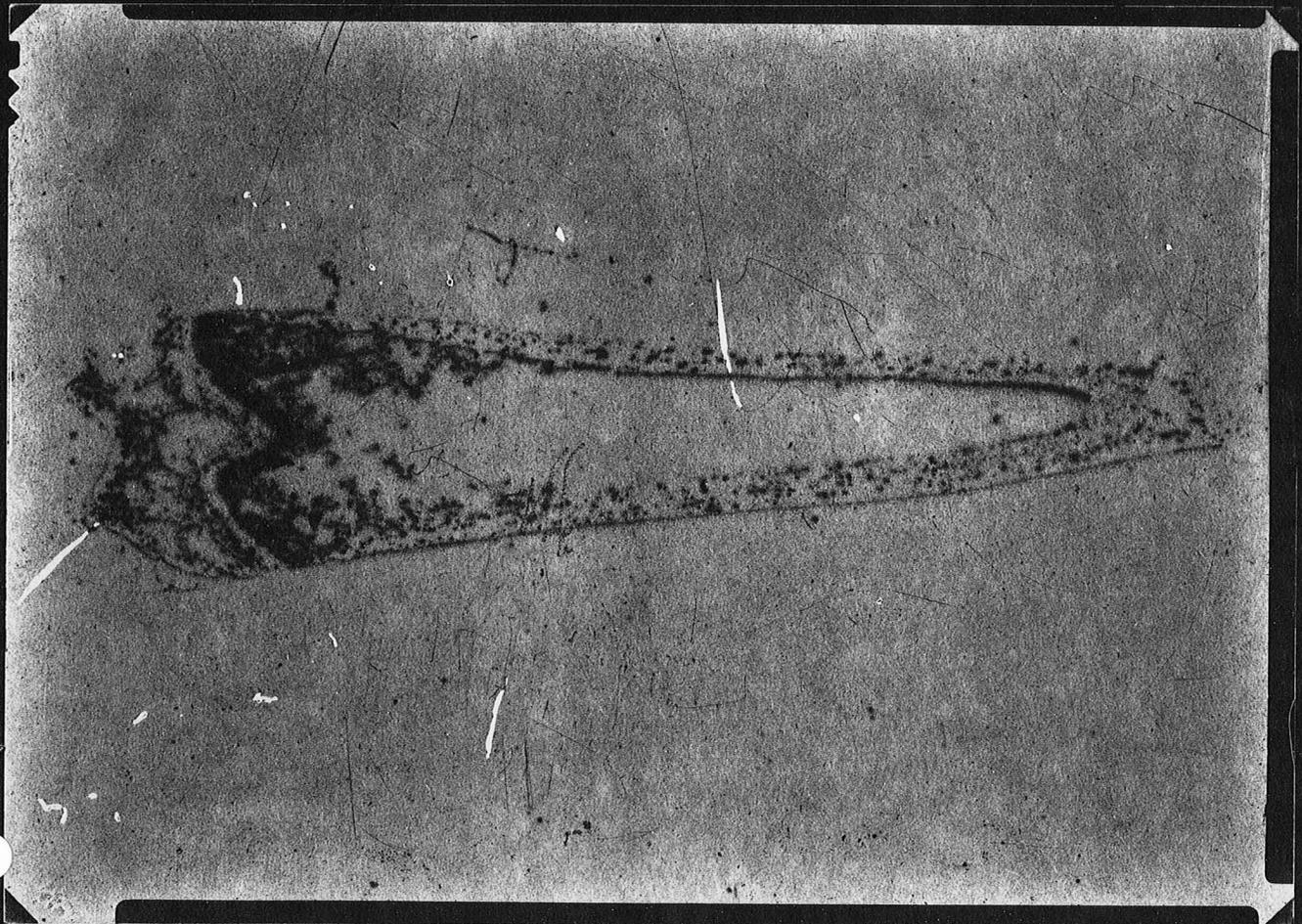
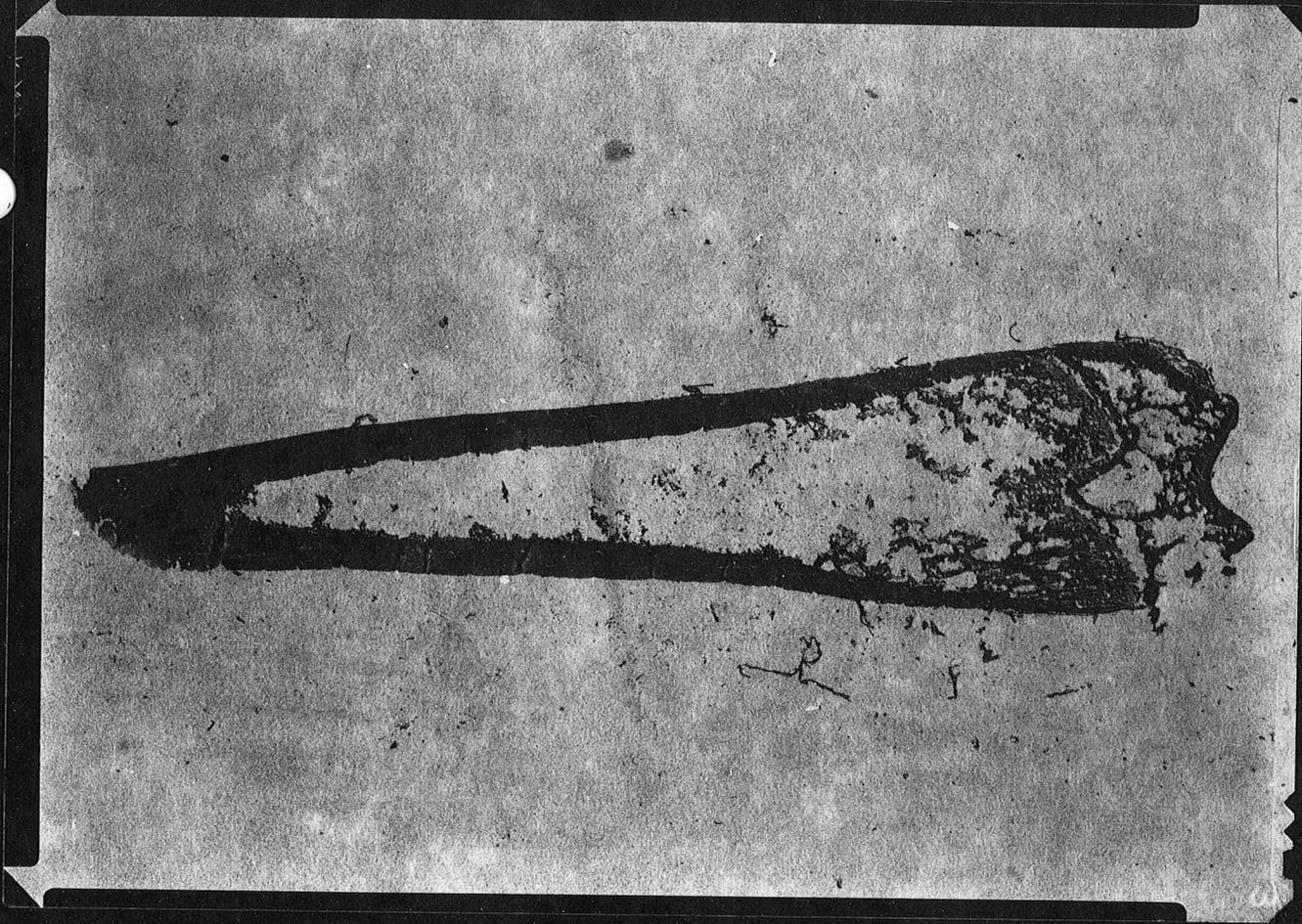


FIGURE 15

Femur from adult rat injected with curium and sacrificed at 7 days. Note similarity to cerium, element 61, actinium, and americium. (X 7)

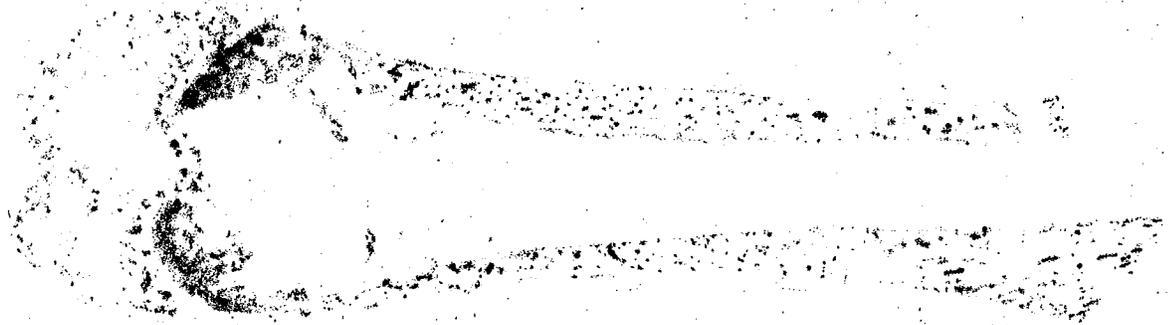


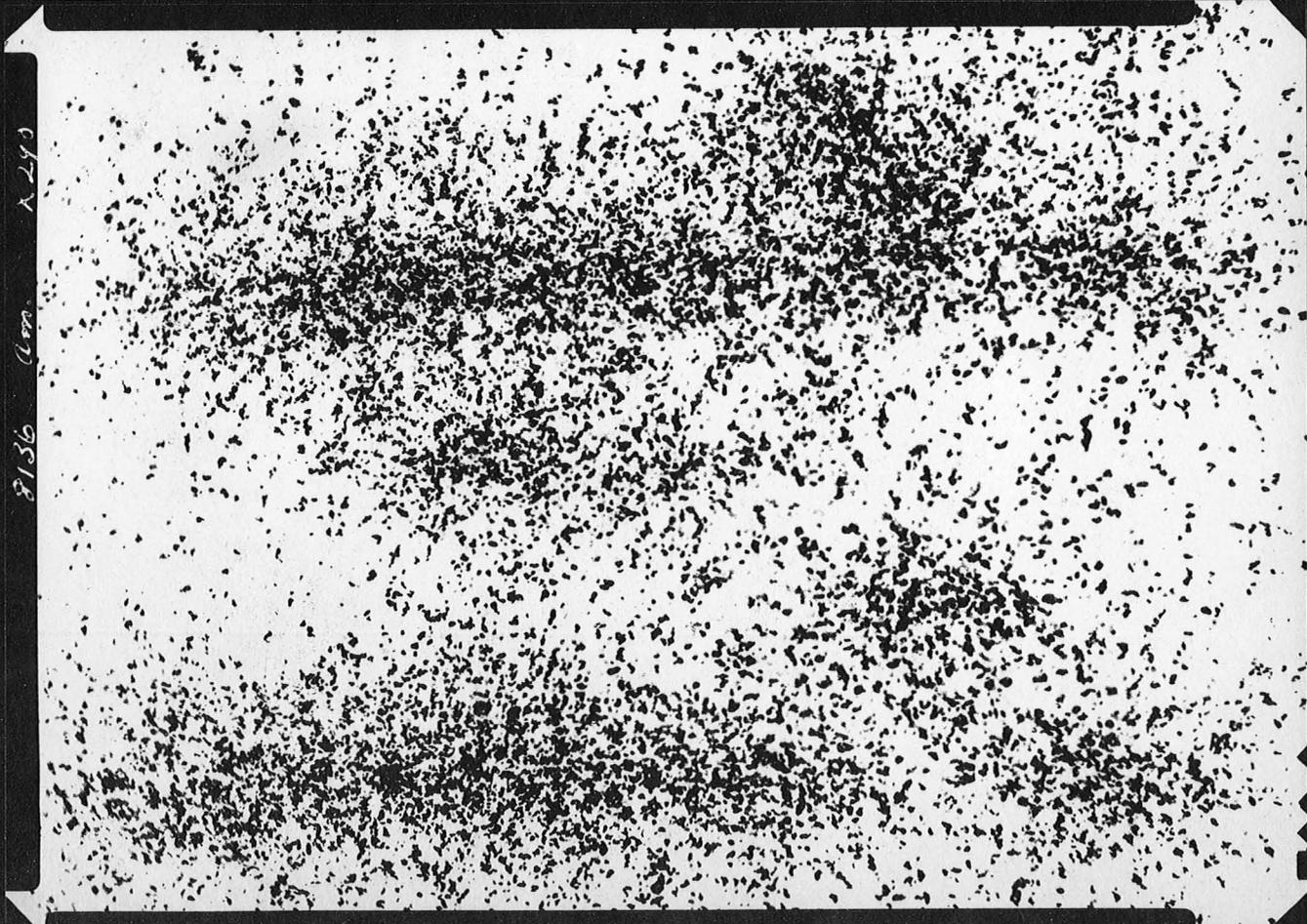
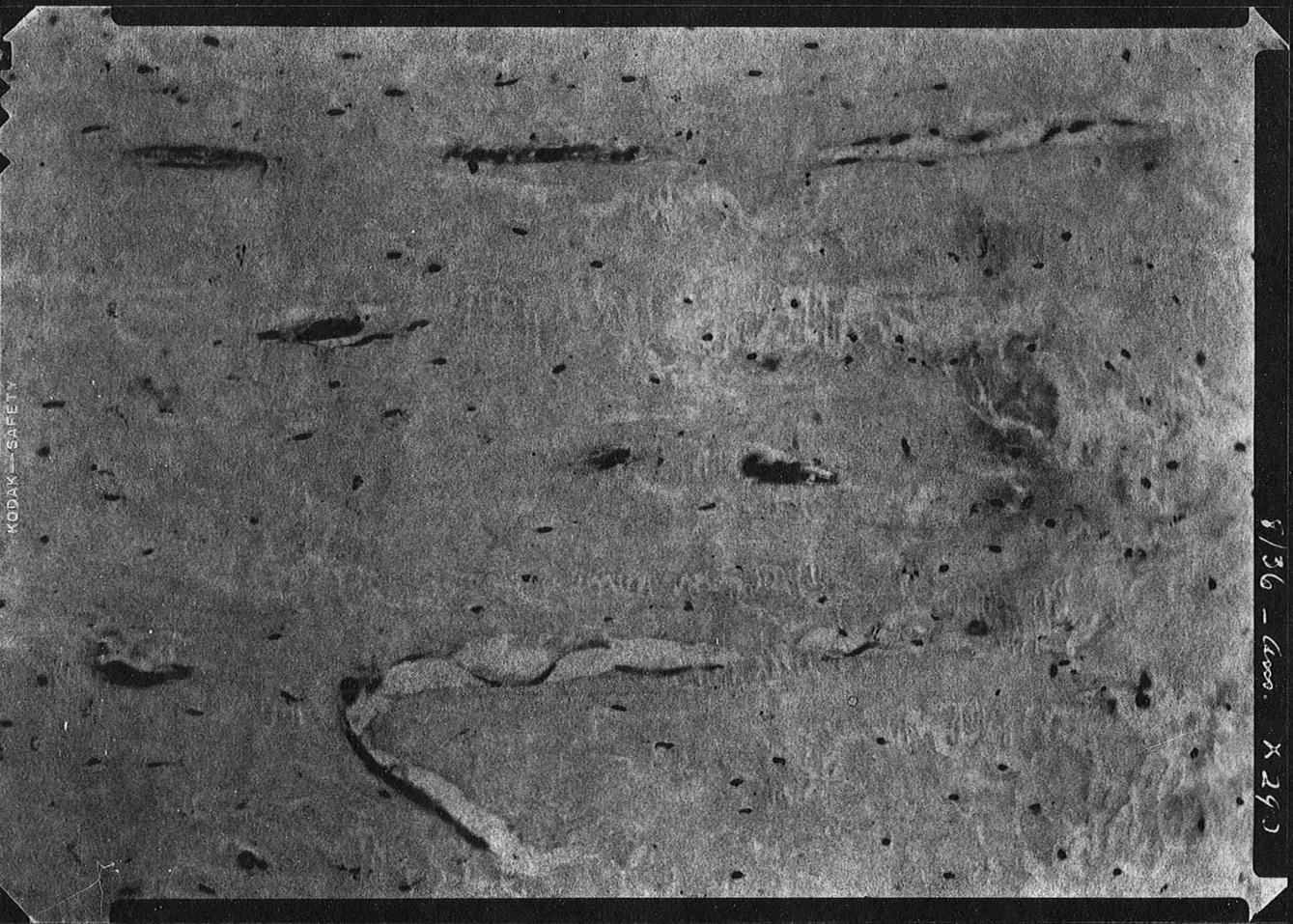
FIGURE 16

Higher power magnification of a section of femur and americium radioautograph shown in Fig. 14. Note deposition of americium in the region adjacent to the blood vessels of the shaft. (X 270)

KODAK SAFETY

8/36 - (1000) X 29)

8/36 (1000) X 29)



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