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TRANSLOCATION DYNAMICS OF 239-PLUTONIUM

By

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A Study of the Translocation of Plutonium and
Americium From Puncture Wounds

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ABSTRACT OF THESIS

TRANSLOCATION DYNAMICS OF ^{239}Pu -PLUTONIUM

The translocation dynamics of $^{239}\text{Pu}(\text{NO}_3)_4$ and $^{239}\text{PuO}_2$ from simulated puncture wounds in the paws of beagle dogs were studied. The difference between the more soluble $\text{Pu}(\text{NO}_3)_4$ form and the insoluble "high fired" PuO_2 was assumed to bring about highly differing translocation dynamics from the wound site, through lymphatic channels into the system's circulation and organs of deposition and of excretion. The study provided data on the relative translocation of Pu and Am. Half of the dogs were given chelation therapy with the trisodium calcium salt of diethylenetriaminepentaacetic acid (DTPA).

The first major lymph node draining the site of implant collected a significant fraction of the implanted radioactive material. The kinetics of removal of the material from the paw and the buildup of lymph node activity were studied by in vivo measurement techniques and by radiochemical analysis performed on the alpha activity in selected tissues collected at necropsy. Equations describing the dynamics of the activity were fitted to the data. Both chemical forms reached peaks in activity accumulation followed by a regression. These peaks appeared around 30 to 60 days for the soluble $\text{Pu}(\text{NO}_3)_4$ and

about 30 to 40 days in the "high fired" PuO_2 whose particles had a Geometric Mean Diameter $0.7 \mu\text{m}$.

The relative concentration or retention of Pu and Am was determined for all sample types collected. The dogs were serially necropsied, tissues samples collected and radiochemically analyzed for Pu and Am activity.

A greater relative concentration of Am over Pu occurred in the reticuloendothelial tissues of the PuO_2 dogs, the major soft tissues for concentrating Pu and Am. No significant enhancement of either Pu or Am in these tissues was found in the $\text{Pu}(\text{NO}_3)_4$ study. The thyroid gland was low in activity but did show an enhancement of Am in the PuO_2 study, but, no significant enhancement with the $\text{Pu}(\text{NO}_3)_4$ form. The proximal section of the femur on the other hand showed a high level of activity with a Pu enhancement over Am in the $\text{Pu}(\text{NO}_3)_4$ study but no significant difference for PuO_2 .

Administration of DTPA produced a significant decrease in Pu concentration in all tissues of the $\text{Pu}(\text{NO}_3)_4$ contaminated dogs except the kidney. In the PuO_2 experiment only the hepatic lymph node and proximal section of the femur showed a significant Pu reduction with DTPA. On the other hand, the liver and spleen had decreased uptake of Am with chelation treatment of both chemical forms, but, only in the $\text{Pu}(\text{NO}_3)_4$ form for the kidney and thyroid. The Am concentration appeared not to be affected by DTPA in the kidney for both forms and

in the proximal portion of the femur of the $\text{Pu}(\text{NO}_3)_4$ dogs. An interesting increase appeared to occur in the thyroids of DTPA treated PuO_2 dogs.

There was rapid movement of Pu from the paw to the first major lymph node with a resulting buildup and regression pattern for activity within the node. Differential translocation, concentration, retention, and excretion of Pu and Am were demonstrated with both chemical forms.

The following major points of consideration were borne out by this study:

- 1.) The shape of the buildup curve for Pu in the lymph node suggests a very rapid movement of the Pu from the wound site.
- 2.) The shape of the buildup curve also indicates a mechanism or means by which the plutonium deposited in the lymph node is able to move through the node and into the circulatory system.
- 3.) That the particle size of the contaminant plays an important role in the rate and total movement of the material from the wound site into the lymph nodes and into the systemic system.
- 4.) The chemical form of the contaminant is important in the dynamics and location of deposition within the system (i. e., soft tissue vs. bone).
- 5.) The effectiveness of DTPA administration for Pu removal from the body is dependent on the chemical form of the Pu contaminant.

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Introduction

Plutonium (Pu) is an element of vital interest to people throughout the world. Its fissionable isotope, ^{239}Pu is abundantly produced and has the potential to be the nuclear fuel of the future (Tremmel, 1968; Seaborg, 1972). Dr. Glenn T. Seaborg, stated that: "no single element has ever been given so much undivided attention by so many people of so many different nations over so short a period of time" (Seaborg, 1972).

The processing of Pu has grown from the recovery of microgram quantities by a few individuals to routine industrial processing of kilogram quantities of the element by several thousand persons. Its potential toxicity as a bone seeker is well known (Seaborg, 1972; Norwood, 1972a), as is its high radioactivity, amounting to about 140,000,000 alpha-disintegrations per minute per milligram of ^{239}Pu . No other element has commanded such caution, carefulness and respect.

Much of the metallurgical and chemical processing of Pu requires personal handling in gloveboxes. Although effective exposure control methods have been implemented in production plants, experience has shown that the risk of accidental internal contamination of persons is high. In spite of outstanding safety records in the nuclear industry there are presently upwards to a thousand employees at the Dow

Chemical Company - Rocky Flats Division Plant, a prime contractor for this A.E.C. facility, having measurable amounts of Pu within their bodies as detected through bioassay analysis or by body counter (Seed, 1972). Many of them have become contaminated through repeated low level exposure over the past 20 years of operation. Others were contaminated through numerous recorded or possibly unrecorded low level exposure accidents where inhalation occurred. However, the greater number of internal contaminations occurred following puncture wounds or by skin contact with contaminated acid in the chemical processing areas.

During the production of Pu in nuclear reactors several of its isotopes are formed. One of these, present in nearly all production Pu, is ^{241}Pu and its daughter americium-241 (^{241}Am). This daughter has an abundant yield of gamma rays (0.37 per alpha decay) of 59.6 keV, which makes it a useful in vivo tracer for Pu-239. Therefore, the industrial practice for in vivo evaluation of Pu deposition in the body is based on the detection of ^{241}Am gamma emission. This practice is based on the assumption that Pu and Am are identically metabolized within a biological system. However, recent evidence have shown that this assumption is erroneous as soon as translocation begins (Johnson, 1969) and can present serious problems in the assessment of the quantity deposited internally.

Because of its high toxicity and the difficulty of making in vivo measurements, nearly all biological knowledge of Pu has been gained through animal research. Much of the information has been obtained by using chemical forms not found in normal production conditions, such as, plutonium citrate specifically limited to the Pu(IV) form used for intravenous injection (Norwood, 1972b; Thompson, 1972). However, under normal production conditions workers are usually exposed to mixtures of chemical states and forms of the oxides, hydroxides, nitrates, fluorides, or chlorides. It is evident that very limited information is available to the applied health physicist at production facilities on the dynamics of movement following the most prevalent form of accident, the puncture wound. It is of utmost importance in clinical wound management to know the dynamic rate of movement and the most probable deposition points for the various types of exposure materials.

The purpose of this study was to investigate the translocation rates of Pu and Am from simulated puncture wounds contaminated with $\text{Pu}(\text{NO}_3)_4$ and PuO_2 in Beagles. The specific objectives of this research were to:

1. Determine the rates of Pu translocation from wounds to the various organs in the body.
2. Determine the effect of different physico-chemical form, upon these dynamics.

3. Determine the relative translocation of Pu and Am for these chemical forms to better assess the use of ^{241}Am as a tracer for in vivo Pu determinations.
4. Determine the effectiveness of chelation therapy (DTPA) upon the above parameters.

Literature Review

Plutonium was discovered, in February 1941, by a group of scientists headed by Dr. Glenn T. Seaborg (Seaborg, 1963). It is a silvery white metallic element and it was the second transuranic element to be discovered. It is found in concentrations of the order of one part per 10^{11} parts of uranium (U) following spontaneous fission resulting from neutron capture in $^{238}_{92}\text{U}$ and $\alpha - \frac{1}{0}\text{n}$ reactions (Leonard, 1967). Since the 1940's, Pu also exists in nature as a result of fallout debris from nuclear weapons testing. However, nearly all Pu is produced in reactors from $^{238}_{92}\text{U}$ with any type of neutron energy spectrum: fast, intermediate, or thermal $^{238}_{92}\text{U}(\text{n}, \gamma) ^{239}_{92}\text{U} \xrightarrow{\beta} ^{239}_{92}\text{Np} \xrightarrow{\beta} ^{239}_{94}\text{Pu}$ (Weast, 1964). A large variation in the ratio of Pu isotopes produced results from differences in the average cross sections of the Pu isotopes over the neutron energy range.

As a member of the actinide series, Pu is chemically very similar to the rare earth elements. Metallic Pu undergoes five allotropic modifications below the melting point (Coleman, 1965). It melts at 640°C and boils at 3327°C . It is a highly reactive metal which combines readily with oxygen. It has four oxidation states (III, IV, V, and VI) and forms quite stable compounds with all non-metallic elements with the exception of the rare gases (Norwood, 1972a).

Plutonium III, IV, and VI are considered the most important oxidation states.

In all of the oxidation states Pu exists as highly charged ions in aqueous solution which undergo hydrolysis reactions in dilute acid solutions. This may lead to a hydroxide precipitate or to a colloidal polymer. Water molecules satisfy the coordination tendency (chemical linkage of unknown type) for Pu in an aqueous solution. The formation of the polymer is dependent on acidity, Pu (IV) concentration, presence of other ions, and temperature (Cleveland, 1967). Brunstad (1959) has studied the effects of acidity and Pu concentration and found that polymerization is greatest for solutions of low acid/Pu ratios. The most important hydrolytic reaction of Pu, from a radiochemical standpoint, is colloidal aggregate formation in solution by successive polymerization reactions. The amounts of polymer and monomer influence the distribution of Pu injected into a biological system.

Plutonium dioxide is the most important and most thoroughly studied of all Pu compounds (Cleveland, 1967). Plutonium dioxide is formed when metallic surfaces of Pu are exposed to air or when Pu or its compounds (except the phosphates) are ignited in air.

Plutonium nitrate is occasionally another important chemical form of Pu in regard to potential hazard for people working in a chemical processing plant. A dilute solution of $\text{Pu}(\text{NO}_3)_4$ is initially brown but soon changes to green as colloidal Pu forms. Concentrated solutions of the nitrate in concentrated HNO_3 , a common processing

contaminant, are green, because of the $\text{Pu}(\text{NO}_3)_4$ complex. When the nitrate form comes in contact with tissue a dilution effect could occur and the polymerization or colloidal formation referred to above would take place.

Industrial Plutonium Exposure

It was realized early that Pu possessed a high level of toxicity. Its specific activity and long half-life presented potentially serious biological problems for industrial people involved in its production. The handling of Pu in production and fabrication facilities has led to numerous contaminated wound cases and long term low level chronic exposures. Prior to 1958 these incidents were not reported in the open literature. However, Langham, et al. (1962), Langham (1972), Hempelmann (1973), discussed in great length some of these early cases and the management problems associated with contaminated wounds and inhalation accidents encountered during and following the era of World War II nuclear weapons production. In 1962 and 1972, the Health Physics Society Journal published many articles involving studies and effects of Pu contamination in animal research and man (Health Physics, Vols. 8, 22, 1962, 1972).

Another form of Pu contamination occurring in industrial plants involves accidental explosive reactions at high temperatures which have led to internal depositions of PuO_2 in some individuals primarily

through the mode of inhalation. Plutonium dioxide produced either at high temperatures or by slow oxidation in air are frequent sources of personnel contamination. Hammond and Putzier (1964), Roesch (1964), and Fuqua (1965) concluded in their reports that exposure of personnel to PuO_2 or metal by way of contaminated wounds is the major type of exposure found in industry. In some production plants, such as the Rocky Flats AEC Plant-Prime contracted to the Dow Chemical Company, they have concluded that wound contamination is the most frequent accidental mode of entry of Pu into the body. This mode of entry is quite common where workers handle contaminated tools and sharp pieces of Pu metal shavings. As a result, experience has shown that Pu contaminated industrial wounds occur most frequently on the hands and fingers. Heid et al. (1966) reported on 123 wounds with measurable Pu contamination over a 20 year period at Hanford. Putzier (1967) reported 429 cases of detectable Pu in wounds over a 13 year period at Rocky Flats with the number of persons having detectable quantities in their bodies now reaching approximately a thousand after 20 years of operation of this major Pu processing and fabrication plant.

Unfortunately, Pu contamination does not remain restricted to the point of entry in the body nor is the translocation generally predictable. Contaminated wound management has been complicated by such variables as: different chemical forms, unknown depth of

deposition, tissue types involved, amount of dispersion of the Pu within the wound, particle sizes involved, variations of individual responses and proximity of wound to blood and lymph vessels (Langham et al., 1962; Norwood, 1962). Modes of entry, distribution, excretion, biological processes such as phagocytosis, and methods for evaluating Pu in living systems have been extensively studied (Bair and Thompson, 1972; Thompson, 1967; Stover and Jee, 1972; Durbin, 1971; Wilson, 1967). In 1967, Thompson proposed a classification for industrial Pu exposure hazards based on (a) distribution within the body by way of the blood stream, (b) Pu deposition in the lungs and associated lymph nodes, and (c) biological uptake and deposition of Pu deposited beneath the skin or in muscle in a relatively non-absorbable form as a result of contaminated puncture wounds. Interrelationships of these three classifications obviously do occur. In contaminated puncture wounds (a) and (c) both affect distribution or translocation of the activity (Thompson, 1967).

Although Pu must be considered one of the greatest potential hazards to life on the basis of present limited knowledge, no serious injury has been observed to date in industrial workers due to the internal deposition of Pu (Norwood, 1972a; Thompson, 1967).

Thorough biomedical studies were carried out at Los Alamos and Rocky Flats on employees with measured quantities of Pu in their bodies, covering a period of 27 years that substantiates these findings

(Hempelmann, 1973; Lushbaugh and Langham, 1962; Bistline, 1973).

These studies showed that only a few people have experienced body burdens in excess of the maximum permissible level of $0.04\mu\text{Ci}$ of Pu, as established by the International Commission on Radiation Protection (ICRP) (NBS Handbook H-47, 1951).

Treatment and Therapy of Contaminated Wounds

Using mice, Brues, Lisco, and Finkel (1947) performed some of the earliest subcutaneous injection studies with Pu. They reported a high incidence of malignant fibrosarcoma at the site of $\text{Pu}(\text{NO}_3)_4$ injections. Langham (1962) and Foreman (1960) in describing practices of washing and excision of wounds concluded that decision for or against surgical removal of the Pu from a wound is not an urgent one and can be deliberated for several days since it is absorbed slowly from such sites.

In addition to the practices of excision of contaminated wounds over certain levels chemical chelating agents are used commonly with or even without surgical excision of the wound site. Many reports to this effect have been published in the literature: Weeks et al. (1955) Schubert (1955); Smith (1958); Langham (1959); Foreman (1960); Sowby and Taylor (1960); Norwood (1960); Catsch (1961); Schubert et al. (1961); Ballou (1961); Lindenbaum et al. (1962); Norwood (1962); Taylor and Sowby (1962); Taylor (1962); Norwood (1963); Cable et al.

(1963); Markley (1963); Swanberg and Henle (1964); McClanahan et al. (1964); Lagerquist et al. (1965); Fuqua (1965); Bokowski and Hammond (1965); Heide et al. (1966); Lagerquist, Putzier and Piltingsrud (1967); Boss and Mann (1967); Lindenbaum et al. (1967); McClanahan and Kornberg (1967); Lagerquist, Allen and Holman (1967); and Larson et al. (1968).

The trisodium calcium salt of DTPA is the chelate most commonly used for therapeutic purposes (Lagerquist, 1965; Fuqua, 1965). In 1969 Johnson described for air oxidized Pu the effects of DTPA on the relative translocation ratios of Pu and Am on body distribution as a function of time. Schubert and Lindenbaum (1960) have shown that the chelate specificity, or affinity for a metal relative to that of body proteins, and the distribution of the metal in the body are important to determine the effectiveness of a chelating agent. Chelation is impaired in some cases where the metals complexed very strongly with the proteins. James and Taylor (1971) pointed out the role of local bone resorption in the removal of ^{239}Pu deposited in the bone matrix of immature rats following intravenous injection. They stated that chelation of Pu bound in the bone matrix can occur effectively only if the Pu is first liberated into the interstitial tissues by osteoclastic activity during the process of bone resorption. If therapy is administered after completion of skeletal uptake, the total bone surface area undergoing resorption will dictate the efficacy of

delayed therapy in reducing the skeletal burden. It has been reported that the effectiveness of DTPA therapy given shortly after contamination is largely due to the chelation of Pu in the blood, thus preventing skeletal deposition. The extent of bone remodeling activity in human adults is much smaller than that of continuously growing bones of rats and mice. It is likely therefore that DTPA therapy can have only a marginal effect in removing Pu from human bone, once incorporated in the bone matrix.

More recent studies suggested that, in the human, induction of lung and liver tumors, or leukaemia could be as great, or even greater, than bone tumor occurrences (James, 1971). McClanahan and Ragan (1965) found that DTPA was equally effective in reducing liver and femur concentrations of Pu whether injected subcutaneously or intravenously. Therefore, it is expected that DTPA treatment even when started some time after contamination, will reduce the risk of tumor induction in soft tissues or of leukaemia, assuming that in the case of leukaemia the cells at risk are distributed throughout the bone marrow and not concentrated along endosteal surfaces. However, DTPA is most effective when administered promptly after contamination, when the levels of Pu in the blood are relatively high. Under these circumstances the therapy will prevent or reduce further deposition of Pu in bones as well as reducing the soft tissue Pu burdens. In man, the time of treatment following contamination is regulated by the route and rate of entry of soluble Pu into the bloodstream.

High concentrations of DTPA may be toxic (Seven, 1960), therefore, therapeutic doses of DTPA range from 0.1 to 2.0 grams per day for man. The most common procedure reported has been to give a dose of 1 gram per day for 5 days by slow intravenous infusion at two weeks intervals and then a repeat of the treatment (Larson et al., 1968; Norwood, 1963). Catsch (1961) found that DTPA increased both urinary and fecal excretion rate for as long as 8 days.

Johnson (1969) showed that DTPA treatment enhanced the relative urine Pu content over the Am content. However, Johnson did not see an effect on the relative amount of Pu and Am in the feces. A two-fold or more increase in the relative amount of Pu excreted in the feces was observed when compared to the blood and the untreated urine. Ratios of Pu to Am were normalized to that of the initial implant material. He reported that liver of treated dogs showed a Pu to Am ratio about 5 times greater than that of the liver tissue of untreated dogs which could be due to a preferential Am chelation because of greater availability of Am in the liver. Taylor and Sowby (1962) reported that the effect of DTPA administered 1 hour after the intravenous injection of ^{241}Am or ^{239}Pu , showed that ^{241}Am is more effectively removed from the liver than ^{239}Pu . The level of ^{239}Pu in the liver was reduced by a factor of about 14, whereas the ^{241}Am content was reduced by two hundred fold. In contrast, ^{239}Pu was apparently removed more efficiently from the skeleton than ^{241}Am .

It was proposed as an explanation for the less efficient removal of ^{239}Pu from the liver that Pu could be bound more strongly by the tissue protein, or other constituents, than Am. Treatment with DTPA was most effective when started early after exposure and a short course of repeated treatments was more effective than a single treatment.

Johnson (1969) reported that the proximal end of the femur was the only skeletal tissue showing a significant DTPA treatment effect. A Pu enhancement of about threefold following DTPA treatment was reported. The effectiveness of chelation therapy on absorption of activity from an implant site has been debated by many. Ballou (1961) observed increased absorption of radionuclides as a result of the external use of chelation agents for wound decontamination. McClanahan and Kornberg (1967) reported that rinsing wounds with DTPA had no discernible effect on the subsequent tissue distribution of Pu. The literature does not contain any report showing increased absorption from the wound site following intravenous injection of chelating agents, although, Schulte and Whipple (1967) did issue a dissenting argument to the use of chelation therapy.

Metabolism and Distribution of Pu and Am from Implants

A limited amount of research involving Pu and/or Am in contaminated wounds and its subsequent distribution within the body has

been reported in laboratory animals. On the other hand, rather extensive studies of inhalation, ingestion, and intravenous injection of Pu in animals has been described (Thompson, 1967; Bair, 1970). Plutonium nitrate implanted subcutaneously in mice was studied by Brues, Lisco, and Finkel (1947) with resulting elevated frequency of fibrosarcoma. Scott et al., in 1948, performed metabolic and distribution studies of Pu and Am following intramuscular injections and reported major concentrations in the liver and skeleton. Langham (1959) placed microgram quantities of PuO_2 on abraded areas of rabbit skin and failed to show measurable absorption with the activity sloughing along with the scab. Likewise, Cable et al. (1962) using $\text{Pu}(\text{NO}_3)_4$ intradermally injected in swine showed major loss of activity with the scab. Plutonium nitrate injected intramuscularly in the rat has been shown to remain primarily at the injection site even following DTPA administration (Taylor and Sowby, 1962).

Translocation of subcutaneously administered PuO_2 in swine was reported to be about 100 times lower than that of the nitrate (McClanahan and Ragan, 1965 and 1966; Cable et al., 1962 and 1963). The studies of PuO_2 translocation did lead to the conclusion that the regional lymph nodes were the major point of translocation from the implant. The chemical form of the Pu was reported to be an important factor affecting the translocation rate, the nitrate form being much more rapidly transported than the oxide form (McClanahan and

Kornberg, 1967). Intramuscular injection of $\text{Pu}(\text{NO}_3)_4$ in rabbits resulted in nearly all the Pu initially injected, retained at the injection site (Taylor, 1969). This research showed that subsequent translocation to other organs took place by lymphatic transport as well as by slow migration in the form of soluble Pu complexes directly into the blood stream. Taylor and Sowby (1962) reported on the nature of the physiological complexes of Pu and Am. Serum proteins, particularly transferrin, were isolated as the binding and transport media for both Pu and Am (Stevens et al., 1965; Turner, 1967; Taylor, 1969; Turner and Taylor, 1968; Bruenger et al., 1969; Stover et al., 1968; Boocock and Popplewell, 1966; Chipperfield and Taylor, 1968).

Taylor (1972) demonstrated that ^{239}Pu administered in a colloidal form and in monomeric form showed different association with the lysosomes from centrifugation of liver homogenates. The different time courses for the lysosomal association of monomeric and polymeric ^{239}Pu suggested that different mechanisms are involved in the deposition of the two physio-chemical species. The rapid association of polymeric material with lysosomes probably resulted from direct uptake of colloidal particles; mainly into Kupfer cells, by endocytosis.

There appears to be a close association between ^{239}Pu and iron pigments in a number of tissues. An association between ^{239}Pu and the iron storage protein ferritin has been reported in both rat and dog

liver, and autoradiographic studies in dog liver showed that ^{239}Pu appeared to migrate with iron-containing pigment from parenchymal cells to the Kupfer cells at 200 to 300 days post injection. The coincidental localization of ^{239}Pu and haemosiderin has also been observed in the adrenal gland and in the bone marrow. It was reported that the significance of this association may be concerned with the intra and inter-cellular transport of ^{239}Pu and may represent an attempt by the cells to detoxicate the "foreign" metal, or it may merely reflect a high affinity of Pu for the protein moiety, or of hydrolyzed Pu species for the colloidal "iron hydroxide" complex of ferritin or haemosiderin. The transfer of Pu from transferrin, the primary binding compound to the liver ferritin, parallels the uptake of iron. Whether ^{239}Pu is associated with ferritin in lysosomes is still not known (Taylor, 1972).

The retention of ^{239}Pu in the liver, lung, adrenal, testes, and bone marrow is prolonged in all the species studied so far. It is interesting to note that soft tissue malignancies have generally arisen in these tissues where the retention of the nuclide is very prolonged. It has been suggested by Sanders and Adey that the intracellular localization of ^{239}Pu in the cells of the alveolar wall may account for the prolonged retention of the nuclide in the lung (Taylor, 1972).

Taylor and Benstad reported a much greater concentration of ^{241}Am in the spleen than the liver following intravenous injection of a

neutralized Pu nitrate solution. With ^{241}Am the picture appears to be rather different from that of ^{239}Pu because over long periods of time very little of the ^{241}Am is retained in the liver. Preliminary autoradiographs did not show the "star clusters" in macrophages which were observed in ^{239}Pu containing livers. However, in the spleen ^{241}Am was found in association with iron-containing macrophages.

The strong complex-forming properties of Pu suggested that Pu deposited in the liver may be more firmly bound to cellular constituents than is Am. This suggestion was supported by a more prolonged retention of ^{239}Pu than of ^{241}Am in the liver and by the results of studies on the removal of ^{239}Pu or ^{241}Am from the body by treatment with chelating agents (Taylor, 1962).

While the gross metabolic behavior of ^{239}Pu and ^{241}Am may be similar in some respects, there is increasing evidence that the predominantly tetravalent ^{239}Pu and the trivalent ^{241}Am are handled by different mechanisms in the body (Taylor and Bensted; Turner and Taylor, 1968). Americium-241 is cleared from the blood plasma much more rapidly than ^{239}Pu , and recent studies have shown marked differences in their binding by plasma proteins.

It was reported that Am formed weaker complexes than did Pu with transferrin, which delivers iron to bone marrow (Stevens, Bruenger, and Stover, 1965). Transferrin probably carries Pu and Am to the bone where bone surface interactions are possible. Two

bone glycoproteins, sailoprotein and chondroitin sulphate-protein, have been shown to bind Pu and Am strongly in vitro research.

Transferrin of normal plasma is only about 30 percent saturated with iron, thus many binding sites for transport of Pu and Am would be

available (Stevens, Bruenger, and Stover, 1968). The greater uptake

of ^{241}Am in the liver and its more rapid removal as compared to

^{239}Pu as well as differences in the effects of chelating agents, are

probably indicative of differences in the mechanisms of deposition. In

the bones of animals given $7\mu\text{Ci } ^{241}\text{Am/kg}$ the dose-rate can be calcu-

lated to be at least equal to that in the bones of rats given $2.9\mu\text{Ci}$

$^{239}\text{Pu/kg}$, yet the incidence of tumors reported was only 47% in the

^{241}Am group compared with 80% for ^{239}Pu . Autoradiographic evidence

suggested that ^{239}Pu is deposited more heavily on endosteal surfaces

than does ^{241}Am (Taylor and Bensted). Taylor and Sowby (1962)

reported that both ^{239}Pu and ^{241}Am were deposited extensively in the

skeleton in approximately equal quantities, but that the liver concentra-

tion of ^{241}Am was 5-10 times greater than that of ^{239}Pu . Stover et al.

reported that during the first 2 years, skeletal retention decreased

so that at 2 years following contamination, and at low dose levels,

approximately 1/3 of the intravenously injected ^{239}Pu , injected in

citrate form, is in the skeleton, 1/3 in the liver, while 1/3 was

excreted. At higher dose levels decreases in skeletal retention was

slower than was the case at their P 1 level (Stover et al., 1972, p.

158-159). Taylor's studies (1962) showed the different rates of plasma clearance reflected in the rates of uptake of ^{239}Pu and ^{241}Am into different parts of the femur. Plutonium-239 concentrated slowly in all regions of the bone over the whole period of observation, whereas the ^{241}Am concentration rose fairly rapidly to reach a maximum in about 4 hours in the shaft and proximal end. This level appeared to fall slightly over the next 4 hours and then remained approximately constant. In the distal end, the activity rose to a maximum in about 8 hours and then remained constant. The highest concentrations were found in the distal region, which contains the epiphysis, and the lowest were in the shaft.

In 1969, Taylor suggested that intramuscular injection of Pu in rats and mice followed translocation dynamics similar to wound contamination in man. Therefore, he suggested that more useful information could be derived if larger animals, such as the rabbit were used for these studies. Taylor further pointed out that it was interesting to note that up to 49 days after injection the ratio of the percentage of retention in the liver to that in the skeleton was less than 0.2 whereas from 56 days onwards, except for a single animal studied at 365 days, it was greater than 0.5. Such an increase in liver uptake relative to the skeleton suggested that the deposition was changing towards a more colloidal pattern, which also suggested that lymphatic drainage played a part in the removal of the ^{239}Pu from the site of injection, a suggestion made earlier by Cable et al. (1962).

Johnson (1969) showed that rapid movement of the material from the implant site to the first major lymph node draining the site could be surveyed by in vivo counting techniques. The kinetics of the lymph node concentration could best be described by power function equations. About 100 percent of the node burden was accumulated in the first two days. The percent of the estimated initial amount of the material implanted into the subcutaneous tissues of the paw moving to the superficial cervical lymph node ranged from an average of 3.3 percent after 15 days of implant time to 13.3 percent after 12 months.

For intramuscular injection results suggested that almost all the administered Pu is initially retained at the site of injection but that the subsequent translocation to other organs may involve lymphatic transport, as well as the slow formation of soluble Pu complexes migrating directly into the blood stream (Taylor, 1969). Johnson (1969) also suggested that these two mechanisms of translocation are important pathways in the systemic deposition of subcutaneously placed PuO_2 material.

According to Taylor (1969), the translocation of Pu from an intramuscular injection site is initially slow, and the major sites of deposition are the liver and skeleton, but after about seven weeks a marked uptake increase was observed in the liver. Johnson (1969) also found that the ^{241}Am tracer method for in vivo estimation of the liver Pu content over-estimated the Pu liver burden by an average of

4.5 fold for untreated dogs and by 3.6 fold for DTPA treated dogs.

A significant DTPA treatment effect was observed in urine, liver, and proximal femur tissue samples. Enhancement of the relative Pu content relative to Am was observed in these three samples following DTPA treatment. However, in the thyroid tissue the Am recovery was increased by a factor of about 15 while Pu was enhanced in the vertebrae by a factor of about 6. In general, the results indicated an Am enhancement in soft tissues and a Pu enhancement in skeletal tissue. In the case of skeletal tissue, there seemed to be a direct relationship between the hemopoietic activity of a bone and its Pu collection enhancement. Stover (1972, p. 139) reported the thyroid concentration of ^{241}Am was also high in a study conducted at the University of Utah. In this study the thyroid concentration was second only to that of liver and exceeded that found in the skeleton. The Utah study also reported that injection levels of $2.8\mu\text{Ci/kg}$ produced an accelerated loss of activity from the liver, concomitant with a loss of liver tissue. This effect was accompanied by a recycling of ^{241}Am from the liver to the bone. Liver function tests indicated that significant liver injury were produced in dogs injected with $0.9\mu\text{Ci/kg}$ of ^{241}Am (Lloyd et al., 1972, p. 142).

Although both ^{239}Pu and ^{241}Am are apparently transported and bound by the same proteins, the fact that there is a marked difference in the strength of the complexes is evidence of differential transport dynamics and metabolism (Johnson, 1969).

Radiological Properties of Plutonium

There are presently 15 known isotopes of Pu ranging in atomic weights from 232 through 246. Lederer et al., (1968) tabulated the energies and yields of the major α , β , γ , and x radiation emissions given off by the Pu and Am isotopes commonly encountered in the Pu production and processing industry (Table 1). One of the two most important isotopes of Pu is $^{239}_{94}\text{Pu}$ which has a half-life of 24,360 years. Plutonium-239 decays by one of the 3 major alpha decay schemes of the ten identified for this isotope. These three alphas have energies and abundances of 5.147 MeV, 72.5%; 5.134 MeV, 16.8%; and 5.096 MeV, 10.7% (Snyder, 1967). These alpha particles have an average alpha energy of 5.15 MeV and a range of about 40 microns in soft tissue and about 24 microns in bone (Mays, Sears, 1962; Norwood, 1972a). Uranium-235 emits a series of weak L-x rays of average energy levels of 13.6, 17.2, and 20.2 keV having an average energy of 17 keV and an abundance of 4% of the alpha disintegrations immediately following the alpha decay from ^{239}Pu . This isotope also has a low abundance series of K-x rays in the energy range of 94 through 115 keV and two prominent gamma rays of 51.63 and 129.3 keV with abundances of 0.016% (Falk, 1973), 0.020%, and 0.005% (Lederer et al., 1968) per alpha decay respectively.

The transuranic element americium-241 is also of radiological health importance in the Pu production industry. Americium is a

Table 1. Characteristics of Selected Pu and Am Isotopes.

Isotope	Half Life (yr.)	Radiations	Energy	Abundance (%)
^{238}Pu	86.4	α	5.495 MeV	72
		α	5.452 MeV	28
		U L X-rays	17 keV(ave.)	10.55
		γ	43.5 keV	0.038
		γ	99.8 keV	8×10^{-3}
		γ	153.1 keV	10^{-3}
^{239}Pu	24,390	α	5.16 MeV	83
		α	5.11 MeV	11
		U L X-rays	17 keV(ave.)	4
		γ	38.6 keV	0.007
		γ	51.63 keV	0.020
		γ	129.3 keV	0.005
^{240}Pu	6580	α	5.17 MeV	76
		α	5.12 MeV	24
		U L X-rays	17 keV(ave.)	10
		γ	45.28 keV	
		γ	103.6 keV	
^{241}Pu	13.2	Beta	21 keV	99.97
		γ	145 keV	1.6×10^{-4}
^{242}Pu	3.79×10^{-5}	α	4.90 MeV	76
		α	4.86 MeV	24
		U L X-rays	17 keV(ave.)	10
^{241}Am	458	α	5.49 MeV	85
		α	5.44 MeV	13
		Np L X-rays	17 keV(ave.)	37.6
		γ	26.36 keV	2.5
		γ	43.44 keV	0.07
		γ	55.56 keV	
		γ	59.57 keV	36
		γ	99 keV	0.024
		γ	103 keV	0.019
		γ	106 keV	0.001
		γ	122 keV	0.002
		γ	125 keV	0.005
		γ	146 keV	2×10^{-4}

by-product of all reactor produce Pu as it is a daughter of the relatively short-lived isotope ^{241}Pu ($t_{1/2}=14.03\pm0.3$ yrs.). The presence of this isotope is dependent to a degree on the neutron energy spectra within the reactor and on total irradiation time. The production and chemistry of Am has been reviewed by Penneman and Keenan, 1960; and Dawson, Deonigi, and Eschbach (1965). Americium has several valence states of which Am III predominates in aqueous solutions. Americium decays by alpha emissions of 5.49 and 5.44 MeV and prominent emission of 17 keV average energy neptunian L- x rays and of 59.56 keV gamma rays which have abundances of 0.37 per alpha decay (Swinth, 1968 and 1967).

Internal Exposure and Translocation Measurements

The philosophy, research, and scientific data involved in the evolution of the maximum permissible body burden standards for ^{239}Pu from 5 μg in 1943 to the present 0.6 μg or 0.04 μCi is described at length and in depth in the work of Hempelmann et al., (1973). These standards were based on comparative calculation from studies and knowledge gained through experience with the internal alpha emitter radium. Because of the potential hazard of Pu it was deemed expedient to devise means of quantitatively detecting and/or measuring people exposed to a maximum permissible body burden or less. During the 1940's it was recognized that some workers were excreting

small amounts of Pu in their urine. The interpretation and possible consequences of this urinary Pu excretion in terms of body content of Pu was of necessity based on animal studies (Hamilton, 1948; Scott et al. 1948; Scott et al., 1949; Bloom and Bloom, 1949; Carritt et al., 1947). To improve estimates, data from human excretion patterns, was needed. A cooperative project was then developed between the Manhattan Project Laboratory and Los Alamos Laboratory. Eighteen seriously ill persons were injected intravenously with tracer doses of ^{239}Pu in a citrate form (see 9 and 10 Bair and Thompson; Langham, 1956; Durbin, 1972). Power function models for excretion of Pu were empirically derived from these data. These models have been used and modified by various persons to estimate body burdens of Pu following accidental exposure. This method has many limitations due to the intravenous mode of entry and the non-industrial citrate chemical form used to obtain the model. However, these equation despite their uncertainties have been widely used primarily because they represent the only human data where known amounts of Pu were involved (Snyder, 1962; Hammond and Putzier, 1964; Beach, 1966; Jech, 1972; Lagerquist, 1972).

In vivo determination of Pu on surface wounds can be achieved by counting the U L-x rays from the alpha decay of Pu. However, it has been reported that this technique has several limitations. First, the tissue half-value thickness for the absorption of these x rays is only about 0.6 cm, making them nearly useless for measuring anything

other than surface wounds (Swinth, 1967; Ramsden and Speight, 1967). Second, the element ^{241}Am and several isotopes of Pu other than ^{239}Pu are nearly always present as contaminants. They contribute significant levels of x rays which cannot be resolved from those originating from the decay of ^{239}Pu . Also the level of ^{241}Am changes with time in proportion to the amount of ^{241}Pu (its radioactive precursor) present in the mixture (Bistline and Tyree, 1967). Third, there is a significant effect of self-absorption that occurs for the 17 keV energy photons which is a function of particle size from which they originate (Cloutier, 1967). Nevertheless, wound counting for detection of Pu contamination using this technique is a standard practice at most installations (Johnson, 1969; Boss and Mann, 1967). The low abundance of gamma emissions from the Pu isotopes makes in vivo body burden or lung deposition evaluation very difficult. The industrial practice for in vivo evaluation of Pu deposition in the body based on the ^{241}Am gamma emission is an acceptable procedure immediately following an incident. However, Johnson (1969) has shown that as soon as translocation begins an error occurs with this technique as it is based on the assumption that Pu and Am are identically metabolized within a physiologic system. More recent studies have shown this assumption to be wrong (Johnson, 1969). Studies are now in progress to monitor low abundance and difficult to resolve Pu gamma and U K-x rays with high resolution Ge(Li) detector system (Tyree and Bistline, 1970; Falk, 1973).

The citrate form of Pu, injected intravenously has been the source of most of the published experimental data concerning systemic behavioral studies done on animals. Such a chemical form and direct injection technique create difficulties in interpretation in terms of relevance to authentic exposure conditions. Norwood (1972b) stated that the decay curves relating input with daily output where plutonium citrate was administered intravenously to incurably diseased men are reasonably accurate for cases in which plutonium citrate was injected intravenously. However, while many accidental depositions have occurred, the literature does not contain any reference in which plutonium citrate was injected into a vein. Deposition occurred usually by inhalation or via flesh wounds, and the Pu was usually in the form of a metal, oxide, nitrate, or fluoride. Most of these compounds are poorly soluble in the body fluids and are metabolized in the body quite differently than is the intravenously-administered soluble citrate (Norwood, 1972b). The citrate tends not to polymerize through normal hydrolizing processes as it usually occurs with Pu at physiologic pH. Thus, the citrate form will be of the monomeric form as opposed to the more common "polymeric" Pu most often found in daily exposure conditions. The polymeric form was removed from the blood and deposited in the liver, whereas the monomeric form was translocated to the bone at a slower rate. He conjectured that once the Pu had reached the blood by normal physiologic translocation processes it was usually in a monomeric form and predominantly deposited in the bone. However,

experiments have shown Pu in the blood to be associated with the iron binding protein, transferrin, in a quite stable complex form which is deposited primarily in the liver and bone (Bair and Thompson, 1972).

For convenience one can distinguish between systemic Pu and the directly deposited Pu in a tissue by means of a particular route of entry. Plutonium in bone, liver, or other organ deposited directly from the blood is referred to as systemic and might well be expected to show similar deposition and retention dynamics from a wound, absorption from lung inhalation, or even ingestion and absorption through the intestine. However, Pu deposited in the lung by inhalation or a puncture wound will be much more influenced in its subsequent behavior by the physical and chemical nature of the deposited material (Bair and Thompson, 1972). Experience has shown that in most cases Pu deposited in the lungs does not get into systemic circulation and distribution occurs readily as that from wounds.

Autoradiographic studies of Pu particles concentrated in regional lymph nodes following initial translocation have indicated concentration within and around the medullary sinus but generally not in germinal centers. Autopsy reports and animal research did provide striking evidence of the nonuniformity of Pu distribution in man and dog. Dog studies have indicated that inhaled "soluble" Pu may be primarily cleared from the lung within 1 to 2 years and translocated principally to the bone and liver. However, "insoluble" Pu usually was retained

much longer in the lung and translocated principally to the lymph nodes draining the pulmonary region (Bair and Thompson, 1972).

According to Bair and Thompson (1972), Pu compounds of the soluble form injected subcutaneously or intramuscularly usually move quite slowly but eventually translocate to the regional lymph nodes, bones, and liver. Cable et al. (1962) reported that 7 days after intradermal injection of miniature swine with $\text{Pu}(\text{NO}_3)_4$ in 0.2N nitric acid, 12% of the dose was present in regional lymph nodes, about 7% concentrated in the liver, and slightly less than 5% in the bone. Seventeen percent of air-oxidized Pu implanted subcutaneously in paws of Beagle dogs had moved to the proximal lymph node within a year; during this time only about 0.1% had translocated to the skeleton and about the same to the liver.

Materials and Methods

Animals and Animal Maintenance

Ninety-six male adult Beagles, varying in age from 12 to 36 months were used for this study. The dogs were obtained from the barrier-maintained colony of Colorado State University's Collaborative Radiological Health Laboratory (CRHL). The animals were housed one or two to a run while outside and individually in metabolism cages while inside. The outside runs were located next to the CHRL Building on the Foothills Research Campus of Colorado State University. The dogs were maintained in accordance with provisions of the Laboratory Animal Welfare Act (1967) and inspected routinely by a veterinarian.

The runs were 15 feet by 15 feet in size, 1 foot gravel base, a concrete curb around the pen extending 12 inches above the gravel with a 5 foot high, 2 inch mesh cyclone fence on the curbing. Three feet by six feet galvanized sheet metal panels were placed on the fence to provide shading from the sunlight. Concrete houses with wooden floors provided year around shelter and warmth (Fig. 1 and 2). Each dog was given a complete physical examination monthly and routine visual and palpation examinations were conducted at least weekly. The animal caretakers were under strict supervision to report any abnormal behavior or disease symptoms immediately. The dogs were fed a

guaranteed nutritionally adequate dry ration of Purina Dog Chow ad libitum. Automatic watering devices insured a constant source of fresh water in the summer, but daily filling of watering pans was necessary during winter months.

Experimental Design

Two chemical forms of Pu were used for this study, PuO_2 (high fired) and $\text{Pu}(\text{NO}_3)_4$. Table 2 describes the basic experimental design used for the study of each chemical form. The trisodium-calcium salt of diethylenetriaminepentaacetic acid (DTPA) was used as the chelating agent to study therapeutic treatment effects.

Table 2. Experimental Design

Insult Time from Implant to Necropsy	Number of Dogs Contaminated Without Chelation Treatment	Number of Dogs Contaminated and Receiving Chelation Treatment (DTPA)
2 weeks (Group 1)	4	4
1 Month (Group 2)	4	4
2 Months (Group 3)	4	4
3 Months (Group 4)	4	4
6 Months (Group 5)	4	4
12 Months (Group 6)	4	4

Table 3. Blood Sampling Schedule

First two weeks	Day 1 at 1, 2, 4, and 8 hours post-implant Daily on days 2, 3, 4, 5, 6, 7, 9, 11, 14
1 Month	3 consecutive days one month following implant
Monthly	3 consecutive days monthly until necropsy.

Implant Material and Procedure for $\text{Pu}(\text{NO}_3)_4$ Experiment

The stock plutonium nitrate solution used for implant was prepared at the Dow Chemical Company - Rocky Flats Division Plant by the Chemical Standards Laboratory. It was prepared from air oxidized PuO_2 placed in nitric acid solution of pH 2.4 to obtain the nitrate form. The general physical, chemical, and isotopic attributes of the solution are given in Table 4. The solution was packaged in two 5ml sealed pharmaceutical vials fitted with rubber diaphragms. The solution used for the study was 2.0 N with an activity concentration of $19.9 \mu\text{Ci/ml}$. The Am concentration was 750 parts per million (ppm) at the beginning of the experiment. A dose of 0.10 ml of the $\text{Pu}(\text{NO}_3)_4$ solution was injected in each dog. Implant solution calibrations were performed each time a group of dogs was injected by placing three normal 0.1 ml injection aliquots in three separate one liter volumetric flasks of nitric acid solution, mixing and plancheting a sample for alpha counting in a gas flow proportional counting system.

Injection Procedure

The left fore-paw area was closely clipped of all hair to facilitate necessary decontamination of the surface around the simulated wound site. The dogs were anesthetized with an ultra-short anesthetic (sodium thiamylal for injection N.F. 4% solution). A 21 gauge hypodermic needle was inserted subcutaneously in the left dorsal metacarpus of the

Table 4. Physical, Chemical and Isotopic Characteristics of $\text{Pu}(\text{NO}_3)_4$ Supplied by Rocky Flats.

$\text{Pu}(\text{NO}_3)_4$	Characteristics
Pu	= 273 $\mu\text{g/ml}$
Total alpha activity	= 19.9 $\mu\text{Ci/ml}$
^{241}Am	= 0.13 $\mu\text{g/ml}$ (measured 10/1/69)
^{238}Pu	= 0.008%
^{239}Pu	= 93.54%
^{240}Pu	= 5.94%
^{241}Pu	= 0.51% (measured 1/68)
Measured pH	= 2.4

dog. The proper positioning of the needle was determined by palpation and by ascertaining that no back-flow of blood occurred, thus assuring that accidental intravenous injection was avoided. A 0.5 ml glass tuberculin syringe and a 21 gauge needle were used to withdraw an aliquot of the Pu solution from the vial. The syringe was detached from the needle and attached to the needle previously positioned in the dog's foot and the implant performed.

Implant Material for PuO_2 Experiment

The PuO_2 (high fired oxide) was prepared at Rocky Flats from electrowrefined unalloyed Pu metal dissolved in HCl and precipitated with oxalic acid. The resulting salt was washed and then calcined to the high fired state of plutonium dioxide for 100 hours at 850°C . The stoichiometry of oxide so prepared has been accepted as $\text{PuO}_{1.98}$. The

oxide was then dried at 80°C for approximately 100 hours and pulverized in a tungsten carbide grinding vial employing WC_2 grinding balls for 30 minutes on a high speed mechanical shaker. The particle size was measured by optical microscopy with the results shown in Table 5. The PuO_2 was then packaged in a dry particulate form, in 60 pharmaceutical ampuls fitted with airtight rubber diaphragms. Each vial contained approximately 1 mg with the exact measurement to 3 place accuracy. The physical, chemical, and isotopic properties of this preparation are shown in Table 5.

At the time of injection one ml of physiological saline solution (PSS) was injected with a 1 ml tuberculin syringe and needle into the vial. The vial was shaken vigorously to suspend the insoluble PuO_2 particles immediately before withdrawing a 0.25 ml aliquot for implant. Implant procedures were identical to that previously described in the $\text{Pu}(\text{NO}_3)_4$ experiment. Only two aliquots of PuO_2 were taken from each vial to assure a more homogeneous suspension. Because the suspensions were not homogeneous, settling time was critical and activity calibration of individual implant dosages by direct quantitative assessment was impossible. Therefore, a technique was devised whereby the implant dosage could be determined after the injection with an accuracy of approximately $\pm 5\%$. A germanium lithium drifted detector $\text{Ge}(\text{Li})$ was used to measure the amount of material contained in the vial prior to implant. Following implant, the

Table 5. Physical, Chemical and Isotopic Characteristics of PuO_2
Supplied by Rocky Flats.

Pu	= 0.8826 g/g
Cation impurities	= 200 ppm (based on Pu)
^{241}Am	= 360 ppm based on Pu as of Oct. 1, 1970
^{241}Am growth rate	= 15 ppm/month based on Pu
^{238}Pu	= 0.0105 wt %, based on Pu
^{239}Pu	= 93.898 wt %, based on Pu
^{240}Pu	= 5.695 wt %, based on Pu
^{241}Pu	= 0.377 wt %, based on Pu as of June, 1970
^{242}Pu	= 0.019 wt %, based on Pu
Atomic wt of Pu	= 239.116 as of June, 1970

Particle Size

1 μ or less	68%
1 μ	
3 μ to 5 μ	4%
5 μ to 10 μ	6%
>10 μ	< 1%

Mass Median Diameter approximates 0.7 .

activity was once again determined for each vial with the Ge(Li) detector. The injected paws were measured and a ratio of activity in the 2 paws could be correlated to an accurate measurement of the total amount withdrawn from each vial.

Monitoring and Contamination Control Procedures

The laboratory room used for implanting the Pu contaminant was protected from accidental contamination by lining the floor, walls, and surgical table areas with polyethylene sheeting. All persons in the room were required to wear protective equipment, including respirators and the complete protective gear with the exception of respirators during all sample periods. The implants were made under the surveillance of radiation monitoring personnel from the Health Physics Group of the Dow Chemical Company - Rocky Flats Plant. A continuous air sampler was run and contamination surveys were taken throughout the procedure. Following implants, an alpha survey meter was used to monitor the implant site for any accidental external contamination or back drainage. The implant wound site was then washed with hypochlorite solution and if contamination was detected the procedure was repeated until background levels were detected with the survey instrument. Following implant smear samples were taken around the entire room and the air sample filter recovered. These samples were counted for low level contamination. The cage room

and cages were smeared routinely when dogs were maintained in the metabolic cages and the smears analyzed for any low level contamination.

In Vivo Detection Procedure and Equipment

Immediately following implant in vivo measurements of activity were obtained at the implant site and over the left superficial cervical lymph node (LSCLN). This lymph node is the first major node draining the contaminated area of the paw (Yoffey and Courtice, 1970). The dog's paw and LSCLN were monitored with a NaI(Tl) in vivo wound counter and the dog returned to its metabolism cage for quantitative excreta collection.

Activity measurements of the paw and LSCLN were taken immediately after implant and thereafter on the same schedule as the blood sampling (Table 3). The detector used for these measurements was a NaI(Tl) crystal 2 inches in diameter by 4mm thick with a 0.010 inch beryllium window. The single channel analyzer window was set to detect the x-ray region from approximately 10 keV through 24 keV. This wound counter system was capable of detecting the 17 keV, average energy, U and Np L-x rays from the decay of the Pu and Am respectively. All counts were 40 seconds in length. This time interval was found optimum for counting the unanesthetized dogs. The count rate was one to five orders of magnitude above the 3 sigma MDA value (ICRP Handbook 80). Because of the tissue absorption of the low

energy X-rays (half value tissue thickness of approximately 6mm.), all counts taken had to be corrected for the approximate overlying tissue thickness.

A Ge(Li) system was used for simultaneous in vivo measurement of ^{239}Pu and ^{241}Am in the paw and LSCLN of the dogs. Because of the following characteristics of this detector it is capable of independently measuring these two elements in vivo. The Ge(Li) detector was of a planar drifted type with an active entrance surface of 10cm^2 , a depletion depth of 8mm, "P" layer of 13mm, and a diameter of 36mm. The detector was mounted in the cryostat 9mm behind the thin 0.010 inch beryllium window. The resolution of the detector system was approximately 1.9 keV full width at half maximum (FWHM) at 59.57 keV (gamma ray energy of ^{241}Am).

A special plexiglass restraining device was built to hold the dogs in a fixed geometry position for the necessary period, 1000 seconds for lymph nodes, 200 seconds for paw counts, and 600 seconds for liver counts.

The Ge(Li) system was coupled to a 512 channel analyzer calibrated at 1.00 keV per channel. The readout consisted of oscilloscope display, teletype hard copy, and scalers connected to three single channel analyzer centered on the 51.63 and 129.3 keV gamma photo-peaks from ^{239}Pu and the 59.57 gamma peak from ^{241}Am . The wound site was shielded with a lead shield to count over the LSCLN and liver regions. Problems which had to be resolved included: (1) The contribution from the 59.57 keV photopeak into the 51.63 keV energy region,

(2) the expected baseline background counts to be anticipated from the body regions of interest, and (3) the contribution of the Ge escape peak in the 51.63 keV region. It has been shown (Bistline, 1967; Speight and Ramsden, 1967) that differences in counts can be expected from scatter and compton radiation depending on the mass of tissue and natural background activity present.

DTPA Chelation Therapy

A dose of one gram per infusion is administered in man for clinical treatment where industrial use of DTPA is allowed (Lagerquist, et al., 1965; Norwood, 1962). For the dogs, a dose of 0.25 grams of DTPA in 10ml of PSS was injected intravenously. This dose was derived from comparison of standard blood volume between man (Radiological Health Handbook, 1960) and dog (Altman, 1961). The DTPA injections started at 2 hours post-implant on the first day and were routinely administered according to the schedule followed for the blood sampling Table 3, following the first day.

Measurement of Activity

Collection of Excreta and Blood Samples

Following implant of the Pu each dog was maintained in an individual metabolism cage for 14 days and for 3 consecutive days each month thereafter beginning with the 30th day post-implant. All 24-hour urine and feces samples were collected in the metabolism

cages on days 2 through 7, 9, 11, 14, and 3 days each month thereafter beginning on day 30 post-implant. Ten milliliter blood samples were obtained from each dog from the external jugular vein with a 10cc syringe and needle. Samples were taken at 1, 2, 4, and 8 hours post-implant and continued on the same schedule listed above for excreta sample collection.

Necropsy Procedure

The dogs were anesthetized with pentobarbital sodium and bled by a direct heart puncture until death. The following tissue samples were collected at necropsy: left testis, left kidney, left adrenal gland, spleen, liver (total mass was recorded but only about 1/3 taken for radiochemical analysis), left eye, trachea (approximately 3 inches to represent body cartilage), lung (a portion of one lobe), sternum, rib (left 10th), vertebrae (2-lumbar), skull (approximately 1 inch square section), left femur (sectioned into the proximal end, shaft and the distal end), left superficial cervical lymph node (LSCLN), left axillary lymph node, (the implant site & the left front paw sectioned at the carpo-metacarpal joint), right superficial cervical lymph node (RSCLN), thyroid gland, bile, and the hepatic lymph nodes. Each sample was collected in an individual plastic bag and care was taken to prevent cross contamination by instruments from sample to sample and from one necropsy to the next by washing the instruments in a special K-W solution (formulated mixture of citric acid, detergent,

and ethylenediaminetetracetic acid (EDTA) (Putzier, 1967). All samples were ashed and radiochemically assayed for Pu and Am at the Rocky Flats Health Physics Laboratories.

Analysis of Data

The data were grouped according to treatment groups and time of samples. Because of the extreme closeness of the data points on the time scale for the first several days, most of the data were grouped for plotting and standard errors calculated for the grouped data. All grouped data were analyzed for range and mean values. Extreme data points for individual dogs lying greater than 3 sigma were discarded. The mean, standard deviation, and standard error was calculated for each individual group of data including wound counter measurements and radiochemical analysis data on blood, urine and tissue samples. All tables and graphs are presented with standard error values. Generally it can be said that the standard error values are smaller in the figures during the earlier values of time because through the 14th day each treatment group consisted of 24 dogs decreasing to 4 dogs at 6 months. Thus the sample size decreased greatly with time.

The determination of the curve models best fitting the data presented in the graphs was accomplished by comparisons of a least-squares fit of their linear transforms. Indexes of determinations were obtained for three functions including linear, power, and

exponential. The indexes approaching 1.00 were calculated to be the best fit curve for the data.

Data values given in the tables with no standard error values included are single data values.

Results

To be able to group the data and compare time, treatment and enhancement effects for different chemical forms, it was necessary to normalize all data to the fraction of the initial implant dose administered to each dog. Monthly values are presented as an average of the 3 daily counts or samples taken on each dog.

The results obtained with the in vivo Na(T) wound counter measurements of the 17 keV L-x rays from the implant site on the left paw are shown in Table 6. The data reflects the average values obtained at the time of sampling or counting for dogs in each treatment group for the chemical form implanted. The animals listed under No Treatment (Table 6) headings were implanted with Pu but receiving no chelation therapy and those listed under DTPA received DTPA chelation therapy according to the schedule described in the experimental design. Figures 1 and 2 show plots of the best curve fit analysis for this data. It was found that the best curve fit models for the $\text{Pu}(\text{NO}_3)_4$ No Treatment and DTPA groups were the following power functions:

A. No Treatment

$$y = AX^B$$

where y = time in days, x = fraction of initial implant dose, A = 0.6359, B = 0.1239

Table 6. Fraction of Initial Implant Dose of Plutonium in Paw with Exposure Time.

Time Following Implant (days)	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment	DTPA	No Treatment	DTPA
0.0417	0.90 $\pm$ 0.13	0.71 $\pm$ 0.15	0.762 $\pm$ 0.097	0.702 $\pm$ 0.105
0.333	0.65 $\pm$ 0.08	0.50 $\pm$ 0.08	0.865 $\pm$ 0.098	0.804 $\pm$ 0.108
5 Days	0.57 $\pm$ 0.07	0.33 $\pm$ 0.06	0.808 $\pm$ 0.091	0.788 $\pm$ 0.107
11 "	0.63 $\pm$ 0.085	0.34 $\pm$ 0.06	0.737 $\pm$ 0.087	0.758 $\pm$ 0.101
14 "	0.51 $\pm$ 0.08	0.33 $\pm$ 0.07	0.660 $\pm$ 0.089	0.745 $\pm$ 0.099
31 "	0.35 $\pm$ 0.06	0.22 $\pm$ 0.06	0.879 $\pm$ 0.067	0.930 $\pm$ 0.119
60 "	0.31 $\pm$ 0.11	0.22 $\pm$ 0.06	0.546 $\pm$ 0.073	0.552 $\pm$ 0.089
90 "	0.31 $\pm$ 0.05	0.24 $\pm$ 0.05	0.470 $\pm$ 0.123	0.516 $\pm$ 0.137
125 "	0.49 $\pm$ 0.15	0.31 $\pm$ 0.08	0.421 $\pm$ 0.055	0.370 $\pm$ 0.047
170 "	0.37 $\pm$ 0.07	0.21 $\pm$ 0.09	0.452 $\pm$ 0.074	0.380 $\pm$ 0.043
221 "	0.33 $\pm$ 0.12	0.17 $\pm$ 0.03	0.133 $\pm$ 0.016	0.160 $\pm$ 0.020
248 "	0.36 $\pm$ 0.12	0.21 $\pm$ 0.02	0.090 $\pm$ 0.006	0.147 $\pm$ 0.024
304 "	0.38 $\pm$ 0.12	0.21 $\pm$ 0.02	0.116 $\pm$ 0.011	0.164 $\pm$ 0.021
357 "	0.18 $\pm$ 0.06	0.11 $\pm$ 0.03	0.109 $\pm$ 0.012	0.163 $\pm$ 0.021

Figure 1. Power function curve for fraction of
initial dose retained in paw of $\text{Pu}(\text{NO}_3)_4$
dogs. Solid line = No Treatment.
Broken line = DTPA treatment.

FRACTION OF DOSE
LOG SCALE

TIME IN DAYS

Figure 2. Exponential function curve for fraction
of initial dose retained in paw of PuO_2
dogs. Solid line = No Treatment.
Broken line = DTPA Treatment.

B. DTPA

$$y = AX^B$$

where y = time in days,
X = fraction of initial
implant dose, A =
0.4436, B = 0.545

For the PuO_2 data the best curve fit analysis found was an
exponential curve for both sets of data:

A. No Treatment,

$$y = Ae^{BX}$$

where y and X are the
same as above, A =
0.8368, B = 0.006601

B. DTPA

$$y = Ae^{BX}$$

where y and X are the
same as above, A =
0.797, B = -0.005419

The data on the Pu buildup from the wound site to the left
superficial cervical lymph node, is presented in Table 7. This data
was derived from the in vivo NaI(Tl) wound counter measurements,
taken over the LSCLN. Figures 3 and 4 are plots of the data obtained
from the wound counter measurements. Radiochemical analysis of the
LSCLN's taken at the 6 necropsy times is shown in Tables 14-17.
These data show a similar shaped curve for buildup and regression.
These data reinforce the compatibility of the two completely separate
measurement techniques. The activity in the LSCLN rose to a maxi-
mum around 30 to 90 days for both $\text{Pu}(\text{NO}_3)_4$ and PuO_2 forms. This
data was best fitted by a power function model. After reaching this
maximum a gradual linear regression in the data occurred throughout
the remainder of the 1 year study. The curve fit models for the
 $\text{Pu}(\text{NO}_3)_4$ data was found to be:

Table 7. Fraction of Initial Implant Dose of Plutonium in Lymph Node with Exposure Time.

Time Following Implant (days)	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment	DTPA	No Treatment	DTPA
0.0417	0.053±0.001	0.04±0.007	0.00125±0.00071	0.00113±0.00050
0.333	0.16±0.029	0.12±0.022	0.00595±0.00143	0.00786±0.00492
5 Days	0.22±0.036	0.17±0.030	0.05086±0.01106	0.02134±0.00548
11 "	0.24±0.066	0.20±0.043	0.08909±0.01593	0.05050±0.01435
14 "	0.17±0.039	0.15±0.037	0.09292±0.01363	0.05275±0.01062
31 "	0.11±0.02	0.08±0.02	0.20119±0.02471	0.08074±0.00913
60 "	0.31±0.06	0.35±0.07	0.13148±0.02037	0.09331±0.01554
90 "	0.20±0.04	0.23±0.05	0.21260±0.03606	0.11565±0.01565
125 "	0.57±0.12	0.60±0.10	0.13548±0.02358	0.07553±0.00754
170 "	0.10±0.03	0.09±0.04	0.14917±0.05433	0.08157±0.01568
221 "	0.37±0.13	0.30±0.03	0.09288±0.02640	0.04981±0.00501
248 "	0.40±0.13	0.30±0.03	0.09395±0.02635	0.04716±0.00770
304 "	0.43±0.13	0.43±0.04	0.16514±0.09294	0.05842±0.00361
357 "	0.07±0.017	0.06±0.017	0.11203±0.02736	0.05056±0.00488

Figure 3. Fraction of initial dose in superficial
cervical lymph node of $\text{Pu}(\text{NO}_3)_4$ dogs.
X = No Treatment.
Square = DTPA Treatment.

Figure 4. Fraction of initial dose in superficial
cervical lymph node of PuO_2 dogs.
X = No Treatment
Square = DTPA Treatment.

No Treatment

1st component a power function

$$Y = AX^B \quad \begin{array}{l} A = 0.1268 \\ B = 0.1609 \end{array}$$

2nd component a linear function

$$Y = A + BX \quad \begin{array}{l} A = 0.3599 \\ B = -2.7259 \times 10^{-4} \end{array}$$

DTPA

1st component a power function

$$Y = AX^B \quad \begin{array}{l} A = 0.1002 \\ B = 0.1928 \end{array}$$

2nd component a linear function

$$Y = A + BX \quad \begin{array}{l} A = 0.3976 \\ B = -3.0032 \times 10^{-3} \end{array}$$

The curve fit models for the PuO_2 data was:

No Treatment

1st component a power function

$$Y = AX^B \quad \begin{array}{l} A = 0.014006 \\ B = 0.76235 \end{array}$$

2nd component a linear function

$$Y = A + BX \quad \begin{array}{l} A = 0.18134 \\ B = -2.1013 \times 10^{-4} \end{array}$$

DTPA

1st component a power function

$$Y = AX^B \quad \begin{array}{l} A = 0.01020 \\ B = 0.61822 \end{array}$$

2nd component a linear function

$$A = .10098$$

$$B = -1.59127 \times 10^{-4}$$

Johnson (1969) showed a high correlation of coefficient of 0.993 for his PuO_2 (air oxidized) data. Thus, the fact that the power function had a good index of determination for the data in the first components of these curves is strongly supported.

Systemic transport of Pu from the lymph or lymph node as well as the wound site occurred in the blood. The results of the radiochemical analysis of 10ml blood samples taken according to the schedule presented in Table 3 are given in Tables 8 and 9. The concentration of Pu in the blood increased with time reaching a peak at 2 to 24 hours. However, in the curve fit analysis plots of Fig. 5 and 6 the values for the first components are so near day 0 on the time scale that only the 2nd components of the curves have been plotted. The best curve fit functions for these data was found to be:

A. $\text{Pu}(\text{NO}_3)_4$

a) No Treatment Group

Plot is a power function:

$$Y = AX^B$$

$$A = 28.7102 \times 10^{-6}$$

$$B = -0.7004$$

b) DTPA Group

Plot is a power function:

$$Y = AX^B$$

$$A = 13.5395 \times 10^{-6}$$

$$B = 0.68237$$

Table 8. Fraction of Initial Implant Dose of Plutonium in Blood with Exposure Time -- Pu(NO₃)₄ Group.

Time Following Implant (days)	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)
0.021	63.88± 9.90	54.25±10.27
0.042	33.13± 7.13	22.15± 5.15
0.083	54.15± 5.42	36.69± 5.54
0.167	61.07±16.80	40.75± 7.55
0.250	123.20±47.34	70.50±27.56
0.333	67.01±20.24	27.16± 5.87
2	48.25± 4.80	42.01±10.13
3	23.21± 3.23	11.63± 2.02
4	11.09± 0.88	6.09± 1.90
5	9.28± 1.18	2.79± 0.47
6	8.64± 1.87	--
7	--	1.38± 0.21
9	3.11± 0.43	1.95± 0.44
11	2.34± 0.26	1.38± 0.24
14	3.42± 0.73	1.73± 0.28
31	1.50± 0.17	0.95± 0.15
34	1.33± 0.19	0.49± 0.05
59	1.15± 0.13	0.64± 0.15
65	0.61± 0.15	0.31± 0.06
88	0.59± 0.10	0.21± 0.04
93	0.60± 0.14	0.25± 0.05
121	1.09± 0.09	0.53± 0.05
129	1.12± 0.24	0.96± 0.16
157	1.04± 0.14	0.74± 0.07
165	0.78± 0.08	0.38± 0.05
188	1.48± 0.31	1.19± 0.32
221	0.49± 0.07	0.47± 0.15
248	0.65± 0.15	0.24± 0.06
276	0.97± 0.24	0.55± 0.06
304	0.99± 0.17	0.67± 0.12
336	1.06± 0.23	0.64± 0.10
366	0.83± 0.28	0.15± 0.03

Table 9. Fraction of Initial Implant Dose of Americium in Blood with Exposure Time--Pu(NO₃)₄ Group.

Time Following Implant (days)	No. Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)
0.021	1.810±0.714	1.804±0.700
0.042	18.472±7.396	4.618±1.715
0.083	7.273±1.782	4.129±0.953
0.167	7.135±1.695	4.041±1.263
0.250	5.508±0.925	2.390±0.669
0.333	6.103±1.887	4.031±1.037
2	2.736±0.537	1.619±0.331
3	1.469±0.523	0.466±0.101
4	2.152±0.705	1.593±0.488
5	0.897±0.202	0.350±0.103
6	0.459±0.091	0.573±0.187
7	0.369±0.085	0.880±0.657
9	0.278±0.083	0.689±0.248
11	0.621±-.322	0.317±0.108
14	0.449±0.172	0.230±0.050
31	0.231±0.049	0.204±0.055
65	0.159±0.074	0.084±0.024
93	0.018±0.003	0.031±0.016
121	0.072±0.037	0.027±-.008
129	3.491±0.826	1.596±0.185
165	0.016±0.003	0.022±0.006
187	4.704±1.912	2.057±0.443
221	0.854±0.148	1.840±0.561
248	2.864±1.405	0.864±0.140
276	1.964±0.573	1.619±0.283
304	1.603±0.371	2.561±0.669
336	1.764±0.612	5.318±1.511

Figure 5. Power function curve for fraction of initial dose in blood of $\text{Pu}(\text{NO}_3)_4$ dogs. Solid line = No Treatment. Broken line = DTPA treatment.

Figure 6. Power function curve for fraction of
initial dose in blood of PuO_2 dogs.
Solid line = No Treatment.
Broken line = DTPA Treatment.

B. PuO_2

a) No Treatment Group

Plot is a power function:

$$Y = AX^B \quad \begin{array}{l} A = 0.62977 \times 10^{-8} \\ B = 0.26896 \end{array}$$

b) DTPA Group

Plot is a power function:

$$Y = -AX^B \quad \begin{array}{l} A = 0.47545 \times 10^{-8} \\ B = 0.31112 \end{array}$$

The radiochemical analysis of the Am concentration in the blood shows a nearly identical pattern to the of Pu. The data is presented in Tables 10 and 11.

As a fraction of the systemically circulating Pu is excreted through the urine pathway, 24-hour urine samples were collected and analyzed for Pu and Am content. Tables 12 and 13 show the fractions of these isotopes excreted via the urine in 24-hour periods. Curve fit analysis of these data indicate a best fit by using a power function model. The following functions were best fitted to these data:

A. $\text{Pu}(\text{NO}_3)_4$

a) No Treatment Group:

$$Y = AX^B \quad \begin{array}{l} A = 189.07 \times 10^{-5} \\ B = 0.5378 \end{array}$$

b) DTPA Group:

$$Y = AX^B \quad \begin{array}{l} A = 1617.18 \times 10^{-5} \\ B = -0.7013 \end{array}$$

B. PuO_2

a) No Treatment Group:

$$Y = AX^B \quad \begin{array}{l} A = 0.2915 \times 10^{-5} \\ B = -0.4035 \end{array}$$

Table 10. Fraction of Initial Implant Dose of Plutonium in Blood with Exposure Time--PuO₂ Group.

Time Following Implant (days)	No Treatment (X10 ⁻⁸)	DTPA (X10 ⁻⁸)
0.042	0.397±0.088	0.468±0.170
0.083	1.512±0.470	1.107±0.446
0.167	1.439±0.337	0.773±0.215
0.333	1.181±0.384	1.124±0.401
2	1.116±0.470	1.304±0.552
3	0.847±0.207	0.419±0.154
4	0.575±0.113	0.453±0.143
5	0.381±0.079	0.236±0.054
6	0.338±0.076	0.274±0.091
7	0.386±0.092	0.352±0.127
9	0.440±0.075	0.253±0.076
11	0.291±0.064	0.283±0.102
14	0.189±0.085	0.186±0.109
31	0.158±0.048	0.135±0.022
36	0.575±0.413	0.038±0.015
65	0.133±0.025	0.114±0.026
70	0.130±0.034	0.108±0.025
103	0.146±0.032	0.077±0.013
140	0.113±0.020	0.067±0.013
183	0.228±0.109	0.124±0.033
217	0.181±0.045	0.097±0.024
258	0.103±0.035	0.081±0.043
287	0.160±0.091	0.175±0.116

Table 11. Fraction of Initial Implant Dose of Americium in Blood with Exposure Time--PuO₂ Group.

Time Following Implant (days)	No Treatment ($\times 10^{-9}$)	DTPA ($\times 10^{-9}$)
0.042	92.507 $\pm$ 56.855	89.211 $\pm$ 68.819
0.083	80.015 $\pm$ 35.859	60.979 $\pm$ 31.758
0.167	102.297 $\pm$ 47.470	151.304 $\pm$ 105.912
0.333	24.611 $\pm$ 7.907	9.870 $\pm$ 3.917
2	28.862 $\pm$ 11.545	33.980 $\pm$ 19.816
3	32.067 $\pm$ 22.996	99.800 $\pm$ 60.990
4	9.800 $\pm$ 2.293	17.540 $\pm$ 7.840
5	8.526 $\pm$ 2.663	18.990 $\pm$ 14.035
6	12.284 $\pm$ 4.428	19.036 $\pm$ 6.852
7	8.548 $\pm$ 2.682	10.285 $\pm$ 3.396
9	6.803 $\pm$ 2.182	7.290 $\pm$ 2.722
11	45.999 $\pm$ 15.818	28.708 $\pm$ 13.905
14	28.976 $\pm$ 8.890	4.083 $\pm$ 1.054
31	16.072 $\pm$ 4.911	25.223 $\pm$ 6.909
46	7.043 $\pm$ 1.498	--
65	27.890 $\pm$ 24.390	3.602 $\pm$ 0.363
70	8.937 $\pm$ 4.199	19.610 $\pm$ 6.425
78	46.390 $\pm$ 27.939	43.383 $\pm$ 20.942
103	31.752 $\pm$ 12.866	13.128 $\pm$ 5.961
163	15.307 $\pm$ 12.583	40.900 $\pm$ 36.887
183	20.100 $\pm$ 8.278	5.618 $\pm$ 1.314
217	21.496 $\pm$ 8.765	19.096 $\pm$ 7.904

Table 12. Fraction of Initial Implant Dose of Plutonium in 24 hour Urine with Exposure Time.

Time Following Implant (days)	Pu(NO ₃) ₄		Time Following Implant (days)	PuO ₂	
	No Treatment (X10 ⁻⁵)	DTPA (X10 ⁻⁵)		No Treatment (X10 ⁻⁵)	DTPA (X10 ⁻⁵)
2	1233.312±278.032	3676.244±561.894	2	0.344±0.147	6.549±4.616
3	305.322±100.462	2124.812±583.909	3	0.274±0.157	1.355±0.459
4	109.972± 21.183	516.749± 73.452	4	0.981±0.781	0.448±0.226
5	88.234± 15.185	606.613±103.547	5	0.221±0.070	0.432±0.132
6	34.522± 4.418	326.617± 50.231	6	0.034±0.009	0.564±0.216
7	35.746± 5.749	277.699± 45.621	7	0.099±0.029	0.694±0.232
9	22.555± 3.345		9	0.073±0.018	0.280±0.072
11	21.196± 2.921	115.185± 21.525	11	0.071±0.014	0.169±0.066
14	16.294± 2.998	55.544± 9.757	14	0.174±0.075	0.262±0.075
31	11.464± 1.837	49.103± 9.840	33	0.129±0.029	0.414±0.071
59	23.207± 4.817	66.694± 10.089	48	0.006±0.004	0.214±0.161
65	7.251± 1.461	90.448± 22.651	68	0.005±0.004	0.168±0.042
93	9.764± 0.933	73.731± 14.080	78	0.035±0.005	0.050
121	7.004± 0.825	75.246± 19.310	104	0.061±0.011	0.143±0.041
129	30.319± 5.450	104.560± 22.984	137	0.099±0.035	0.168±0.040
157	52.448± 12.389	226.582± 57.475			
165	6.026± 0.843	50.980± 13.441			
187	32.675± 6.022	45.091± 12.423	183	0.110±0.046	0.040±0.021
221	19.376± 5.531	44.865± 25.070	217	0.108±0.031	0.178±0.095
248	16.313± 3.108	51.764± 11.353	258	0.033±0.015	0.068±0.019
276	8.752± 0.993	37.829± 15.709	287	0.030±0.007	0.050±0.027
304	13.843± 2.147	22.041± 5.010			
336	5.540± 1.472	8.978± 4.310			

Table 13. Fraction of Initial Implant Dose of Americium in 24-hour Urine with Exposure Time.

Time Following Implant (days)	$\text{Pu}(\text{NO}_3)_4$		Time Following Implant (days)	PuO_2	
	No Treatment ($\times 10^{-5}$)	DTPA ($\times 10^{-5}$)		No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
2	467.4 $\pm$ 279.7	1214.6 $\pm$ 631.6	2	24.38 $\pm$ 13.82	52.04 $\pm$ 24.33
3	92.5 $\pm$ 32.6	429.6 $\pm$ 123.6	3	10.66 $\pm$ 4.01	87.99 $\pm$ 26.11
4	29.1 $\pm$ 9.5	424.2 $\pm$ 250.2	4	8.61 $\pm$ 1.98	19.13 $\pm$ 4.02
5	49.3 $\pm$ 15.8	115.7 $\pm$ 31.9	5	7.80 $\pm$ 3.71	28.02 $\pm$ 15.49
6	47.6 $\pm$ 19.1	120.9 $\pm$ 43.5	6	19.54 $\pm$ 15.32	12.19 $\pm$ 6.93
7	15.4 $\pm$ 6.9	166.2 $\pm$ 88.3	7	2.35 $\pm$ 1.09	8.74 $\pm$ 3.07
9	15.2 $\pm$ 6.3	69.6 $\pm$ 26.8	9	7.87 $\pm$ 5.22	7.11 $\pm$ 6.26
11	11.4 $\pm$ 4.2	43.4 $\pm$ 12.9	11	4.39 $\pm$ 1.34	11.77 $\pm$ 4.50
14	15.6 $\pm$ 7.3	30.2 $\pm$ 12.3	14	11.73 $\pm$ 2.37	25.65 $\pm$ 9.30
31	6.5 $\pm$ 1.5	15.5 $\pm$ 2.3	33	10.40 $\pm$ 9.26	--
59	--	--	48	3.10 $\pm$ 1.52	6.80 $\pm$ 2.76
65	8.3 $\pm$ 1.9	72.1 $\pm$ 22.3	68	--	--
93	6.8 $\pm$ 1.6	103.6 $\pm$ 42.3	78	--	--
121	9.8 $\pm$ 3.4	59.5 $\pm$ 24.3	104	7.84 $\pm$ 2.03	2.38 $\pm$ 0.75
129	--	--	137	17.94 $\pm$ 10.59	10.01 $\pm$ 3.75
157	--	--	183	0.64 $\pm$ 0.38	0.94 $\pm$ 0.36
165	6.7 $\pm$ 1.4	111.1 $\pm$ 27.9	217	4.74 $\pm$ 4.54	9.02 $\pm$ 4.95
			258	2.32 $\pm$ 1.96	1.87 $\pm$ 0.93
			287	--	1.09 $\pm$ 0.36

b) DTPA Group:

$$Y = AX^B \quad \begin{array}{l} A = 1.9581 \times 10^{-5} \\ B = -0.6202 \end{array}$$

Plots of these functions are shown in Figs. 7 and 8.

Figures 9 and 10 show plots of the data obtained from the radiochemical analysis of the liver. This organ has been recognized as a critical organ and as expected, did show a buildup of activity with time. Data from the analysis of spleen is plotted in Figures 11 and 12. As the hepatic lymph node drains from the liver, it was analyzed for increased activity above other normal soft tissue. The plots of this data are shown in Figures 13 and 14.

The proximal portion of the femur was taken as being representative of trabecular bone. The radiochemical analysis of this data is shown in Figures 15 and 16.

The liver, spleen, hepatic lymph node, and proximal portion of the femur all indicate a trend toward a peak occurring about 6 months, followed by an apparent decrease from 6 months through 1 year.

Because of translocation occurring from the implant site, small quantities of Pu and Am began to appear in the various organs of the body. Specific organs described in the previous section were removed at prescribed sacrifice times and analyzed for Pu and Am content.

Tables 14 and 15 give the normalized concentrations of Pu and Am for the No Treatment and DTPA treatment groups using the two different

Figure 7. Power function curve of fraction of initial dose in urine of $\text{Pu}(\text{NO}_3)_4$ dogs. Solid line = No Treatment. Broken line - DTPA Treatment.

Figure 8. Power function curve of fraction of
initial dose in urine of PuO_2 dogs.
Solid line = No Treatment.
Broken line = DTPA Treatment.

Figure 9. Fraction of initial dose in liver of
 $\text{Pu}(\text{NO}_3)_4$ dogs. X = No Treatment
Square = DTPA Treatment.

Figure 10. Fraction of initial dose in liver of
PuO₂ dogs. X = No Treatment.
Square = DTPA Treatment.

Figure 11. Fraction of initial dose in spleen of
 $\text{Pu}(\text{NO}_3)_4$ dogs. X = No Treatment.
Square = DTPA Treatment.

b

Figure 12. Fraction of initial dose in spleen of
PuO₂ dogs. X = No Treatment.
Square = DTPA Treatment.

b

Figure 13. Fraction of initial dose in hepatic lymph
node of $\text{Pu}(\text{NO}_3)_4$ dogs. X = No Treatment.
Square = DTPA Treatment.

Figure 14. Fraction of initial dose in hepatic lymph
node of PuO_2 dogs. X = No Treatment.
Square = DTPA Treatment.

Figure 15. Fraction of initial dose in proximal
section of femur of $\text{Pu}(\text{NO}_3)_4$ dogs.
X = No Treatment. Square = DTPA
Treatment.

1. The first part of the paper is devoted to a discussion of the general principles of the theory of the structure of the atom. It is shown that the structure of the atom is determined by the laws of quantum mechanics, and that the structure of the atom is a function of the atomic number.

Figure 16. Fraction of initial dose in proximal
section of femur of PuO_2 dogs.
X = No Treatment. Square = DTPA
Treatment.

Table 14. Fraction of Initial Implant Dose of Plutonium per Gram of Organ Tissue.

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Left Testis</u>				
2 wks.	0.74 $\pm$ 0.40	0.29 $\pm$ 0.24	0.0020 $\pm$ 0.0005	0.0010 $\pm$ 0.0008
1 mo.	4.84 $\pm$ 1.49	1.26 $\pm$ 0.33	0.0048 $\pm$ 0.0008	0.0035 $\pm$ 0.0008
2 mo.	2.80 $\pm$ 0.47	1.01 $\pm$ 0.19	0.0716 $\pm$ 0.0377	0.0217 $\pm$ 0.0098
3 mo.	--	--	0.0244 $\pm$ 0.0097	0.0521 $\pm$ 0.0265
6 mo.	8.39 $\pm$ 2.66	2.61 $\pm$ 1.18	0.0483 $\pm$ 0.0237	0.0497 $\pm$ 0.0440
1 yr.	4.51 $\pm$ 0.06	1.33 $\pm$ 0.28	0.0316 $\pm$ 0.0193	0.0036 $\pm$ 0.0014
<u>Left Kidney</u>				
2 wks.	7.62 $\pm$ 3.77	0.52 $\pm$ 0.11	0.0156 $\pm$ 0.0047	0.0113 $\pm$ 0.0039
1 mo.	1.99 $\pm$ 0.34	3.49 $\pm$ 1.21	0.0132 $\pm$ 0.0096	0.1985 $\pm$ 0.1886
2 mo.	21.65 $\pm$ 7.27	6.69 $\pm$ 2.79	0.1360 $\pm$ 0.0192	0.0900 $\pm$ 0.0312
3 mo.	--	--	0.0753 $\pm$ 0.0169	0.3073 $\pm$ 0.1757
6 mo.	4.69 $\pm$ 2.35	6.24 $\pm$ 2.00	0.3397 $\pm$ 0.2348	0.0222 $\pm$ 0.0124
1 yr.	8.27 $\pm$ 4.58	25.12 $\pm$ 21.87	0.0235 $\pm$ 0.0060	0.0115 $\pm$ 0.0067
<u>Left Adrenal</u>				
2 wk.	8.00 $\pm$ 3.78	1.42 $\pm$ 0.72	0.1493 $\pm$ 0.1031	0.1729 $\pm$ 0.1298
1 mo.	23.48 $\pm$ 2.86	30.34 $\pm$ 19.92	0.0595 $\pm$ 0.0524	0.1020 $\pm$ 0.0850
2 mo.	17.49 $\pm$ 2.86	6.23 $\pm$ 1.69	0.5104 $\pm$ 0.1713	0.5335 $\pm$ 0.2710

Table 14. Continued

Time Following Implant	Pu(NO ₃) ₄		PuO ₂	
	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)
<u>Left Adrenal (Continued)</u>				
3 mo.	--	--	43.9351+30.2519	0.6924+0.3698
6 mo.	24.83+4.56	8.76+1.50	3.4660+2.0249	11.6884+5.7430
1 yr.	32.38+11.48	--	0.0765+0.0332	0.0704+0.0323
<u>Spleen</u>				
2 wk.	73.67+40.45	8.30+3.30	0.0276+0.0116	0.0608+0.0540
1 mo.	258.99+129.02	34.22+2.66	0.0132+0.0047	0.0098+0.0009
2 mo.	30.42+12.13	18.57+2.78	0.2577+0.1124	0.0588+0.0116
3 mo.	--	--	0.2661+0.0559	0.0204+0.0060
6 mo.	68.77+26.40	21.85+2.78	0.1195+0.0802	0.2067+0.1837
1 yr.	158.49+102.16	10.67+3.85	0.0189+0.0137	0.0582+0.0512
<u>Liver</u>				
2 wks.	94.04+35.88	17.13+10.81	0.0237+0.0218	0.0012+0.0006
1 mo.	83.03+39.68	10.71+4.01	0.1256+0.1158	0.0005+0.0002
2 mo.	80.04+32.48	2.58+0.77	0.5221+0.2852	0.0576+0.0344
3 mo.	66.31+13.05	15.77+4.26	0.0092+0.0018	0.0419+0.0267

Table 14. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Liver (Continued)</u>				
6 mo.	108.82 $\pm$ 58.64	11.56 $\pm$ 4.45	0.0492 $\pm$ 0.0323	0.2873 $\pm$ 0.0421
1 yr.	474.29 $\pm$ 82.75	49.16 $\pm$ 10.24	0.6637 $\pm$ 0.5728	0.5257 $\pm$ 0.3334
<u>Left Eye</u>				
2 wks.	1.42 $\pm$ 0.47	0.41 $\pm$ 0.02	0.0171 $\pm$ 0.0061	0.0021 $\pm$ 0.0010
1 mo.	3.40 $\pm$ 0.72	0.94 $\pm$ 0.31	0.0095 $\pm$ 0.0010	0.0201 $\pm$ 0.0049
2 mo.	1.55 $\pm$ 0.35	1.08 $\pm$ 0.22	0.8271 $\pm$ 0.6884	0.0655 $\pm$ 0.0278
3 mo.	--	--	3.6910 $\pm$ 2.7599	0.1333 $\pm$ 0.0890
6 mo.	7.86 $\pm$ 2.76	2.83 $\pm$ 1.31	0.1035 $\pm$ 0.0498	4.1157 $\pm$ 2.3345
1 yr.	2.21 $\pm$ 0.21	--	0.0594 $\pm$ 0.0383	0.0136 $\pm$ 0.0075
<u>Trachea</u>				
2 wks.	3.53 $\pm$ 2.49	0.26 $\pm$ 0.23	0.0025 $\pm$ 0.0010	0.0006 $\pm$ 0.0004
1 mo.	7.43 $\pm$ 1.18	2.45 $\pm$ 0.94	0.0480 $\pm$ 0.0462	0.0204 $\pm$ 0.0068
2 mo.	3.99 $\pm$ 1.36	16.65 $\pm$ 8.90	0.0841 $\pm$ 0.0329	0.2621 $\pm$ 0.1573
3 mo.	--	--	1.2437 $\pm$ 0.8674	0.1906 $\pm$ 0.1370
6 mo.	10.33 $\pm$ 2.41	4.34 $\pm$ 0.50	0.1003 $\pm$ 0.0347	0.1241 $\pm$ 0.0756
1 yr.	3.82 $\pm$ 0.64	1.13 $\pm$ 0.42	0.0760 $\pm$ 0.0394	0.1039 $\pm$ 0.0391

Table 14. Continued

Time Following Implant	Pu(NO ₃) ₄		PuO ₂	
	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)
<u>Lung</u>				
2 wks.	15.31± 6.22	8.45± 7.66	0.0019±0.0007	0.0062±0.0058
1 mo.	6.68± 1.86	2.98± 1.01	0.0306±0.0297	0.0109±0.0092
2 mo.	5.37± 1.01	3.14± 1.63	0.0129±0.0039	0.0293±0.0121
3 mo.	--	--	0.0791±0.0351	0.4423±0.2338
6 mo.	8.43± 0.63	3.43± 0.29	0.0187±0.0036	0.1467±0.1037
1 yr.	132.51±67.96	42.94±39.23	0.0100±0.0031	0.0051±0.0029
<u>Sternum</u>				
2 wks.	158.31±21.94	14.05± 7.84	0.0113±0.0030	0.0057±0.0018
1 mo.	167.17±67.86	95.04±46.46	0.0109±0.0038	0.0072±0.0016
2 mo.	121.40±32.65	58.21±16.02	0.1280±0.0138	0.0362±0.0037
3 mo.	133.04±22.25	24.26± 9.42	0.1596±0.0199	0.0936±0.0129
6 mo.	313.77±53.93	84.73±10.34	0.0303±0.0189	0.0281±0.0047
1 yr.	281.49±34.66	252.78±20.59	0.0483±0.0125	0.0064
<u>Rib</u>				
2 wks.	110.81±20.63	28.86±10.99	0.0223±0.0049	0.0356±0.0310
1 mo.	255.74±74.81	133.60±44.89	0.0628±0.0164	0.0870±0.0640
2 mo.	153.54±32.16	38.55± 9.45	0.2229±0.0145	0.0686±0.0101

Table 14. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment	DTPA	No Treatment	DTPA
	($\times 10^{-6}$)	($\times 10^{-6}$)	($\times 10^{-6}$)	($\times 10^{-6}$)
<u>Rib. (Continued)</u>				
3 mo.	129.60 $\pm$ 35.60	29.72 $\pm$ 3.92	1.1819 $\pm$ 1.0335	0.1090 $\pm$ 0.0399
6 mo.	354.61 $\pm$ 29.01	124.96 $\pm$ 16.71	0.2628 $\pm$ 0.0612	0.0431 $\pm$ 0.0095
1 yr.	280.52 $\pm$ 31.04	58.06 $\pm$ 9.13	0.0613 $\pm$ 0.0145	0.0385 $\pm$ 0.0212
<u>Vertebrae</u>				
2 wks.	46.85 $\pm$ 11.06	17.02 $\pm$ 10.44	0.0062 $\pm$ 0.0009	0.0030 $\pm$ 0.0010
1 mo.	26.29 $\pm$ 15.85	31.56 $\pm$ 9.00	0.0248	0.0065 $\pm$ 0.0009
2 mo.	64.55 $\pm$ 8.25	27.91 $\pm$ 6.98	0.2398 $\pm$ 0.0329	0.0374 $\pm$ 0.0074
3 mo.	95.82 $\pm$ 6.42	24.50 $\pm$ 4.65	0.0928 $\pm$ 0.0122	0.0567 $\pm$ 0.0166
6 mo.	387.22 $\pm$ 40.45	145.17 $\pm$ 30.12	0.1251 $\pm$ 0.0134	0.3613 $\pm$ 0.3190
1 yr.	196.44 $\pm$ 52.42	85.79 $\pm$ 36.59	0.0278 $\pm$ 0.0119	0.0101 $\pm$ 0.0025
<u>Skull</u>				
2 wks.	11.07 $\pm$ 5.43	10.19 $\pm$ 6.06	0.0068 $\pm$ 0.0035	0.0092 $\pm$ 0.0059
1 mo.	5.17 $\pm$ 0.86	11.41 $\pm$ 2.10	0.0104 $\pm$ 0.0078	0.0060 $\pm$ 0.0038
2 mo.	47.66 $\pm$ 13.68	11.98 $\pm$ 2.09	0.0456 $\pm$ 0.0075	0.1748 $\pm$ 0.1600
3 mo.	16.01 $\pm$ 1.72	15.38 $\pm$ 5.25	0.0369 $\pm$ 0.0078	0.0183 $\pm$ 0.0052
6 mo.	58.85 $\pm$ 15.38	57.15 $\pm$ 7.64	0.1977 $\pm$ 0.1617	0.0464 $\pm$ 0.0325
1 yr.	61.94 $\pm$ 12.17	28.10 $\pm$ 1.92	0.0929 $\pm$ 0.0785	0.0155 $\pm$ 0.0089

Table 14. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Femur (Proximal)</u>				
2 wks.	78.77 $\pm$ 23.59	12.72 $\pm$ 3.39	0.0145 $\pm$ 0.0044	0.0059 $\pm$ 0.0021
1 mo.	51.88 $\pm$ 18.58	61.83 $\pm$ 13.46	0.0734 $\pm$ 0.0457	0.0101 $\pm$ 0.0050
2 mo.	125.99 $\pm$ 26.69	34.21 $\pm$ 19.43	0.2509 $\pm$ 0.1168	0.0676 $\pm$ 0.0227
3 mo.	65.06 $\pm$ 7.75	28.33 $\pm$ 3.90	0.2216 $\pm$ 0.0503	0.1138 $\pm$ 0.0245
6 mo.	380.37 $\pm$ 18.89	121.61 $\pm$ 23.65	0.1832 $\pm$ 0.0159	0.0567 $\pm$ 0.0178
1 yr.	244.93 $\pm$ 12.72	41.28 $\pm$ 8.12	0.0579 $\pm$ 0.0232	0.0238 $\pm$ 0.0047
<u>Femur (Shaft)</u>				
2 wks.	7.89 $\pm$ 1.44	2.55 $\pm$ 0.53	0.0052 $\pm$ 0.0013	0.0038 $\pm$ 0.0028
1 mo.	34.04 $\pm$ 25.72	17.18 $\pm$ 2.97	0.0052 $\pm$ 0.0012	0.0092 $\pm$ 0.0035
2 mo.	28.43 $\pm$ 6.07	9.23 $\pm$ 3.05	0.0928 $\pm$ 0.0237	0.0497 $\pm$ 0.0131
3 mo.	15.53 $\pm$ 2.16	7.44 $\pm$ 1.23	0.0928 $\pm$ 0.0196	0.0430 $\pm$ 0.0218
6 mo.	57.30 $\pm$ 13.56	21.70 $\pm$ 4.69	0.1309 $\pm$ 0.0934	0.0371 $\pm$ 0.0142
1 yr.	71.00 $\pm$ 20.57	39.65 $\pm$ 18.37	0.0254 $\pm$ 0.0150	0.0189 $\pm$ 0.0100
<u>Femur (Distal)</u>				
2 wks.	23.88 $\pm$ 3.06	6.70 $\pm$ 1.75	0.0052 $\pm$ 0.0005	0.0043 $\pm$ 0.0010
1 mo.	79.13 $\pm$ 9.78	32.58 $\pm$ 5.32	0.0239 $\pm$ 0.0061	0.0401 $\pm$ 0.0287
2 mo.	67.65 $\pm$ 14.01	26.44 $\pm$ 7.88	0.1068 $\pm$ 0.0390	0.0894 $\pm$ 0.0488

Table 14. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Femur (Distal--Continued)</u>				
3 mo..	41.20 $\pm$ 11.82	16.04 $\pm$ 1.98	0.2805 $\pm$ 0.0599	0.1151 $\pm$ 0.0292
6 mo.	138.91 $\pm$ 25.17	58.48 $\pm$ 5.95	0.3560 $\pm$ 0.2212	0.0390 $\pm$ 0.0110
1 yr.	168.88 $\pm$ 40.65	47.10 $\pm$ 28.14	0.0308 $\pm$ 0.0143	0.0149 $\pm$ 0.0008
<u>L.S.C.L.N.</u>				
2 wks.	8,778.73 $\pm$ 5091.12	5,156.25 $\pm$ 1919.42	269.5903 $\pm$ 15.9417	191.3983 $\pm$ 88.7938
1 mo.	23,893.30 $\pm$ 5425.61	17,603.36 $\pm$ 1475.39	541.7794 $\pm$ 111.2964	467.2939 $\pm$ 189.2330
2 mo.	23,829.14 $\pm$ 10081.96	27,849.98 $\pm$ 8383.35	1013.1064 $\pm$ 271.5225	1364.0595 $\pm$ 357.1127
3 mo.	8,106.08 $\pm$ 4221.59	2,582.45 $\pm$ 1507.32	--	614.9849 $\pm$ 298.0859
6 mo.	11,138.89 $\pm$ 1920.26	31,825.02 $\pm$ 3222.00	1092.9112 $\pm$ 619.1151	1538.8583 $\pm$ 235.8470
1 yr.	2,149.79 $\pm$ 1489.54	2,423.96 $\pm$ 763.69	352.6104 $\pm$ 244.2531	222.4972 $\pm$ 60.5927
<u>Left Axillary Lymph Node</u>				
2 wks.			0.0732 $\pm$ 0.0347	0.3762 $\pm$ 0.3532
1 mo.			0.9682 $\pm$ 0.4421	1.0091 $\pm$ 0.9946
2 mo.			0.5719 $\pm$ 0.0986	0.7163 $\pm$ 0.4561
3 mo.			289.2001 $\pm$ 270.8544	2.8866 $\pm$ 1.9800
6 mo.			42.1758 $\pm$ 40.2670	3696.3124 $\pm$ 3657.3957
1 yr.			19.8371 $\pm$ 19.1655	67.0706 $\pm$ 66.9542

Table 14. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>R. S. C. L. N.</u>				
2 wks.	25.96 $\pm$ 6.96	2.19 $\pm$ 0.88	0.0175 $\pm$ 0.0098	0.0069 $\pm$ 0.0033
1 mo.	31.12 $\pm$ 6.39	20.57 $\pm$ 5.86	0.1382 $\pm$ 0.0816	0.2067 $\pm$ 0.1752
2 mo.	50.01 $\pm$ 10.06	18.28 $\pm$ 5.58	1.9920 $\pm$ 0.5539	0.4929 $\pm$ 0.1930
3 mo.	37.70 $\pm$ 28.28	12.34 $\pm$ 4.41	5.0852 $\pm$ 1.3400	1.5230 $\pm$ 0.7963
6 mo.	43.04 $\pm$ 12.36	11.84 $\pm$ 2.47	1.4010 $\pm$ 1.0649	1.8660 $\pm$ 1.2960
1 yr.	26.56 $\pm$ 7.18	18.70 $\pm$ 3.89	0.6754 $\pm$ 0.3547	0.0629 $\pm$ 0.0403
<u>Thyroid</u>				
2 wks.	2.91 $\pm$ 2.32	2.32 $\pm$ 2.14	0.1606 $\pm$ 0.0497	0.1203 $\pm$ 0.0497
1 mo.	6.97 $\pm$ 1.59	10.69 $\pm$ 2.23	0.0800 $\pm$ 0.0191	0.2788 $\pm$ 0.2057
2 mo.	8.71 $\pm$ 4.20	42.16 $\pm$ 17.34	1.1591 $\pm$ 0.3752	1.8733 $\pm$ 1.4609
3 mo.	15.63 $\pm$ 5.27	139.10 $\pm$ 0.45	2.6771 $\pm$ 1.5360	0.3978 $\pm$ 0.2077
6 mo.	31.93 $\pm$ 21.58	25.77 $\pm$ 16.27	1.5991 $\pm$ 0.9928	3.8689 $\pm$ 0.6434
1 yr.	12.45 $\pm$ 0.78	42.48 $\pm$ 20.99	0.2314 $\pm$ 0.1022	0.1246 $\pm$ 0.1087
<u>Bile</u>				
2 wks.	0.04 $\pm$ 0.02	0.15 $\pm$ 0.03	0.0173 $\pm$ 0.0146	0.0031 $\pm$ 0.0010
1 mo.	1.09 $\pm$ 0.36	0.60 $\pm$ 0.13	0.2508 $\pm$ 0.2444	0.0333 $\pm$ 0.0225
2 mo.	0.26 $\pm$ 0.13	0.08 $\pm$ 0.05	0.0291 $\pm$ 0.0273	0.0835 $\pm$ 0.0587

Table 14. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Bile (Continued)</u>				
3 mo.	0.10 $\pm$ 0.03	0.05 $\pm$ 0.01	0.0186 $\pm$ 0.0085	0.0485
6 mo.	0.09 $\pm$ 0.03	0.05 $\pm$ 0.01	0.0870 $\pm$ 0.0211	0.2739 $\pm$ 0.1511
1 yr.	1.53 $\pm$ 0.81	0.19 $\pm$ 0.12	0.0090	0.0051
<u>Hepatic Lymph Node</u>				
2 wks.		3.06 $\pm$ 0.98	0.1662 $\pm$ 0.1115	0.0162 $\pm$ 0.0080
1 mo.	9.20 $\pm$ 4.18	13.57 $\pm$ 5.66	0.0346 $\pm$ 0.0112	0.1183 $\pm$ 0.0593
2 mo.	31.16 $\pm$ 12.92	13.16 $\pm$ 4.84	0.2399 $\pm$ 0.1177	0.8734 $\pm$ 0.4750
3 mo.	10.35 $\pm$ 7.95	3.85 $\pm$ 1.53	85.8200 $\pm$ 41.7989	2.0331 $\pm$ 1.1349
6 mo.	51.97 $\pm$ 9.55	46.27 $\pm$ 6.55	14.5571 $\pm$ 12.0065	8.9578 $\pm$ 6.0884
1 yr.	123.31 $\pm$ 19.16	25.50 $\pm$ 7.08	1.1012 $\pm$ 1.0501	1.9155 $\pm$ 1.3479

Table 15. Fraction of Initial Implant Dose of Americium per Gram of Organ.

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Left Testis</u>				
2 wks.	1.059 $\pm$ 0.558	0.412 $\pm$ 0.826	0.433 $\pm$ 0.335	0.046 $\pm$ 0.041
1 mo.	1.161 $\pm$ 0.669	3.311 $\pm$ 2.692	0.058 $\pm$ 0.029	0.284 $\pm$ 0.056
2 mo.	0.949 $\pm$ 0.255	0.728 $\pm$ 0.114	0.057 $\pm$ 0.030	1.608 $\pm$ 0.839
3 mo.	1.420 $\pm$ 1.040	1.086	0.066	1.886 $\pm$ 1.530
6 mo.	1.793 $\pm$ 0.536	2.097 $\pm$ 1.460	0.351 $\pm$ 0.203	0.090 $\pm$ 0.042
1 yr.	--	--	0.460	0.072
<u>Left Kidney</u>				
2 wks.	32.484 $\pm$ 14.979	2.795 $\pm$ 0.972	0.127 $\pm$ 0.065	0.050 $\pm$ 0.009
1 mo.	--	--	0.291	0.310 $\pm$ 0.304
2 mo.	47.429 $\pm$ 10.270	68.793 $\pm$ 19.373	0.365 $\pm$ 0.105	0.537 $\pm$ 0.230
3 mo.	45.790 $\pm$ 9.719	2.920 $\pm$ 1.270	0.549	4.442 $\pm$ 2.911
6 mo.	82.835 $\pm$ 55.083	7.410 $\pm$ 2.278	0.062 $\pm$ 0.013	0.040 $\pm$ 0.034
1 yr.	--	--	0.045	0.130 $\pm$ 0.102
<u>Left Adrenal Gland</u>				
2 wks.	6.698 $\pm$ 3.608	3.353 $\pm$ 1.218	0.969 $\pm$ 0.348	0.494 $\pm$ 0.080
1 mo.	6.088 $\pm$ 6.032	3.774 $\pm$ 0.739		3.918 $\pm$ 1.946
2 mo.	12.241 $\pm$ 1.315	1.820 $\pm$ 0.581	0.695 $\pm$ 0.271	7.141 $\pm$ 1.087

Table 15. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Left Adrenal Gland (Continued)</u>				
3 mo.	--	1.136 ± 0.256	5.596	6.977 ± 3.629
6 mo.	13.270 ± 1.116	3.758 ± 0.744	0.181 ± 0.092	2.254 ± 2.218
1 yr.	--	--	0.87	--
<u>Spleen</u>				
2 wks.	26.329 ± 8.010	3.638 ± 1.380	0.091 ± 0.030	0.039 ± 0.033
1 mo.	63.998 ± 26.388	--	0.214	0.120
2 mo.	28.748 ± 26.324	7.769 ± 1.797	0.282 ± 0.109	0.108 ± 0.031
3 mo.	1.910	5.004 ± 4.925	1.420	0.296 ± 0.132
6 mo.	27.647 ± 9.337	9.060 ± 2.325	0.285 ± 0.131	0.346 ± 0.318
1 yr.	37.780 ± 4.430	--	0.020	0.014
<u>Liver</u>				
2 wks.	37.690 ± 14.177	8.154 ± 3.642	0.308 ± 0.119	0.215 ± 0.156
1 mo.	40.658 ± 8.182	1.593 ± 1.031	--	--
2 mo.	118.979 ± 57.314	2.542 ± 1.962	2.065 ± 1.079	0.521 ± 0.298
3 mo.	57.078 ± 53.823	9.405 ± 5.533	2.075 ± 0.902	1.182 ± 0.715
6 mo.	142.303 ± 97.392	16.883 ± 6.249	0.869 ± 0.367	0.548 ± 0.191
1 yr.	--	--	0.034	0.481 ± 0.469

Table 15. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Left Eye</u>				
2 wks.	2.300 $\pm$ 1.101	0.842 $\pm$ 0.331	1.158 $\pm$ 0.562	0.346 $\pm$ 0.172
1 mo.	3.388 $\pm$ 0.791	2.348 $\pm$ 1.304	1.906 $\pm$ 0.466	9.518 $\pm$ 5.599
2 mo.	1.202 $\pm$ 0.174	0.754 $\pm$ 0.422	2.344 $\pm$ 1.602	24.195 $\pm$ 19.109
3 mo.	--	--	6.180	3.918 $\pm$ 0.632
6 mo.	2.345 $\pm$ 0.394	0.90 $\pm$	0.598 $\pm$ 0.334	2.911 $\pm$ 2.906
1 yr.	113.210 $\pm$ 8.642	--	4.740	0.452 $\pm$ 0.194
<u>Trachea</u>				
2 wks.	2.675 $\pm$ 0.695	5.989 $\pm$ 5.697	0.204 $\pm$ 0.106	0.175 $\pm$ 0.119
1 mo.	7.706 $\pm$ 1.966	1.211 $\pm$ 0.466	0.974 $\pm$ 0.579	1.880
2 mo.	6.463 $\pm$ 0.973	15.562 $\pm$ 13.066	0.542 $\pm$ 0.298	2.031 $\pm$ 1.244
3 mo.	--	--	6.180	0.098 $\pm$ 0.052
6 mo.	18.260 $\pm$ 3.484	3.433 $\pm$ 0.915	0.297 $\pm$ 0.110	0.303 $\pm$ 0.160
1 yr.	--	--	3.325 $\pm$ 0.785	1.794 $\pm$ 1.620
<u>Lung</u>				
2 wks.	2.592 $\pm$ 0.589	1.232 $\pm$ 0.929	0.037 $\pm$ 0.012	
1 mo.	6.367 $\pm$ 3.616		0.397 $\pm$ 0.009	0.906 $\pm$ 0.190
2 mo.	3.146 $\pm$ 1.136	4.873 $\pm$ 2.316	1.139 $\pm$ 0.418	0.849 $\pm$ 0.361

Table 15. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Lung (Continued)</u>				
3 mo.	2.437 $\pm$ 0.497	5.949 $\pm$ 1.171	1.028 $\pm$ 0.159	1.490 $\pm$ 0.269
6 mo.	10.220 $\pm$ 3.062	2.380 $\pm$ 0.739	0.303 $\pm$ 0.216	0.030 $\pm$ 0.028
1 yr.	--	--	1.352 $\pm$ 1.200	--
<u>Sternum</u>				
2 wks.	7.547 $\pm$ 2.012	2.980 $\pm$ 0.996	0.058 $\pm$ 0.029	0.036 $\pm$ 0.018
1 mo.	1.531 $\pm$ 1.056	17.953 $\pm$ 8.122	0.348	0.296
2 mo.	42.647 $\pm$ 15.459	20.621 $\pm$ 11.171	1.688 $\pm$ 0.254	0.907 $\pm$ 0.330
3 mo.	--	2.771 $\pm$ 1.613	0.693 $\pm$ 0.179	0.880 $\pm$ 0.289
6 mo.	54.940 $\pm$ 41.353	27.583 $\pm$ 10.645	0.333 $\pm$ 0.039	0.432 $\pm$ 0.317
1 yr.	--	--	1.080 $\pm$ 0.518	0.026
<u>Rib</u>				
2 wks.	4.427 $\pm$ 1.221	2.423 $\pm$ 1.116	0.127 $\pm$ 0.091	0.132 $\pm$ 0.070
1 mo.	2.106 $\pm$ 1.120	14.081 $\pm$ 9.443	0.424	1.583 $\pm$ 0.690
2 mo.	25.418 $\pm$ 6.119	15.487 $\pm$ 4.927	4.591 $\pm$ 0.826	4.083 $\pm$ 0.850
3 mo.	49.400 $\pm$ 21.202	6.490 $\pm$ 3.288	2.421 $\pm$ 1.764	5.940 $\pm$ 3.393
6 mo.	199.093 $\pm$ 27.455	52.003 $\pm$ 13.938	1.619 $\pm$ 0.506	1.880 $\pm$ 1.406
1 yr.	--	--	3.566 $\pm$ 3.262	0.830

Table 15. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Vertebrae</u>				
2 wks.	7.021 $\pm$ 2.481	3.576 $\pm$ 1.985	0.002 $\pm$ 0.001	0.013 $\pm$ 0.007
1 mo.	0.874 $\pm$ 0.181	5.391 $\pm$ 1.602	0.435 $\pm$ 0.275	0.225 $\pm$ 0.218
2 mo.	11.725 $\pm$ 8.998	10.370 $\pm$ 6.436	1.890 $\pm$ 0.352	0.881 $\pm$ 0.463
3 mo.	39.995 $\pm$ 14.988		0.851 $\pm$ 0.318	0.345 $\pm$ 0.280
6 mo.	178.520 $\pm$ 99.431	33.520 $\pm$ 30.353	0.288 $\pm$ 0.134	0.023 $\pm$ 0.017
1 yr.	--	--	1.260 $\pm$ 1.233	0.028
<u>Skull</u>				
2 wks.	1.693 $\pm$ 0.395	1.903 $\pm$ 0.571	0.020 $\pm$ 0.011	0.123 $\pm$ 0.032
1 mo.	2.132 $\pm$ 0.553	1.870 $\pm$ 1.015	0.757 $\pm$ 0.227	0.912 $\pm$ 0.909
2 mo.	38.258 $\pm$ 8.695	11.892 $\pm$ 5.437	0.313 $\pm$ 0.029	0.246 $\pm$ 0.097
3 mo.	9.513 $\pm$ 3.909	5.800 $\pm$ 3.708	0.518 $\pm$ 0.107	0.578 $\pm$ 0.230
6 mo.	33.335 $\pm$ 21.065	22.958 $\pm$ 11.870	0.425 $\pm$ 0.312	0.826 $\pm$ 0.649
1 yr.	--	--	0.567 $\pm$ 0.530	0.209 $\pm$ 0.200
<u>Femur (Proximal)</u>				
2 wks.	5.210 $\pm$ 1.835	2.498 $\pm$ 1.426	0.181 $\pm$ 0.165	0.030 $\pm$ 0.020
1 mo.	7.568 $\pm$ 6.994	25.550 $\pm$ 23.912	0.328 $\pm$ 0.221	0.257 $\pm$ 0.148
2 mo.	38.700 $\pm$ 16.855	13.329 $\pm$ 9.975	0.593 $\pm$ 0.175	1.505 $\pm$ 1.404

Table 15. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Femur (Proximal--Continued)</u>				
3 mo.	22.187 $\pm$ 15.033	19.607 $\pm$ 19.506	0.736 $\pm$ 0.322	0.758 $\pm$ 0.282
6 mo.	121.943 $\pm$ 59.877	45.513 $\pm$ 23.413	0.413 $\pm$ 0.075	0.133 $\pm$ 0.047
1 yr.	327.240 $\pm$ 296.080	132.50	0.099	0.166 $\pm$ 0.100
<u>Femur (Shaft)</u>				
2 wks.	2.272 $\pm$ 0.950	0.833 $\pm$ 0.218	0.113 $\pm$ 0.098	0.392 $\pm$ 0.334
1 mo.	1.254 $\pm$ 0.222	4.800 $\pm$ 4.292	0.347 $\pm$ 0.293	0.21
2 mo.	42.706 $\pm$ 25.376	8.417 $\pm$ 4.075	1.142 $\pm$ 0.760	0.494 $\pm$ 0.231
3 mo.	20.590 $\pm$ 15.330	6.903 $\pm$ 3.457	1.241 $\pm$ 0.416	0.922 $\pm$ 0.679
6 mo.	32.278 $\pm$ 18.061	60.625 $\pm$ 52.035	1.002 $\pm$ 0.557	0.097 $\pm$ 0.037
1 yr.	--	--	0.292	1.993 $\pm$ 1.801
<u>Femur (Distal)</u>				
2 wks.	3.815 $\pm$ 0.998	2.390 $\pm$ 1.201	0.021 $\pm$ 0.007	0.030 $\pm$ 0.021
1 mo.	3.167 $\pm$ 1.463	10.544 $\pm$ 3.980	0.575 $\pm$ 0.042	0.787 $\pm$ 0.513
2 mo.	2.185 $\pm$ 0.929	16.093 $\pm$ 0.950	0.412 $\pm$ 0.140	0.316 $\pm$ 0.107
3 mo.	18.203 $\pm$ 7.541	0.473 $\pm$ 0.237	0.855 $\pm$ 0.069	0.327 $\pm$ 0.063
6 mo.	37.635 $\pm$ 14.421	20.635 $\pm$ 10.733	0.604 $\pm$ 0.519	0.108 $\pm$ 0.074
1 yr.	--	--	0.167 $\pm$ 0.124	0.199 $\pm$ 0.162

Table 15. Continued

Time Following Implant	Pu(NO ₃) ₄		PuO ₂	
	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)
<u>L.S.C.L.N.</u>				
2 wks.	3686.372 ₊ 1924.405	2275.064 ₊ 886.907	419.776 ₊ 145.236	307.717 ₊ 216.101
1 mo.	--	6766.855 ₊ 1906.181	--	1776.254 ₊ 1418.584
2 mo.	6740.956 ₊ 3888.250	12072.526 ₊ 6313.369	805.420 ₊ 787.942	6548.312 ₊ 3118.764
3 mo.	3368.305 ₊ 1808.409	270.715 ₊ 136.678	--	1061.665 ₊ 358.728
6 mo.	4230.410 ₊ 784.746	5264.473 ₊ 3152.922	2364.987 ₊ 466.102	1036.924 ₊ 123.582
1 yr.	--	3531.700 ₊ 1100.780	1165.875 ₊ 800.683	1252.100
<u>Left Axillary Lymph Node</u>				
2 wks.	251.981 ₊ 180.149	957.458 ₊ 669.127	2.538 ₊ 1.944	6.446 ₊ 5.599
1 mo.	--	8.644 ₊ 7.062	12.904	16.875 ₊ 0.207
2 mo.	422.072 ₊ 248.129	333.401 ₊ 328.960	248.050 ₊ 245.885	31.914 ₊ 20.859
3 mo.	574.453 ₊ 429.619	2.990 ₊ 0.780	7.989 ₊ 3.370	5.769 ₊ 3.391
6 mo.	215.553 ₊ 202.161	190.883 ₊ 155.448	3.601 ₊ 1.704	0.114 ₊ 0.068
1 yr.	93.745 ₊ 77.055	--	59.779 ₊ 6.049	3.057 ₊ 1.663
<u>Left Paw</u>				
2 wks.	--	--	1662.442 ₊ 1052.418	1793.902 ₊ 334.544
1 mo.	--	--	1266.892	1131.261

Table 15. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Left Paw (Continued)</u>				
2 mo.	--	--	21.284 $\pm$ 12.073	8.540 $\pm$ 5.752
3 mo.	--	--	36.273 $\pm$ 5.553	44.204 $\pm$ 11.091
6 mo.	--	2343.230 $\pm$ 1885.940	58.295 $\pm$ 38.420	39.486 $\pm$ 9.837
1 yr.	--	--	17.561 $\pm$ 9.232	18.115
<u>R. S. C. L. N.</u>				
2 wks.	21.728 $\pm$ 13.971	9.655 $\pm$ 4.783	0.829 $\pm$ 0.261	2.900 $\pm$ 1.814
1 mo.	--	7.324 $\pm$ 2.880	107.242 $\pm$ 102.126	--
2 mo.	126.882 $\pm$ 93.74	24.528 $\pm$ 10.444	4.625 $\pm$ 1.475	8.461 $\pm$ 4.608
3 mo.	--	12.780 $\pm$ 6.772	--	1.265 $\pm$ 0.976
6 mo.	12.003 $\pm$ 3.917	10.908 $\pm$ 4.970	2.808 $\pm$ 1.982	2.856 $\pm$ 1.629
1 yr.	97.750 $\pm$ 71.610	--	41.174 $\pm$ 36.412	0.634 $\pm$ 0.536
<u>Thyroid</u>				
2 wks.	6.617 $\pm$ 3.925	3.898 $\pm$ 1.337	1.168 $\pm$ 0.182	4.906 $\pm$ 4.241
1 mo.	16.189 $\pm$ 0.967	35.318 $\pm$ 35.093	4.711 $\pm$ 4.391	1.146 $\pm$ 0.537
2 mo.	60.006 $\pm$ 43.344	18.044 $\pm$ 8.802	8.745 $\pm$ 2.936	2.633 $\pm$ 0.371
3 mo.	10.455 $\pm$ 2.641	15.410 $\pm$ 9.913	8.644 $\pm$ 5.390	2.153 $\pm$ 0.898

Table 15. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Thyroid (Continued)</u>				
6 mo.	25.750 $\pm$ 8.545	40.280 $\pm$ 20.708	1.290 $\pm$ 0.668	2.529 $\pm$ 2.432
1 yr.	--	--	19.005 $\pm$ 4.088	15.552 $\pm$ 14.647
<u>Bile</u>				
2 wks.	--	--	0.146 $\pm$ 0.040	0.226 $\pm$ 0.111
1 mo.	1.115 $\pm$ 0.548	3.581 $\pm$ 1.343	0.037	0.038 $\pm$ 0.032
2 mo.	2.283 $\pm$ 1.943	0.780 $\pm$ 0.303	0.530 $\pm$ 0.304	0.770 $\pm$ 0.359
3 mo.	0.379 $\pm$ 0.241	0.500 $\pm$ 0.211	0.430 $\pm$ 0.235	--
6 mo.	0.238 $\pm$ 0.061	0.275 $\pm$ 0.105	0.810 $\pm$ 0.413	0.988 $\pm$ 0.532
1 yr.	13.403 $\pm$ 10.968	3.670 $\pm$ 2.648	0.923	0.153
<u>Hepatic Lymph Node</u>				
2 wks.	--	9.720 $\pm$ 5.770	0.675 $\pm$ 0.547	0.625 $\pm$ 0.279
1 mo.	--	--	13.199 $\pm$ 11.058	7.301 $\pm$ 6.333
2 mo.	40.984 $\pm$ 14.977	7.653 $\pm$ 2.211	2.147 $\pm$ 1.278	1.664 $\pm$ 0.995
3 mo.	4.095 $\pm$ 1.765	3.568 $\pm$ 0.719	--	6.421 $\pm$ 2.446
6 mo.	19.478 $\pm$ 8.946	19.145 $\pm$ 3.436	1.479 $\pm$ 1.236	7.146 $\pm$ 5.661
1 yr.	--	--	--	18.249 $\pm$ 6.381

chemical forms. Tables 16 and 17 show the total content of Pu concentrated in each organ or section, such as bone samples. A good example of the buildup of Pu that occurred in tissue of contaminated animals is shown in Fig. 9 and 10, where the fraction of initial implant dose per gram of liver versus time following implant is plotted.

Data included in Tables 14-17 were derived from the radiochemical analysis for Pu and Am concentrating in other organs of interest. These organs included soft tissues such as testes, kidney, adrenal gland, eye, lung, left axillary lymph node, RSCLN, thyroid, and bile. The kidney was of interest because of the amount of urine filtered through this organ. The kidney contained high activity of Pu and Am with preferential levels of Am over Pu. The lung was radiochemically analyzed to find out if significant levels were deposited in this organ through blood exchange.

There are evidences in the literature which suggest that the left axillary lymph node can become the first major lymph node draining the paw if the implant is deposited slightly off the medial area of the metacarpal region. There is also suggestion that there could be variation among dogs in the distribution of lymphatic channels which would account for larger intake in the axillary lymph node observed in some dogs. The data (Tables 14-17) show some dogs with higher concentrations of Pu in the left axillary lymph node than in the LSCLN

Table 16. Fraction of Initial Implant Dose of Plutonium per Total Organ.

Time Following Implant	Pu(NO ₃) ₄		PuO ₂	
	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)
<u>Left Testis</u>				
2 wks.	12.3 ± 7.8	4.20 ± 3.24	0.012 ± 0.004	0.003 ± 0.001
1 mo.	250.35 ± 172.81	19.85 ± 6.36	0.06 ± 0.02	0.05 ± 0.01
2 mo.	36.63 ± 5.28	9.88 ± 2.63	0.77 ± 0.39	0.28 ± 0.13
3 mo.	18.84 ± 2.58	3.74 ± 1.68	0.35 ± 0.16	0.66 ± 0.36
6 mo.	92.65 ± 18.93	32.12 ± 13.09	0.71 ± 0.37	0.51 ± 0.43
1 yr.	49.37 ± 4.59	17.43 ± 3.00	--	--
<u>Left Kidney</u>				
2 wks.	140.18 ± 27.97	21.75 ± 5.86	0.44 ± 0.12	0.43 ± 0.15
1 mo.	74.32 ± 12.97	156.45 ± 6.47	0.45 ± 0.32	0.38 ± 0.19
2 mo.	761.98 ± 250.63	203.40 ± 78.69	5.31 ± 0.67	3.05 ± 1.13
3 mo.	429.90 ± 101.40	69.68 ± 4.30	2.49 ± 0.56	8.50 ± 4.89
6 mo.	147.20 ± 71.30	272.09 ± 22.65	9.79 ± 6.64	0.96 ± 0.62
1 yr.	201.88 ± 110.19	837.31 ± 720.21	0.87 ± 0.38	0.35 ± 0.26
<u>Left Adrenal</u>				
2 wks.	16.06 ± 7.51	2.03 ± 0.85	0.10 ± 0.07	0.13 ± 0.11
1 mo.	31.16 ± 3.80	31.98 ± 18.34	0.05 ± 0.03	0.11 ± 0.08
2 mo.	20.78 ± 3.49	5.49 ± 1.33	0.60 ± 0.21	0.79 ± 0.47

Table 16. Continued

Time Following Implant	Pu(NO ₃) ₄		PuO ₂	
	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)
<u>Left Adrenal (Continued)</u>				
3 mo.	9.06± 2.58	1.09± 0.43	39.90±28.10	0.50±0.25
6 mo.	53.59±19.50	9.14± 1.43	1.05± 0.43	12.67±6.45
1 yr.	31.64±10.59	--	0.07± 0.05	0.05±
<u>Spleen</u>				
2 wks.	2,081.64± 957.21	414.55± 78.03	0.62± 0.28	0.19±0.08
1 mo.	6,854.20±3,389.84	972.74± 142.03	0.34± 0.12	0.31±0.08
2 mo.	1,301.12± 211.94	337.10± 105.85	7.27± 2.61	1.37±0.49
3 mo.	860.63± 87.50	213.36± 48.66	6.25± 1.54	0.64±0.18
6 mo.	1,886.06± 783.87	619.55± 120.37	2.64± 1.88	0.73±0.10
1 yr.	3,790.00±2,495.30	299.55± 111.54	1.29± 0.96	4.04±3.54
<u>Liver</u>				
2 wks.	40,167.75±17,409.09	5,338.54±2,478.00	0.59± 0.31	0.39± 0.17
1 mo.	37,466.21±12,101.01	4,814.30±1,288.12	38.86±37.69	0.19± 0.06
2 mo.	26,366.97±10,042.65	957.68± 283.09	203.14±107.20	18.39±10.33
3 mo.	19,505.52± 3,645.01	5,154.80±1,722.26	2.89± 0.46	17.01±11.06
6 mo.	35,551.42±18,749.29	4,154.46±1,934.07	18.88± 12.17	104.67±18.86
1 yr.	141,006.39±17,300.36	18,813.76±6,321.77	298.82±293.22	312.22±206.81

Table 16. Continued.

Time Following Implant	Pu(NO ₃) ₄		PuO ₂	
	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)
<u>Left Eye</u>				
2 wks.	11.05± 3.39	3.27± 0.14	0.11±0.04	0.013±0.006
1 mo.	25.21± 5.30	6.26± 2.01	0.06±0.01	0.14 ±0.04
2 mo.	9.02± 1.87	6.97± 1.85	0.96±0.83	0.40 ±0.15
3 mo.	3.11± 0.59	2.37± 0.64	20.54±15.11	0.78 ±0.53
6 mo.	50.53± 18.80	17.35± 7.21	0.64±0.31	25.33 ±14.44
1 yr.	14.20± 1.28	4.59	0.16±0.07	0.15 ±0.05
<u>Sternum</u>				
2 wks.	2412.96±239.97	225.77± 128.81	0.28±0.09	0.10 ±0.03
1 mo.	2413.08±822.42	2519.13± 727.03	0.28±0.09	0.20 ±0.05
2 mo.	2648.36±792.09	1121.14± 281.17	4.10±0.47	0.89 ±0.10
3 mo.	2167.12±454.20	484.23± 102.66	4.79±0.69	1.10 ±0.23
6 mo.	4718.06±867.61	1356.24± 232.65	3.64±0.60	0.89 ±0.15
1 yr.	3957.95±655.96	2887.98±2229.78	1.33±0.66	--
<u>Rib</u>				
2 wks.	723.36± 95.50	251.24± 44.74	0.14±0.03	0.21 ±0.19
1 mo.	1134.19± 29.22	676.34± 243.55	0.44±0.11	0.59 ±0.42
2 mo.	879.31±257.64	246.59± 70.12	1.44±0.21	0.42 ±0.15
3 mo.	919.07±193.06	235.10± 40.86	0.96±0.22	0.78 ±0.26
6 mo.	2105.58±224.53	864.43± 89.28	1.57±0.64	0.33 ±0.07
1 yr.	1460.89±149.76	436.26± 97.48	0.47±0.25	0.37 ±0.20

Table 16. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA $\times 10^{-6}$
<u>Vertebrae</u>				
2 wks.	1367.52 $\pm$ 87.97	166.85 $\pm$ 50.96	0.21 $\pm$ 0.02	0.10 $\pm$ 0.03
1 mo.	794.56 $\pm$ 519.88	714.15 $\pm$ 179.41	0.62 $\pm$	0.22 $\pm$ 0.01
2 mo.	1396.58 $\pm$ 318.83	513.29 $\pm$ 187.83	6.11 $\pm$ 0.98	0.91 $\pm$ 0.16
3 mo.	904.29 $\pm$ 55.29	220.86 $\pm$ 19.71	2.79 $\pm$ 0.32	1.93 $\pm$ 0.46
6 mo.	4224.21 $\pm$ 366.04	1601.94 $\pm$ 224.18	3.32 $\pm$ 0.38	1.20 $\pm$ 0.45
1 yr.	2584.39 $\pm$ 475.68	1547.00 $\pm$ 707.85	0.62 $\pm$ 0.36	0.34 $\pm$ 0.11
<u>Skull</u>				
2 wks.	50.74 $\pm$ 27.20	32.61 $\pm$ 18.07	0.04 $\pm$ 0.02	0.06 $\pm$ 0.03
1 mo.	87.16 $\pm$ 19.45	150.24 $\pm$ 32.94	0.08 $\pm$ 0.05	0.05 $\pm$ 0.03
2 mo.	323.56 $\pm$ 89.37	80.37 $\pm$ 16.83	0.67 $\pm$ 0.12	2.68 $\pm$ 0.67
3 mo.	98.87 $\pm$ 7.54	108.49 $\pm$ 39.50	0.87 $\pm$ 0.20	0.39 $\pm$ 0.07
6 mo.	438.42 $\pm$ 131.27	371.77 $\pm$ 39.88	0.79 $\pm$ 0.12	0.70 $\pm$ 0.40
1 yr.	350.64 $\pm$ 66.21	53.19 $\pm$ 20.61	0.92 $\pm$ 0.87	0.07 $\pm$ 0.03
<u>Femur (Proximal)</u>				
2 wks.	931.92 $\pm$ 285.26	133.72 $\pm$ 33.28	0.16 $\pm$ 0.05	0.06 $\pm$ 0.02
1 mo.	669.55 $\pm$ 319.15	663.33 $\pm$ 155.04	0.40 $\pm$ 0.08	0.14 $\pm$ 0.07
2 mo.	1674.53 $\pm$ 285.95	299.06 $\pm$ 106.89	1.77 $\pm$ 0.23	0.76 $\pm$ 0.23

Table 16. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Femur (Proximal--Continued)</u>				
3 mo.	739.58 $\pm$ 58.84	300.15 $\pm$ 51.98	3.06 $\pm$ 0.96	1.35 $\pm$ 0.43
6 mo.	4326.25 $\pm$ 318.45	1345.63 $\pm$ 142.18	2.69 $\pm$ 0.19	0.81 $\pm$ 0.27
1 yr.	2548.67 $\pm$ 182.28	530.21 $\pm$ 149.40	0.67 $\pm$ 0.34	0.29 $\pm$ 0.09
<u>Femur (Shaft)</u>				
2 wks.	104.88 $\pm$ 12.86	29.67 $\pm$ 6.63	0.05 $\pm$ 0.01	0.03 $\pm$ 0.02
1 mo.	129.50 $\pm$ 54.33	239.62 $\pm$ 41.69	0.05 $\pm$ 0.01	0.12 $\pm$ 0.03
2 mo.	357.92 $\pm$ 67.56	104.75 $\pm$ 30.65	0.82 $\pm$ 0.14	0.47 $\pm$ 0.12
3 mo.	176.76 $\pm$ 5.65	78.59 $\pm$ 16.27	0.97 $\pm$ 0.31	0.39 $\pm$ 0.18
6 mo.	600.37 $\pm$ 117.37	266.86 $\pm$ 54.32	1.26 $\pm$ 0.46	0.39 $\pm$ 0.14
1 yr.	614.21 $\pm$ 167.98	551.07 $\pm$ 103.33	0.28 $\pm$ 0.19	0.19 $\pm$ 0.11
<u>Femur (Distal)</u>				
2 wks.	374.88 $\pm$ 48.40	101.84 $\pm$ 29.79	0.08 $\pm$ 0.01	0.04 $\pm$ 0.01
1 mo.	728.24 $\pm$ 206.08	486.21 $\pm$ 104.74	0.39 $\pm$ 0.06	1.16 $\pm$ 0.93
2 mo.	1062.47 $\pm$ 205.51	372.45 $\pm$ 110.26	2.66 $\pm$ 0.61	1.60 $\pm$ 0.95
3 mo.	498.79 $\pm$ 121.48	227.83 $\pm$ 38.57	5.04 $\pm$ 1.10	1.87 $\pm$ 0.47
6 mo.	2183.94 $\pm$ 402.90	939.94 $\pm$ 145.58	2.16 $\pm$ 0.36	0.73 $\pm$ 0.19
1 yr.	2176.51 $\pm$ 504.86	2768.07 $\pm$ 2088.11	0.51 $\pm$ 0.36	0.25 $\pm$ 0.01

Table 16. Continued

Time Following Implant	Pu(NO ₃) ₄				PuO ₂			
	No Treatment		DTPA		No Treatment		DTPA	
	(X10 ⁻⁶)		(X10 ⁻⁶)		(X10 ⁻⁶)		(X10 ⁻⁶)	
<u>L. S. C. L. N.</u>								
2 wks.	16,781.60±	3,887.36	14,388.00±	6,123.67	366.45±	48.02	0.39±	0.17
1 mo.	22,244.99±	3,345.64	15,492.02±	2,137.56	622.80±	308.30	511.98±	193.69
2 mo.	20,844.30±	3,239.69	18,610.39±	3,687.96	1,317.97±	478.07	1,774.14±	523.14
3 mo.	5,912.03±	2,235.27	4,096.96±	148.48	54,655.64±	34,842.17	4,508.64±	3,568.70
6 mo.	11,657.65±	3,281.39	34,184.64±	4,227.60	19,487.19±	17,061.89	4,631.02±	2,647.91
1 yr.	1,724.31±	1,029.17	2,423.03±	491.64	263.83±	187.04	199.54±	89.57
<u>Left Axillary Lymph Node</u>								
2 wks.	11,566.31±	10,254.44	10,795.23±	9,041.16	0.022±	0.007	0.044±	0.038
1 mo.	674.99±	419.66	1,349.38±	1,187.24	0.413±	0.206	0.66 ±	0.65
2 mo.	11,346.99±	6,410.11	11,178.95±	11,135.23	0.470±	0.105	0.183±	0.082
3 mo.	12,288.08±	11,698.97	114.72±	93.90	5.225±	4.995	1.390±	0.855
6 mo.	14,692.16±	7,928.92	316.88±	122.61	0.527±	0.251	18.573±	17.827
1 yr.	855.97±	398.77	835.27±	511.73	6.340±	5.846	50.967±	50.887

Table 16. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>R. S. C. L. N.</u>				
2 wks.	46.20 $\pm$ 20.60	4.38 $\pm$ 1.77	0.02 $\pm$ 0.01	0.01 $\pm$ 0.01
1 mo.	35.27 $\pm$ 5.55	16.90 $\pm$ 4.68	0.05 $\pm$ 0.02	1.01 $\pm$ 0.95
2 mo.	31.72 $\pm$ 7.09	15.08 $\pm$ 5.36	1.55 $\pm$ 0.29	0.47 $\pm$ 0.17
3 mo.	32.19 $\pm$ 17.46	6.05 $\pm$ 2.17	5.26 $\pm$ 2.38	1.19 $\pm$ 0.54
6 mo.	52.37 $\pm$ 18.97	12.48 $\pm$ 1.77	3.71 $\pm$ 2.51	1.28 $\pm$ 0.73
1 yr.	27.00 $\pm$ 6.05	32.39 $\pm$ 11.27	0.27 $\pm$ 0.07	0.07 $\pm$ 0.02
<u>Thyroid</u>				
2 wks.	6.20 $\pm$ 2.46	4.64 $\pm$ 4.27	0.02 $\pm$ 0.01	0.04 $\pm$ 0.01
1 mo.	9.41 $\pm$ 1.67	13.09 $\pm$ 2.47	0.06 $\pm$ 0.02	0.26 $\pm$ 0.17
2 mo.	6.50 $\pm$ 2.64	10.06 $\pm$ 7.56	0.77 $\pm$ 0.25	1.50 $\pm$ 1.20
3 mo.	9.41 $\pm$ 2.27	2.62 $\pm$ 0.59	3.33 $\pm$ 2.22	1.68 $\pm$ 1.52
6 mo.	26.06 $\pm$ 17.11	16.98 $\pm$ 10.79	1.08 $\pm$ 0.63	5.80 $\pm$ 2.80
1 yr.	9.63 $\pm$ 1.44	29.47 $\pm$ 9.52	0.13 $\pm$ 0.09	0.10 $\pm$ 0.09
<u>Bile</u>				
2 wks.	0.37 $\pm$ 0.09	1.37 $\pm$ 0.41	0.17 $\pm$ 0.15	0.02 $\pm$ 0.01
1 mo.	11.06 $\pm$ 3.57	5.86 $\pm$ 1.60	2.51 $\pm$ 2.44	0.36 $\pm$ 0.25
2 mo.	2.55 $\pm$ 1.27	0.76 $\pm$ 0.57	0.29 $\pm$ 0.27	0.61 $\pm$ 0.36

Table 16. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Bile (Continued)</u>				
3 mo.	0.82 ± 0.23	0.39 ± 0.10	0.16 ± 0.06	0.16 ± 0.14
6 mo.	0.76 ± 0.22	0.40 ± 0.08	7.38 ± 6.51	2.50 ± 1.56
1 yr.	14.70 ± 8.06	1.70 ± 0.99		
<u>Hepatic Lymph Node</u>				
2 wks.		5.08 ± 3.00	0.06 ± 0.03	0.01 ± 0.01
1 mo.	3.75 ± 1.39	6.68 ± 2.89	0.05 ± 0.02	1.01 ± 0.90
2 mo.	43.74 ± 15.92	16.75 ± 8.45	4.08 ± 3.88	1.45 ± 0.96
3 mo.	5.36 ± 4.35	1.69 ± 0.61	58.34 ± 7.94	1.94 ± 1.26
6 mo.	31.60 ± 7.72	27.65 ± 8.39	18.07 ± 14.58	16.20 ± 12.90
1 yr.	41.46 ± 13.28	13.18 ± 4.90	0.11	3.39 ± 3.02

Table 17. Fraction of Initial Implant Dose of Americium per Total Organ.

Time Following Implant	Pu(NO ₃) ₄				PuO ₂			
	No Treatment		DTPA		No Treatment		DTPA	
	(X10 ⁻⁶)		(X10 ⁻⁶)		(X10 ⁻⁶)		(X10 ⁻⁶)	
<u>Left Testis</u>								
2 wks.	15.3428±	7.0775	10.4187±	4.5817	5.618±5.275	0.497±	0.433	
1 mo.	20.064 ±	6.476	6.369		0.672±0.363	4.158±	0.307	
2 mo.	12.3585±	3.0949	7.5470±	1.4410	0.657±0.259	24.700±14.569		
3 mo.	18.921 ±	6.603			--	21.652±17.053		
6 mo.	20.863 ±	3.722	24.027 ±	16.998	4.110±2.307	1.036±	0.416	
1 yr.	92.213		40.984		3.653	0.975		
<u>Left Kidney</u>								
2 wks.	1049.3250±	419.5895	105.7113±	32.2062	3.894±2.005	1.832±	0.302	
1 mo.	150.743		148.620		9.885	11.187±	7.431	
2 mo.	1688.676 ±	392.619	207.5473±	42.6010	14.916±5.292	17.471±	7.151	
3 mo.	1542.857 ±	161.905	86.667 ±	33.115	--	128.861±80.067		
6 mo.	3023.308 ±	1979.915	246.355 ±	71.726	2.233±0.077	1.268±	1.097	
1 yr.	--	--	--	--	--	4.872±	3.991	
<u>Left Adrenal</u>								
2 wks.	6.9230±	0.6920	5.0880±	1.3738	0.706±0.200	0.303±	0.044	
1 mo.	12.474 ±	3.769	4.246 ±	0.000		3.817±	1.986	
2 mo.	66.226 ±	50.378	1.6038±	0.4184	0.774±0.330	8.517±	1.487	

Table 17. Continued

Time Following Implant	Pu(NO ₃) ₄				PuO ₂			
	No Treatment		DTPA		No Treatment		DTPA	
	(X10 ⁻⁶)		(X10 ⁻⁶)		(X10 ⁻⁶)		(X10 ⁻⁶)	
<u>Left Adrenal (Continued)</u>								
3 mo.							5.748±	3.676
6 mo.	15.870 ±	3.112	4.115 ±	1.043	1.664±	1.502	1.931±	1.897
1 yr.	--		--		0.805		25.522	
<u>Spleen</u>								
2 wks.	842.1598±	283.4901	200.1558±	36.6216	1.898±	0.566	2.275±	1.137
1 mo.	1684.7487±	370.4723			5.203		3.861	
2 mo.	137.8460±	89.4826	172.4318±	46.5535	8.939±	2.388	2.700±	1.1270
3 mo.			181.905				9.296±	3.901
6 mo.	757.813 ±	300.417	237.550 ±	48.652	5.766±	3.037	9.192±	7.953
1 yr.	804.303		--		1.579		0.935	
<u>Liver</u>								
2 wks.	13085.644 ±	3274.607	3202.830 ±	1624.369	34.859		20.154±	7.389
1 mo.	8371.505 ±	4485.505	1092.144 ±	585.572	--		19.476	
2 mo.	63931.038 ±	18305.802	811.747 ±	539.388	771.297±	460.710	165.714±	87.236
3 mo.	22241.492 ±	20792.448	5993.832 ±	1910.073	710.730±	325.040	459.610±	290.924
6 mo.	36332.695 ±	30012.773	5195.298 ±	1959.708	346.776±	149.427	196.615±	59.568
1 yr.	--		--		10.300		234.661±	230.751

Table 17... Continued

Time Following Implant	Pu(NO ₃) ₄		PuO ₂	
	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)	No Treatment (X10 ⁻⁶)	DTPA (X10 ⁻⁶)
<u>Left Eye</u>				
2 wks.	17.238 ₊ 7.726	6.724 ₊ 2.647	9.806 ₊ 3.720	2.448 ₊ 1.441
1 mo.	24.576 ₊ 3.026	15.216 ₊ 8.276	12.838 ₊ 2.473	66.012 ₊ 39.965
2 mo.	7.170 ₊ 0.847	4.505 ₊ 2.400	15.619 ₊ 10.745	537.524 ₊ 406.548
3 mo.	7.619	23.429 ₊ 19.810	--	23.183 ₊ 3.234
6 mo.	14.753 ₊ 2.729	65.415 ₊ 53.335	3.561 ₊ 1.977	18.817 ₊ 18.783
1 yr.	719.945 ₊ 57.988	--	30.836	3.547 ₊ 1.877
<u>Sternum</u>				
2 wks.	117.783 ₊ 34.528	40.447 ₊ 8.753	1.362 ₊ 0.741	0.637 ₊ 0.356
1 mo.	19.356 ₊ 10.576	263.022 ₊ 110.290	9.206	6.805
2 mo.	944.575 ₊ 378.301	536.163 ₊ 227.944	54.304 ₊ 9.104	22.588 ₊ 9.757
3 mo.	780.000	81.619 ₊ 20.286	20.348 ₊ 4.778	22.811 ₊ 5.283
6 mo.	950.660 ₊ 710.270	537.150 ₊ 110.757	9.496 ₊ 1.674	12.952 ₊ 9.474
1 yr.	8022.541	--	38.024 ₊ 24.953	0.650
<u>Rib</u>				
2 wks.	31.231 ₊ 9.806	16.979 ₊ 7.804	0.773 ₊ 0.541	0.649 ₊ 0.328
1 mo.	19.604 ₊ 10.339	26.646 ₊ 19.215	3.029	11.167 ₊ 5.252
2 mo.	171.069 ₊ 25.607	92.013 ₊ 27.152	30.769 ₊ 6.647	25.938 ₊ 7.298
3 mo.	349.079 ₊ 129.402	44.500 ₊ 21.382	15.446 ₊ 10.912	41.065 ₊ 22.937
6 mo.	1011.720 ₊ 112.901	347.395 ₊ 72.856	9.998 ₊ 4.266	14.194 ₊ 10.681
1 yr.	3739.754	229.508	25.146 ₊ 23.970	6.056

Table 17. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No. Treatment	DTPA	No. Treatment	DTPA
	($\times 10^{-6}$)	($\times 10^{-6}$)	($\times 10^{-6}$)	($\times 10^{-6}$)
<u>Vertebrae</u>				
2 wks.	185.592 $\pm$ 71.858	78.583 $\pm$ 35.338	0.085 $\pm$ 0.023	0.257 $\pm$ 0.040
1 mo.	26.327 $\pm$ 6.223	125.902 $\pm$ 39.620	10.977 $\pm$ 6.737	6.581 $\pm$ 6.363
2 mo.	69.340 $\pm$ 25.985	123.019 $\pm$ 106.969	47.620 $\pm$ 5.909	20.777 $\pm$ 13.139
3 mo.	383.691 $\pm$ 147.815	46.572 $\pm$ 18.953	26.029 $\pm$ 9.833	10.668 $\pm$ 8.309
6 mo.	2403.127 $\pm$ 1167.048	401.080 $\pm$ 364.628	7.619 $\pm$ 3.552	0.680 $\pm$ 0.534
1 yr.	13323.77	--	56.837	
<u>Skull</u>				
2 wks.	6.906 $\pm$ 1.282	6.542 $\pm$ 2.277	0.208 $\pm$ 0.183	0.834 $\pm$ 0.278
1 mo.	31.078 $\pm$ 3.124	21.842 $\pm$ 11.446	5.845 $\pm$ 0.388	7.607 $\pm$ 7.576
2 mo.	260.613 $\pm$ 54.768	80.283 $\pm$ 38.233	6.045 $\pm$ 1.049	3.293 $\pm$ 1.150
3 mo.	57.365 $\pm$ 22.585	37.334 $\pm$ 21.911	11.606 $\pm$ 0.897	12.667 $\pm$ 5.533
6 mo.	194.010 $\pm$ 126.473	141.613 $\pm$ 71.751	8.123 $\pm$ 5.608	9.797 $\pm$ 8.987
1 yr.	--	307.377	4.220 $\pm$ 3.594	1.551 $\pm$ 1.465
<u>Femur (Proximal)</u>				
2 wks.	66.952 $\pm$ 27.771	25.262 $\pm$ 18.572	0.391 $\pm$ 0.214	0.646 $\pm$ 0.438
1 mo.	71.231 $\pm$ 63.195	18.047	4.498 $\pm$ 2.970	3.127 $\pm$ 1.488
2 mo.	543.145 $\pm$ 254.581	147.736 $\pm$ 118.456	7.754 $\pm$ 2.231	0.988 $\pm$ 0.465

Table 17. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment	DTPA	No Treatment	DTPA
	($\times 10^{-6}$)	($\times 10^{-6}$)	($\times 10^{-6}$)	($\times 10^{-6}$)
<u>Femur (Proximal--Continued)</u>				
3 mo.	232.698 $\pm$ 153.064	327.381 $\pm$ 326.905	9.959 $\pm$ 4.959	9.557 $\pm$ 3.008
6 mo.	1516.320 $\pm$ 740.267	681.773 $\pm$ 259.679	6.182 $\pm$ 1.038	1.868 $\pm$ 0.668
1 yr.	3721.312 $\pm$ 3399.591	1731.557	1.448	1.994 $\pm$ 1.251
<u>Femur (Shaft)</u>				
2 wks.	33.203 $\pm$ 14.736	9.710 $\pm$ 2.775	1.186 $\pm$ 1.146	4.693 $\pm$ 3.866
1 mo.	17.463 $\pm$ 2.173	67.728 $\pm$ 60.616	4.143 $\pm$ 2.172	0.265
2 mo.	556.164 $\pm$ 315.869	95.346 $\pm$ 43.799	10.004 $\pm$ 6.095	2.984 $\pm$ 1.841
3 mo.	280.159 $\pm$ 214.873	67.555 $\pm$ 35.995	13.618 $\pm$ 5.289	8.523 $\pm$ 6.182
6 mo.	288.255 $\pm$ 153.623	106.040 $\pm$ 82.303	10.219 $\pm$ 6.030	1.040 $\pm$ 0.388
1 yr.	4067.623	104.508	12.744	20.624 $\pm$ 18.680
<u>Femur (Distal)</u>				
2 wks.	64.486 $\pm$ 20.180	29.388 $\pm$ 11.980	0.314 $\pm$ 0.117	0.643 $\pm$ 0.427
1 mo.	36.731 $\pm$ 13.767	155.096 $\pm$ 72.081	7.338 $\pm$ 2.672	15.887 $\pm$ 12.018
2 mo.	34.245 $\pm$ 14.154	238.051 $\pm$ 46.934	7.831 $\pm$ 3.208	5.527 $\pm$ 2.173
3 mo.	311.111 $\pm$ 91.983	9.762 $\pm$ 2.810	15.246 $\pm$ 0.742	5.295 $\pm$ 1.025
6 mo.	587.630 $\pm$ 199.523	294.713 $\pm$ 148.614	104.961 $\pm$ 96.467	1.979 $\pm$ 1.332
1 yr.	10348.36		2.532 $\pm$ 1.805	3.282 $\pm$ 2.725

Table 17. Continued.

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)

L. S. C. L. N.

2 wks.	7434.949 $\pm$ 1195.923	6545.517 $\pm$ 2700.444	550.238 $\pm$ 214.447	323.868 $\pm$ 266.241
1 mo.	14225.053	8040.287 $\pm$ 3262.261	1541.796 $\pm$ 1052.033	1558.441 $\pm$ 912.532
2 mo.	3808.725 $\pm$ 2219.860	8646.713 $\pm$ 5088.612	1193.660 $\pm$ 1174.838	9387.937 $\pm$ 5602.968
3 mo.	2550.048 $\pm$ 1059.899	253.714 $\pm$ 103.995	10557.863	1597.704 $\pm$ 885.412
6 mo.	4775.535 $\pm$ 2132.386	5024.738 $\pm$ 3312.662	3235.710 $\pm$ 328.647	957.510 $\pm$ 45.348
1 yr.	649.590	2922.132 $\pm$ 1538.935	840.575 $\pm$ 650.309	413.193

Left Axillary Lymph Node

2 wks.	687.851 $\pm$ 557.762	2615.784 $\pm$ 2032.693	0.683 $\pm$ 0.607	0.825 $\pm$ 0.581
1 mo.	38.747	3.610 $\pm$ 2.548	5.794	9.172 $\pm$ 2.022
2 mo.	385.409 $\pm$ 212.489	390.849 $\pm$ 388.585	209.557 $\pm$ 207.788	9.861 $\pm$ 6.354
3 mo.	439.143 $\pm$ 397.001	1.095 $\pm$ 0.619	5.071 $\pm$ 1.926	3.371 $\pm$ 1.683
6 mo.	93.267 $\pm$ 77.674	96.720 $\pm$ 83.990	0.946 $\pm$ 0.483	0.046 $\pm$ 0.012
1 yr.	77.869 $\pm$ 67.623		28.933 $\pm$ 12.277	1.980 $\pm$ 0.804

Left Paw

2 wks.		1662.440 $\pm$ 780.148	1793.902 $\pm$ 334.544
1 mo.	Used for Pathology	1266.892	726.307 $\pm$ 404.954
2 mo.		1607.204 $\pm$ 964.057	628.879 $\pm$ 397.585

Table 17. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Left Paw (Continued)</u>				
3 mo.			3296.095 $\pm$ 580.248	3682.351 $\pm$ 732.409
6 mo.	Used for Pathology		4990.678 $\pm$ 3379.605	3477.467 $\pm$ 693.962
1 yr.			1492.678 $\pm$ 794.470	3149.501 $\pm$ 1128.952
<u>R. S. C. L. N.</u>				
2 wks.	28.349 $\pm$ 12.430	19.289 $\pm$ 9.555	0.512 $\pm$ 0.056	2.270 $\pm$ 1.337
1 mo.	12.208	7.431 $\pm$ 4.671	74.126 $\pm$ 68.873	--
2 mo.	52.537 $\pm$ 28.274	26.470 $\pm$ 15.507	3.802 $\pm$ 1.092	8.083 $\pm$ 4.290
3 mo.	10.571	4.968 $\pm$ 2.654	--	1.026 $\pm$ 0.633
6 mo.	13.873 $\pm$ 5.474	14.050 $\pm$ 6.155	2.456 $\pm$ 1.702	2.491 $\pm$ 1.316
1 yr.	84.017 $\pm$ 63.525		22.296 $\pm$ 20.914	0.327 $\pm$ 0.274
<u>Thyroid</u>				
2 wks.	19.214 $\pm$ 12.062	6.984 $\pm$ 2.832	0.528 $\pm$ 0.117	
1 mo.	23.779 $\pm$ 7.113	36.837 $\pm$ 36.625	3.208 $\pm$ 3.008	1.020 $\pm$ 0.491
2 mo.	12.327 $\pm$ 5.631	5.708 $\pm$ 3.584	5.614 $\pm$ 1.884	2.029 $\pm$ 0.329
3 mo.	6.905 $\pm$ 1.560	8.423 $\pm$ 5.478	4.148 $\pm$ 2.513	1.197 $\pm$ 0.463
6 mo.	20.867 $\pm$ 4.693	22.813 $\pm$ 14.690	0.952 $\pm$ 0.562	1.177 $\pm$ 1.120
1 yr.	141.393		11.468 $\pm$ 4.904	9.878 $\pm$ 9.147

Table 17. Continued

Time Following Implant	$\text{Pu}(\text{NO}_3)_4$		PuO_2	
	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)	No Treatment ($\times 10^{-6}$)	DTPA ($\times 10^{-6}$)
<u>Bile</u>				
2 wks.	--	--	1.508 $\pm$ 0.545	--
1 mo.	11.819 $\pm$ 6.097	34.183 $\pm$ 12.648	0.371	0.376 $\pm$ 0.323
2 mo.	22.830 $\pm$ 19.434	6.274 $\pm$ 2.063	290.586 $\pm$ 285.294	6.151 $\pm$ 2.213
3 mo.	3.214 $\pm$ 2.078	3.691 $\pm$ 1.123	3.518 $\pm$ 1.569	--
6 mo.	2.265 $\pm$ 0.679	2.358 $\pm$ 1.179	8.101 $\pm$ 4.131	8.812 $\pm$ 4.325
1 yr.	17.076 $\pm$ 5.335	32.787 $\pm$ 22.572	--	--
<u>Hepatic Lymph Node</u>				
2 wks.	--	17.446 $\pm$ 13.500	10.406 $\pm$ 10.132	0.222 $\pm$ 0.056
1 mo.	4.565	4.034	7.306 $\pm$ 4.266	12.964 $\pm$ 11.916
2 mo.	40.377 $\pm$ 6.879	9.104 $\pm$ 3.931	5.366 $\pm$ 4.726	25.278 $\pm$ 22.157
3 mo.	2.143 $\pm$ 1.000	1.691 $\pm$ 0.593	12.229	45.654 $\pm$ 40.098
6 mo.	14.248 $\pm$ 7.375	10.833 $\pm$ 2.652	2.032 $\pm$ 1.792	6.396 $\pm$ 4.685
1 yr.	38.934	102.459	--	13.069 $\pm$ 3.463

and some dogs with essentially background activity in the axillary node. Based on work done at the University of Utah and by Johnson (1969) high concentration of Am in the thyroid has been reported. Tables 14-17 show an increased Am concentration of 4-10 in the PuO_2 experiment but no significant difference in the $\text{Pu}(\text{NO}_3)_4$ study. Bile is of interest because this is a pathway for excretion of Pu through the liver and intestinal tract. Data in Tables 14-17 indicate no significant differences from that of non-concentrating soft tissues. A section of trachea was taken as a representative cartilage as a comparison to that of soft tissue and bone. The data (Tables 14-17) are likewise similar to that of non-concentrating soft tissues.

Additional bone samples consisting of sternum, rib, vertebrae, skull, femur (shaft), and femur (distal) were analyzed and the data shown in Tables 14-17. These selections of bone represent various bone types. The data show differences in deposition with different types. The trabecular bone represented by the femur (proximal) showed greater concentrations than the flat bones represented by the femur (shaft).

Because of the continuing decay of ^{241}Pu to ^{241}Am described in the previous section all Am data and the wound count data were corrected for growth of Am from the time of implant until the count time or the time of chemical separation of the Pu and Am.

Because overlying tissue over the LSCLN and over the paw produced a significant absorption of the 17 keV x rays, as was demonstrated by Ramsden and Speight (1967), tissue phantoms were constructed from masonite and from tissue and absorption curves were constructed. Measurements were performed on several dogs to determine the approximate average tissue overlay and all wound count data was corrected for tissue absorption.

Discussion

Wound Counter Measurements of Paw and LSCLN

The chemistry of Pu is a very complex subject even in a simple in vitro system. With the added complexities of a biochemical system such as a mammalian body the interactions and unpredictable reactions become even more compounded. We at Colorado State University have been studying the various chemical forms of Pu normally encountered in an industrial environment by employees. The first experiment dealt with an air oxidized form. This study involved $\text{Pu}(\text{NO}_3)_4$ and PuO_2 prepared under a high fired (calcined at 850°C) condition. Two of the chemical complexities of Pu are its very insoluble characteristics as an oxide and its strong hydrolizing reaction. These characteristics made it difficult to administer the suspension of PuO_2 in consistently reproduceable doses from one animal to the other. Because of insolubility of the PuO_2 particles and their tendency to settle quickly to the bottom of the containment vial, the vials were vigorously shaken immediately before withdrawal of the injection samples. The calibration technique described in the Materials and Methods section gave a reasonably accurate estimate of the implant dose for both chemical forms. This was tested by monitoring the animals with wound count measurements and correlating these results to the radio-chemical alpha analysis following necropsy of the dogs.

On the other hand, a solution, the $\text{Pu}(\text{NO}_3)_4$ has an extremely strong ability to hydrolize and plate on the surfaces of containment vessels, especially glass. Therefore, plastic containers and syringes were used whenever possible.

Data obtained from the routine counting showed a significant reduction in activity at the implant site with time for the more soluble form $\text{Pu}(\text{NO}_3)_4$ (Fig. 1 and Table 6), as well as for PuO_2 (Fig. 2 and Table 6). The data show, after 1 year, a 70% reduction in the amount of $\text{Pu}(\text{NO}_3)_4$ and a 90% reduction for the PuO_2 originally administered. These results are contrasted with Johnson's findings (1969) of a 20% reduction at 1 year using PuO_2 air oxidized. The initial rate of loss appears to be more gradual in the PuO_2 dogs. These data were best fit by power functions that are probably two component curves for the $\text{Pu}(\text{NO}_3)_4$ and an exponential function for the PuO_2 dogs.

The first component of the curve for the $\text{Pu}(\text{NO}_3)_4$ is probably due to movement of the very small particles and/or ionizable Pu which can be removed readily from the implant site. The second component of the curve is probably due to a slower moving fraction that is broken down by phagocytosis and other reactions from large particles. Student "t" tests were performed on the data and no significant DTPA treatment effect on the removal of either chemical form occurred.

Concerning the movement of Pu from the implant site to the LSCLN a very obvious factor stood out and is shown in Table 7 and

Figs. 4 and 5. The rapidity with which measurable activity moved from the paw to the node within a few minutes after implant was remarkable for a system such as the lymphatic circulation. The buildup of activity in this node was first reported to reach a maximum around 10 days (Bistline et al. 1972), however, with the accumulation of more data and refinement of the data for absorption and Am growth, a more accurate value of 30 to 60 days appears to be the case for the $\text{Pu}(\text{NO}_3)_4$ data. This is consistent with the later data obtained from radiochemical analysis of the nodes following necropsy (Table 14) and the intersection of two curves fit to the data shown in Fig. 3. The lines were derived by connecting power function fits to the data preceding the peak times and by fitting a linear function to the data following the peak. These functions were found by a least squares fit which best described the two separate components of the curve.

For the high fired PuO_2 , a similar increase in concentration occurred in the LSCLN (Table 14 and Fig. 4). The deposition reached a maximum around 30-40 days followed by a gradual decrease over the following 9 months. These results are agreed, with radiochemical analysis of the data following necropsy and explain the intersection of a two component fit to the data. It would seem quite logical, as Johnson reported in 1969, that a mirror image of the power function loss from the injection site would be seen in the lymph node. However, two factors do influence the amplitude and shape of buildup dynamics in this

curve. First, some of the loss from the paw is undoubtedly occurring by direct absorption into the blood circulation possibly through lympho-venous shunts (Yoffey, 1970). Second, due to the level of buildup of Pu in the lymph node a significant movement of activity out of the lymph node occurs. This may be due to simple dynamics and from radiation damage to the cellular structure of the lymph node as described by Dagle (1973). The retention curve shown in Figs. 3 and 4 probably are a result of the difference between the mirror loss from the paw and resulting buildup in the lymph node, and the continuous loss of Pu from the node through both efferent channels and blood circulation.

These data on lymph node accumulation of Pu are in marked contrast to the data obtained in earlier PuO_2 (air oxidized) experiments (Johnson, 1969), where the deposition in the LSCLN showed continuous buildup throughout the one-year study. One explanation for this difference may be the particle size of the implant material. In Johnson's experiment, the geometric mean diameter by count was $7\mu\text{m}$, whereas the $\text{Pu}(\text{NO}_3)_4$ was administered in solution and the high fired PuO_2 had a geometric mean diameter by count of $0.7\mu\text{m}$. Thus, the particle size in the air oxidized PuO_2 experiment was much larger, a factor which might explain the lesser mobility of transport to and through the lymph node.

The rapidity with which one can detect measurable quantities of Pu in the node is evident in Table 7. In the high fired PuO_2 studies, measurable quantities were detected in the node at times varying from a few minutes to one or two hours. The speed of initial translocation appeared to depend on exact positioning of the implant and did not correlate with implant dosage. A student "t" test of the high fired PuO_2 data did show a statistically significant difference in LSCLN buildup between the No Treatment and DTPA therapy groups. However, there was no statistical significance between the No Treatment and DTPA groups in the $\text{Pu}(\text{NO}_3)_4$ experiment using the same student "t" test.

Blood and Urine Alpha Activity

A. Blood

Plutonium Analysis

The Pu and Am activity in the blood and urine was determined by the bioassay laboratories of the Health Physics Department at the Dow Chemical Co. - Rocky Flats Division (Table 18). As described earlier, correction for the growth of Am was made on all samples. The long half life of all the α -emitting Pu isotopes made the Pu activity essentially constant over the time of the study.

Except for the first 14 days when the dogs were housed in metabolic cages continuously, DTPA was not given to the treated nor were blood and urine samples taken from them until after they had been in

the metabolic cages for 24 hours. Thus, the animals were held in the cages 24 hours prior to implant and prior to the first sampling of each monthly sample collection series.

After completion of the translocation of the Pu from the wound site to the efferent lymph pathways, the blood is the primary mode of transport throughout the systemic circulation. The concentration of Pu in the blood (Figs. 5 and 6) rose quickly reaching a peak about 6 hours following implant of the $\text{Pu}(\text{NO}_3)_4$ in both chelation treated and untreated groups. In the PuO_2 experiment, the peak appeared around two hours for the untreated group and between 8 and 24 hours following implant of the DTPA treated group. The data following these peaks is best fit by power functions in both $\text{Pu}(\text{NO}_3)_4$ and PuO_2 experiments for both treatment and no treatment groups. These power functions very strongly suggest a two-component loss. These data are in contrast to that found by Johnson (1969) for concentration of Pu in the blood. The concentration of Pu in the blood of the $\text{Pu}(\text{NO}_3)_4$ dogs was about two orders of magnitude greater than the PuO_2 dogs. However, at 2 to 24 hours (peak time) the concentration of the later group was nearly four orders of magnitude less. One can speculate that these differences are likely related to the nature of the chemical form of the element implanted.

Americium Analysis

The Am data showed that translocation reached a rapid peak in the blood at one hour after implant followed by a power function loss. The PuO_2 data did not peak until four hours, however, it likewise exhibited a power function loss. Thus, all blood data for concentration of Pu and Am in these two experiments exhibited power function loss describing the two component curves. The Am concentration in the $\text{Pu}(\text{NO}_3)_4$ dogs is approximately two orders of magnitude greater than that in the PuO_2 dogs (Tables 10 and 11). Possible explanations for the 2 component curve were the particle size differences and possible ionic state of the chemical forms and the inflammatory reaction (foreign body reaction).

In the $\text{Pu}(\text{NO}_3)_4$ experiment there appears to be a greater concentration of Pu over Am in the blood throughout the one year study. However, in the PuO_2 experiment the Am concentration was greater by approximately an order of magnitude.

B. Urine

Fractions of the Pu and Am circulating in blood are removed by the kidney and excreted through the urine as demonstrated by Langham (1962). In this experiment the removal process was well demonstrated in the data presented in Tables 12 and 13. The excretion patterns for the $\text{Pu}(\text{NO}_3)_4$ and PuO_2 experiments were best fit by power function models for treated and untreated groups and for Pu as well as Am. In

the $\text{Pu}(\text{NO}_3)_4$ and PuO_2 experiments an enhancement appears to occur in the removal of Pu and Am following DTPA treatment. The enhancement was greater in the case of $\text{Pu}(\text{NO}_3)_4$ where the DTPA was observed to give about a threefold increase of Pu and Am excretion. In contrast, a minimum increase in the order of 1.5 to 2.0 fold appeared to prevail in the Pu and Am excretion pattern in the PuO_2 contaminated dogs following DTPA therapy. In the PuO_2 experiment there was a significant enhancement in excretion of Am over Pu by approximately tenfold in the No Treatment group. This agrees well with the data of Hammond et al. (1968) reporting a tenfold enhancement in Am excretion over Pu from that of initial contamination. The DTPA treated PuO_2 dogs showed an Am enhancement of approximately eightfold at the beginning, but, this enhancement in Am excretion did not appear to hold up after about a week.

Tissue Sample Alpha Activity

Activity measurements following chemical analysis of the individual tissue samples for Pu and Am were converted to fraction of initial implant dose in order to normalize the data and make comparisons of fractional translocation. These data are listed on Tables 14, 15, 16, and 17. Tables 14 and 15 give the Pu and Am results as a fractional concentration per gram of tissue and Tables 16 and 17 give the fractional concentration for total organ. Detection of activity in

the various tissues correlates with previous reports by Langham et al. 1962; Newton et al. 1966; and Johnson, 1969 who reported that the lymph nodes, liver, spleen, and bone were the major concentrating tissues.

As expected from previous experiments, (Johnson, 1969), liver and spleen showed the most significant buildup of the soft tissue organs with the liver exhibiting the most dramatic increase in Pu concentration. The buildup of Pu in the liver (Fig. 9 and 10) was about 2 orders of magnitude greater in the $\text{Pu}(\text{NO}_3)_4$ experiment than in the PuO_2 at 1 year following implant. There was a definite DTPA treatment effect in the $\text{Pu}(\text{NO}_3)_4$ experiment showing a fivefold decrease in liver concentration of Pu and Am at 2 weeks and progressively greater differences with time up to about a tenfold reduction at 1 year in the livers of treated dogs. In the PuO_2 experiment the pattern was not as well defined and no statistically significant treatment effect could be seen in Pu concentration. However, an apparent Am reduction by about twofold was seen in the DTPA treated dogs. No significant enhancement for Pu or Am appears to exist in the liver in either treated or untreated dogs in the $\text{Pu}(\text{NO}_3)_4$ experiment. However, an apparent Am enhancement over Pu of approximately twofold occurred in the PuO_2 dogs.

The spleen (Fig. 11 and 12 and Tables 14-17) exhibited an overall similar pattern to that of the liver for both chemical forms. The difference in concentration between $\text{Pu}(\text{NO}_3)_4$ and PuO_2 experiments

showed a greater than two orders of magnitude higher concentration in the $\text{Pu}(\text{NO}_3)_4$ experiment. The overall difference in concentration was about 500 times greater in the $\text{Pu}(\text{NO}_3)_4$ dogs than in the PuO_2 dogs. In the spleen of the $\text{Pu}(\text{NO}_3)_4$ dogs approximately a twofold increase of Pu concentration over Am, relative to the amount implanted, was observed. A statistically significant reduction following DTPA treatment of about 3 to tenfold for Pu was observed in the $\text{Pu}(\text{NO}_3)_4$ dogs. A treatment effect causing an approximate threefold reduction of Am was seen. In the PuO_2 experiment the spleen showed no statistically significant enhancement. However, a trend toward Am enhancement was observed, especially in the treated animals. Because of the range of errors in the values no statistically significant DTPA effect was discernible in the PuO_2 for the Pu and Am data.

The excretion of activity through the kidney created a concentration of Pu and Am in that organ (Tables 14-17). There were approximately 2 orders of magnitude greater concentration of Pu to Am in the $\text{Pu}(\text{NO}_3)_4$ dog kidneys over that of PuO_2 . With the $\text{Pu}(\text{NO}_3)_4$ no statistically significant DTPA treatment reduction in Pu content occurred. However, there was a significant reduction of about 1 order of magnitude in Am activity in the $\text{Pu}(\text{NO}_3)_4$ dogs due to chelation treatment. In the PuO_2 experiment no statistically significant DTPA treatment effect was observed. However, there was greater concentration in the kidney of both the $\text{Pu}(\text{NO}_3)_4$ dogs and the PuO_2 dogs ranging from about

2 to 5 for Am over that of Pu. This fact is understandable since there is preferential excretion of Am through the kidney (Hammond et al. 1968).

The hepatic lymph node draining the liver is another target organ of high interest (Parks et al. 1972). Parks reported translocation of Pu to this node from inhaled $^{239}\text{PuO}_2$ equal to that translocated to the skeleton (5%), however this level occurred in both organs approximately 2,000 days following exposure. In our studies there was no statistically significant difference in concentration of Pu or Am in the hepatic lymph node between $\text{Pu}(\text{NO}_3)_4$ and PuO_2 (high fired), although there is a trend toward slightly higher concentration of Pu and Am in the $\text{Pu}(\text{NO}_3)_4$ dogs. DTPA therapy reduced the concentration of Pu in the $\text{Pu}(\text{NO}_3)_4$ experiment by about twofold and as much as 10 difference in the PuO_2 dogs. The effect of DTPA on Am concentration does not show a significant effect. The higher values for Am in the DTPA dogs of the PuO_2 groups of Table 17 are misleading because 1st, 2nd, and 3rd month data are all elevated by individual animal variations in each group as is indicated by the large standard error values.

For many years the ICRP has considered the liver and bone the critical organs for assessing dose limitations for internally deposited Pu. The bone is considered a prime and critical target organ for most alpha emitting heavy elements. Johnson (1969) points out the fact that skeletal tissue seemed to show a direct relationship between

the hemopoetic activity of the bone and its Pu collection enhancement. This finding supported previous work showing transferrin transport of Pu and Am to the bone where they were transferred to bone glycoproteins (Boocock and Popplewell, 1966; Chipperfield and Taylor, 1968). The proximal end of the femur is a representative sample of trabecular bone with the shaft and skull samples representative of flat bone (appositional growth).

The proximal femur showed a tremendous buildup of Pu and Am in the $\text{Pu}(\text{NO}_3)_4$ experiment as opposed to the (high fired) PuO_2 experiment. The Pu buildup per gram of bone was over 2,000 times as great at 6 months in the $\text{Pu}(\text{NO}_3)_4$ dogs as in the PuO_2 dogs. The Am buildup at 6 months was about 300 times greater for the $\text{Pu}(\text{NO}_3)_4$ dogs. The plots (Fig. 15 and 16) show the buildup that occurred in the $\text{Pu}(\text{NO}_3)_4$ experiment. There was a significant DTPA treatment effect with a reduced concentration of Pu in the bones of treated dogs by threefold in both $\text{Pu}(\text{NO}_3)_4$ and PuO_2 experiments. The DTPA did not show a statistically significant effect on Am in the PuO_2 experiment. There appears to be a Pu enhancement exhibited in the $\text{Pu}(\text{NO}_3)_4$ experiment. The PuO_2 did not show significance at the 5% error level.

Solid or compact bone samples such as femur shaft and skull did show a higher concentration by about 300 to 1,000 fold in the $\text{Pu}(\text{NO}_3)_4$ experiment and demonstrated no significant treatment effect.

The thyroid gland has been singled out as an organ of specific interest because of apparent enhancement of Am reported by the University of Utah researchers (Stover and Jee, 1972), and by Johnson (1969). There was a DTPA effective reduction of Am in the thyroid by a factor of threefold and an Am enhancement of 4-10 in the PuO_2 experiment. However, in the $\text{Pu}(\text{NO}_3)_4$ experiment no statistically significant enhancement could be seen.

The six-month and one-year groups of the $\text{Pu}(\text{NO}_3)_4$ experiment show some differences in buildup patterns when compared to the other groups. This may be due to the administered dose. The six-month study group was erroneously given a dose 2.5 times greater than planned and injected in the 4 earlier groups. The 1 year group was under exposed by approximately a factor of 16 due to a calculation error in the laboratories preparing the implant solutions at the Rocky Flats Plant. Normalizing the data to fractions of initial implant dose smoothed the data, however, some dose dependency does appear to exist in some data.

It became very obvious that proper localization of the implant material was critical. One must avoid intravenous injection and it was found that if the implant was implanted too deep or toward either side of the midline the route of translocation could possibly occur through the axillary lymph node. Thus, the axillary node data has no consistency and produced very large standard errors due to this parameter.

The Pu and Am data were purposely handled separately with no attempt to use Pu to Am ratios. This was done because of the level of Am being extremely low, many times at the minimum detectable limits of α -counting. Thus, very small variability in actual α -counts from sample to sample within groups was large relative to the actual numbers. When this variability is placed in the denominator of the ratio where Pu is generally so much larger than Am, the resulting values have extreme ranges creating enormous standard errors in the final data. Handling the data independently minimized this problem.

An explanation for the differences between PuO_2 and $\text{Pu}(\text{NO}_3)_4$ in translocation dynamics from the paw to the LSCLN and in LSCLN buildup may be due to the particle size and chemical nature of the material implanted. The nature of the inflammatory reaction at the injection site due to the chemical form of the material implanted could possibly be another factor deserving more investigation. In the experiment of Johnson (1969), the geometric mean diameter by count was $7\text{ }\mu\text{m}$ for the more soluble PuO_2 of an air oxidized form. The supposedly insoluble high fired PuO_2 had a geometric mean diameter by count of $0.7\text{ }\mu\text{m}$. Unpublished data from Dr. F. J. Miner of the Dow Chemical Company - Rocky Flats Plant does not support the former theories of insolubility of this oxide form. Rather, he has found the high fired PuO_2 to be much more soluble than previously considered. The $\text{Pu}(\text{NO}_3)_4$ on the other hand was administered as a

solution. This material does not remain stable at physiologic pH values as it hydrolyzes or complexes almost immediately in an environment above pH 3. This would imply that either a particulate form of plutonium hydroxide or plutonium complexes will be formed. Therefore, particles of sizes similar to those of the high fired PuO_2 would be formed. On the other hand, the similarities of the buildup curves in the LSCLN between these two chemical forms could be due to the same factors. The particulate formed could easily agglomerate, a reaction that has been demonstrated with PuO_2 maintained in various aqueous solutions. These reactions could very well explain the difference in the shape of the curves obtained for the removal from the implant site forms.

Johnson (1969) has reported a continued increase by power function curve for buildup of PuO_2 (air oxidized) in the LSCLN in his experiment. However, the data presented in Table 12 would suggest a similar two component curve if the data point plotted for the 1 year group is rejected (this point was derived from a smaller number of dogs than for the previous points).

Ge(Li) Counting

The Ge(Li) detector system was used to analyze the implant site, LSCLN, and liver regions. Data was collected and analyzed for Pu to Am ratios using the 51.63 keV and 129.3 keV gamma rays of ^{239}Pu and

the 59.56 keV gamma ray of ^{241}Am . A plexiglass containment device was constructed and the animals were anesthetized to maintain geometry integrity. The counting was done inside a large 2 inch thick lead shield, 4 feet by 4 feet by 3 feet. The detector had a resolution of 1.9 keV full width half maximum at 60 keV and the lead shield reduced background by a factor of 4 to tenfold in the energy regions of interest. Experiments were run using uncontaminated control dogs to determine the contribution of scatter and compton radiation into the detector from the animal. A series of data was also collected to correlate size parameters of the dog with background counts.

The counting data collected from the PuO_2 dogs and at 2 weeks indicated an increase concentration of Pu over Am by a factor of 2.5. The α -counting data from radiochemical analysis of the 2 week study group showed a Pu concentration increase over Am by a factor of 5. However, the Am data had a very large standard error, so the student "t" test does not show significance.

Summary

The dynamics of translocation and deposition in various organs of Pu and Am from $\text{Pu}(\text{NO}_3)_4$ and "high fired" PuO_2 implanted in the paw of beagle dogs was studied. In vivo measurements of activity were taken over the paw wound site and the left superficial cervical lymph node (LSCLN).

Very rapid movement of activity was observed from the paw to the LSCLN. Activity was seen in the LSCLN within minutes in nearly all dogs with both chemical forms. The data show at 1 year a 70% reduction in Pu from this implant site for the $\text{Pu}(\text{NO}_3)_4$ experiment and a 90% reduction for the high fired PuO_2 . The LSCLN for both forms of Pu injected showed buildup dynamics reaching peaks at approximately 30 to 60 days followed by a linear regression in activity. The buildups are best described kinetically up to 1 year by power function curves, and linear functions fitted to the data. The activity in the blood rose rapidly following implant to a peak reached at 2 to 24 hours following implant. The time of maximum accumulation varied according to the chemical form and the treatment group. This peak in activity was followed by a power function reduction through the 1 year studies.

The major pathway for removal of Pu from the body is by urine elimination. This data showed a power function model for urine excretion. The urine did show a higher excretion of Am by about ten-fold over the ratio of Pu to Am in the implant material. A buildup pattern similar to the LSCLN was demonstrated for liver, spleen, hepatic lymph node, and proximal portion of the femur.

Nearly all tissues analyzed showed a significantly lower concentration of activity when chelation treatment was used. Only the solid or compact bone samples represented by femur shaft and skull failed to show treatment effects.

There was a significantly greater concentration of Pu in bone than Am especially observed in the $\text{Pu}(\text{NO}_3)_4$ experiment. The thyroid did show a greater concentration in the PuO_2 experiment consistent with previous reports.

This study raised several important questions which need to be answered through further experimentation. The following are some of the questions needed to be answered: 1) What effect does particle size have on translocation of Pu from the wound site? This study showed great differences in translocation dynamics for particles having a count median diameter of 0.1 of the previous PuO_2 study. Likewise the $\text{Pu}(\text{NO}_3)_4$ showed even greater translocation dynamics differences. Because of the ranges in particle sizes and agglomeration characteristics of Pu in solution it was impossible to determine if the very small particles were ionized or transported or if any selective processes existed. A study using mono-dispersed particles would be more helpful in investigating this question, 2) All the data obtained so far on the various chemical forms should be selectively analyzed to see if a particular bone can be used as a model for total skeletal deposition, 3) Many questions remain unanswered regarding transport mechanisms, transport forms (ionic or particulate), and routes from the wound site to the systemic system. From previous experiments it is known that the lymphatic system and lymph node are major routes of translocation. However, certainly some Pu gets directly into the

blood stream from the wound site while some may get into the blood through lympho-venous shunts along the lymph channels draining the wound site before reaching the SCLN. In addition, some Pu is probably leaving the lymph node via blood circulation, although most often Pu must leave the lymph node through the efferent ducts leading to the thoracic duct. Thus considerably more study of this system is indicated.

Our data suggest a very rapid movement of Pu from a wound site, an event which should be considered seriously by medical and health physics people when dealing with such cases. Our data also show an active lymph system having an ability to build up Pu in the lymph node and the capability to clear it gradually into the circulation.

LITERATURE CITED

- Altman, P. L. 1961. Blood and other body fluids. Federation of American Societies for Experimental Biology. Washington, D. C.
- Bair, W. J. 1970. Plutonium inhalation studies (A series of lectures given in Japan in 1969 at the invitation of the Japanese Atomic Energy Commission) USAEC Report BNWL-1221.
- Bair, W. J. and R. C. Thompson. 1972. Private communications of biomedical research on plutonium. Pacific Northwest Laboratories, Battelle, Richland, Wash.
- Ballou, J. E. 1961. USAEC Report HW-69500. p. 111.
- Beach, S. A., G. W. Dolphin, K. P. Duncan and H. J. Dunster. 1966. A basis for routine urine sampling of workers exposed to plutonium-239. Health Physics 12:12.
- Bistline, R. W. 1968. A method for predicting subject background for in vivo plutonium measurements. AEC Report RFP-893.
- Bistline, R. W. 1973. Unpublished biomedical research of employees at Rocky Flats Division, Dow Chemical Co., Golden, Colo.
- Bistline, R. W. and W. H. Tyree. 1967. A comparison of low energy photon detectors for plutonium and americium wound counting. USAEC Report RFP-1068.
- Bloom, M. A. and W. Bloom. 1949. Late effects of radium and plutonium on bone. Arch. Pathol. 47:494.
- Bokowski, D. L. and S. E. Hammond. 1965. Diethylenetriaminepenta-acetic acid analysis and excretion following therapy for plutonium exposure. USAEC Report RFP-510.
- Boocock, G. and D. S. Popplewell. 1966. In vitro distribution of americium in human blood serum proteins. Nature 210:1283.
- Boocock, G. and D. S. Popplewell. 1966. In vitro distribution of plutonium and americium in blood serum. AWRE-O-37/66.

- Boss, M. R. and J. R. Mann. 1967. Body counter evaluation of plutonium exposures. *Health Physics* 13:259.
- Bruenger, F. W., W. Stevens and B. J. Stover. 1969. Americium-241 in the blood: in vivo and in vitro observations. *Radiation Research* 38:349-360.
- Brues, A. M., H. Lisco and M. D. Finkel. 1947. Carcinogenic action of some substances which may be a problem in certain future industries. *Cancer Research* 7:49.
- Brunstad, A. 1959.
- Cable, J. W., V. G. Horstman, W. J. Clarke and L. K. Bustad. 1962. Effects of intradermal injections of plutonium in swine. *Health Physics* 8:629.
- Cable, J. W., B. J. McClanahan, V. G. Horstman, D. H. Wood and L. K. Bustad. 1963. Effects of plutonium in skin and its removal. USAEC Report HW-76000 p. 149.
- Carritt, J., R. Fryxell, J. Kleinschmidt, R. Kleinschmidt, W. Langham, A. San Pietro, R. Schaffer and B. Schnap. 1947. Distribution and excretion of plutonium administered intravenously to the rat. *Biol. Chem.* 171:273.
- Catsch, A. 1961. Radioactive metal mobilization. *Federation Proceedings* 20:206.
- Chipperfield, A. R. and D. M. Taylor. 1968. Binding of plutonium and americium to bone glycoproteins. *Nature* 219:609.
- Cleveland, J. M. 1967. Compound of plutonium, In *Plutonium Handbook*. O. J. Wick (Ed.) Gandon and Breach, New York, pp. 335-402.
- Cloutier, R. J. and E. E. Watson. 1967. Measuring plutonium in wounds: Advantages of using the americium gamma ray. *Health Physics* 13:811.
- Coleman, G. H. 1965. The radiochemistry of plutonium. University of California. Livermore Radiation Laboratory, Livermore, California. NAS-NS-3058.

- Dagle, G. E. 1973. Lymph node clearance of plutonium. Special Report to the USAEC, COO-1787 (Ph.D. Dissertation).
- Dawson, F. G., D. E. Deonigi and E. A. Eschbach. 1965. Plutonium buildup and depletion. *Nucleonics* 23:101.
- Durbin, P. W. 1971. Plutonium in man: A twenty-five year review. UCRL-20850.
- Durbin, P. W. 1972. Plutonium in man: A new look at the old data. In *Radiobiology of Plutonium*, Stover, B. J., and W. S. S. Jee (eds.) J. W. Press, University of Utah, Salt Lake City.
- Falk, R. 1973. Unpublished; high resolution Ge(Li) spectrum analysis of pure plutonium-239. Rocky Flats Division, Dow Chemical Co., Golden, Colo.
- Foreman, H. 1960. The application of chelating agents for hastening excretion of radioelements, In *Metal-Binding in Medicine*. J. B. Lippincott, Philadelphia, pp. 160-168.
- Fuqua, P. A. 1965. Plutonium absorption--Evaluation and treatment. *Industrial Medicine and Surgery* 34:335.
- Hamilton, J. G. 1947. Plutonium project; metabolism of fission products and heaviest elements. *Radiology* 49:325.
- Hammond, S. E. and E. A. Putzier. 1963. Observed effects of plutonium in wounds over a long period of time, In *Proceedings of the Ninth Annual Conference on Bio-Assay and Analytical Chemistry*. TID-7695 pp. 140-165.
- Hammond, S. E. and E. A. Putzier. 1964. Observed effects of plutonium in wounds over a long period of time. *Health Physics* 10:399.
- Health Physics, Vol. 8. 1962. *Proceedings of the Hanford Symposium; The biology of the transuranic elements*, Richland, Wash., 28-30, May, 1962.
- Health Physics, Vol. 22. 1972. *Proceedings of the Hanford Symposium on the Biological Implications of the Transuranium Elements*, Richland, Washington, 27-29 Sept. 1971. *Health Physics*, Vol. 22, June, 1972.

Heid, K. R., R. C. Henle and J. M. Selby. 1966. Prompt mitigatory action after accidental exposure to radionuclides. USAEC Report BNWL-SA-962.

International Commission on Radiological Protection (ICRP). 1961. Handbook 80, A manual of radioactivity procedures.

James, A. C. and D. M. Taylor. 1971. DTPA therapy for chelation of ^{239}Pu in bone: the influence of bone remodelling. Health Physics 21, pp. 31-39.

Jech, J. J., B. V. Andersen and K. R. Heid. 1972. Interpretation of human urinary excretion of plutonium for cases treated with DTPA. Health Physics 22: pp. 787-792.

Johnson, L. J. 1969. Relative translocation and distribution of Pu and Am from experimental PuO_2 subcutaneous implants in beagles. Special Report to the USAEC, COO-1787-6 (Ph. D. Dissertation).

Lagerquist, C. R., I. B. Allen and K. L. Holman. 1967. Plutonium excretion following contaminated acid burns and prompt DTPA treatments. Health Physics 13:1.

Lagerquist, C. R., S. E. Hammond and D. B. Hylton. 1972. Distribution of plutonium and americium in the body 5 years after an exposure via contaminated puncture wound. Health Physics 22:pp. 929-934.

Lagerquist, C. R., S. E. Hammond, E. A. Putzier and C. W. Piltingsrud. 1965. Effectiveness of early DTPA treatments in two types of plutonium exposures in humans. Health Physics 11:1177.

Lagerquist, C. R., E. A. Putzier, and C. W. Piltingsrud. 1967. Bioassay and body counter results for the first 2 years following an acute plutonium exposure. Health Physics 13:965.

Larson, H. V., C. E. Newton, W. V. Baumgartner and K. R. Heid. 1968. The management of an extensive plutonium wound and the evaluation of the residual internal deposition of plutonium. Physics in Medicine and Biology 13:45.

Langham, W. H. 1956. Determination of internally deposited radioactive isotopes for excretion analysis. Am. Ind. Hygiene Assoc. Quart. 17:305.

- Langham, W. H. 1959. Physiology and toxicology of plutonium-239 and its industrial medical control. *Health Physics* 2:172.
- Langham, W. H. 1972. Biological implications of the transuranium elements for man. *Health Physics* 22 pp. 943-952.
- Langham, W. H., J. N. P. Lawrence, J. McClelland and L. H. Hempelmann. 1962. The Los Alamos Scientific Laboratory's experience with plutonium in man. *Health Physics* 8:753-760.
- Lederer, C. M., J. M. Hollander and I. Perlman. 1968. Table of Isotopes. John Wiley and Sons, Inc., New York.
- Leonard, B. R., Jr. 1967. Properties of plutonium isotopes, *In* Plutonium Handbook. O. J. Wick (Ed.) Gordon and Breach, New York pp. 1-10.
- Lindenbaum, A., J. F. Markley and M. W. Rosenthal. 1962. Removal of Pu from the blood as a function of DTPA treatment and of the physical state of the Pu. *Health Physics* 8:695.
- Lindenbaum, A., M. W. Rosenthal, C. J. Lund, J. J. Russell, M. H. Smoler and E. S. Moretti. 1967. Metabolic and therapeutic studies of plutonium. USAEC Report ANL-7409.
- Lloyd, R. L., W. S. S. Jee, D. R. Atherton, G. N. Taylor and C. W. Mays. 1972. Americium-241 in beagles: Biological effects and skeletal distribution, *In* Radiobiology of Plutonium. Stover, B. J., and W. S. S. Jee (Eds.), J. W. Press, University of Utah, Salt Lake City.
- Lushbaugh, C. C. and W. H. Langham. 1962. A dermal lesion from implanted plutonium. *Archives of Dermatology* 86:461.
- Markley, J. F. 1963. Removal of polymeric plutonium from mice by combined therapy with the calcium chelate and penta-ethyl ester of DTPA. *International Journal of Radiation Biology* 7:405.
- Mays, C. W. and K. A. Sears. 1962. Determination of localized alpha dose III from surface and volume deposits of ^{239}Pu , ^{228}Th , and ^{226}Ra , *In* Research in Radiobiology. COO-226, University of Utah, pp. 78-85.
- McClanahan, B. J. and H. A. Kornberg. 1967. Treatment of plutonium-contaminated wounds with diethylenetriaminepentaacetic acid in rats. USAEC Report BNWL-SA-1253.

- McClanahan, B. J. and H. A. Ragan. 1965. Translocation of subcutaneously administered $^{239}\text{PuO}_2$. USAEC Report BNWL-122. pp. 81-82.
- McClanahan, B. J. and J. A. Ragan. 1966. Translocation of subcutaneously deposited plutonium. USAEC Report BNWL-280.
- McClanahan, B. J., D. H. Wood, V. G. Horstman, H. A. Ragan and L. K. Bustad. 1964. Effects of plutonium in swine skin and its removal USAEC Report HW-80500. p. 120.
- National Bureau of Standards Handbook H-47. 1951. Recommendations of the International Commission on Radiological Protection and the International Commission on Radiological Unit 1950, Handbook H-47, 29 June 1957.
- Newton, C. E., Jr., K. R. Heid, H. V. Larson, I. C. Nelson. 1966. Tissue Sampling. USAEC Report BNWL-SA-918 (CONF-661018-3).
- Norwood, W. D. 1960. DTPA-Effectiveness in removing internally deposited plutonium from humans. Journal of Occupational Medicine 2:371.
- Norwood, W. D. 1962. Therapeutic removal of plutonium in humans. Health Physics 8, pp. 747-750.
- Norwood, W. D. 1963. Removal of plutonium and other transuranic elements from man. Diagnosis and treatment of radioactive poisoning. International Atomic Energy Agency, Vienna. pp. 307-317.
- Norwood, W. D. 1972a. Plutonium (^{239}Pu) toxicity, diagnosis and therapy. Journal of Occupational Medicine 14, p. 37.
- Norwood, W. D. 1972b. U. S. Transuranium Registry: Progress and Expectations, In Radiobiology of Plutonium. Stover, B. J., and W. S. S. Jee (Eds.). J. W. Press, University of Utah, Salt Lake City.
- Parks, J. F., W. J. Bair, R. H. Busch. 1972. Progress in Beagle dog studies with transuranium elements at Battelle-Northwest. Health Physics 22:803-810.

- Penneman, R. A. and T. K. Keenan. 1960. The radiochemistry of americium. National Academy of Sciences (NAS-NC-3006). National Research Council, Washington, D. C.
- Putzier, E. A. 1967. Problems in evaluating and treating plutonium exposures. Private communication, In Special Report to the USAEC, COO-1787-6 (Ph.D. Dissertation) Johnson, L. J. 1969.
- Radiological Health Handbook. 1960. U. S. Department of Health, Education, and Welfare. Public Health Service, Washington, D. C.
- Ramsden, D. and Speight. 1967. The measurement of plutonium-239 "in vivo"; a progress report. AEEW-R494.
- Roesch, W. C. 1964. Progress in Radiological Physics. USAEC Report HW-83605.
- Schubert, J. 1955. Removal of radioelements from the mammalian body, In Annual Review of Nuclear Science. J. G. Beckerley, (Ed.). p. 369.
- Schubert, J., J. F. Fried, M. W. Rosenthal and A. Lindenbaum. 1961. Tissue distribution of monomeric and polymeric plutonium as modified by a chelating agent. Radiation Research 15:220.
- Schubert, J. and A. Lindenbaum. 1960. The mechanism of action of chelating agents on metallic elements in the intact animal, In Metal-Binding in Medicine. M. J. Seven (Ed.), J. B. Lippincott Co., Philadelphia, pp. 68-74.
- Schulte, H. F. and H. O. Whipple. 1967. Chelating agents in plutonium deposition: A minority view. USAEC Report LA-DC-8433. CONF-670521-2.
- Scott, K. G., D. J. Axelrod, J. Crowley and J. G. Hamilton. 1949. Deposition and fate of plutonium, uranium, and their fission products inhaled as aerosols by rats and man. Arch. Pathol. 48: 31.
- Scott, K. G., D. J. Axelrod, H. Risher, J. F. Crowley and J. G. Hamilton. 1948. The metabolism of plutonium in rats following intramuscular injection. Journal of Biological Chemistry. 176: 283.

- Seaborg, G. T. 1963. Man-Made Transuranium Elements. Prentice-Hall, Inc., Englewood Cliffs, New Jersey.
- Seaborg, G. T. 1972. Plutonium Revisited, *In Radiobiology of Plutonium*. Stover, B. J. and W. S. S. Jee (Eds.). J. W. Press, University of Utah, Salt Lake City.
- Seed, J. R. 1972. Personal communication. Rocky Flats Division, Dow Chemical Co., Golden, Colo.
- Seven, M. J. 1960. Observation on the toxicity of intravenous chelating agents, *In Metal-Binding In Medicine*. M. J. Seven (Ed.), J. B. Lippincott Company, Philadelphia, pp. 95-103.
- Smith, V. H. 1958. Removal of internally deposited plutonium. *Nature* 181:1792.
- Smith, V. H. 1972. Therapeutic removal of internally deposited transuranium elements. *Symposium Issue-Health Physics* 22: pp. 765-778.
- Snyder, W. S. 1962. Major sources of error in interpreting urinalysis data to estimate the body burden of ^{239}Pu : A preliminary study. *Health Physics* 8:6.
- Snyder, W. S., M. R. Ford and G. C. Warner. 1967. Use of excretion data to predict the systemic body burden of plutonium. USAEC Report ORNL-4168. p. 273.
- Sowby, F. D. and D. M. Taylor. 1960. Removal of internally deposited Americium by chelating agents. *Nature* 187:612.
- Stevens, W., F. W. Bruenger and B. J. Stover. 1965. *In Vitro* studies of the interactions of Pu IV with blood proteins. *Radiation Research* 26:114-123.
- Stevens, W., F. W. Bruenger and B. J. Stover. 1968. *In Vivo* studies on the interactions of Pu IV with blood constituents. *Radiation Research* 33:490.
- Stover, B. J., F. W. Bruenger and W. Stevens. 1968. The reaction of Pu IV with the iron transport system in human blood serum. *Radiation Research* 33:381-394.
- Stover, B. J. and W. S. S. Jee (Eds.) 1972. *Radiobiology of plutonium*. J. W. Press, University of Utah, Salt Lake City.

- Swanberg, F. and R. C. Henle. 1964. Excretion of ^{239}Pu in a patient with a plutonium-contaminated injury. *Journal of Occupational Medicine* 6:174.
- Swinth, K. L. 1967. Interpreting counting data for internally deposited plutonium. USAEC Report BNWL-SA-997.
- Swinth, K. L. 1968. Measurement of the photon to alpha for plutonium isotopes. USAEC Report BNWL-715.
- Taylor, D. M. and F. D. Sowby. 1962. The removal of Americium and Plutonium from the rat by chelating agents. *Physics in Medicine and Biology* 7:83.
- Taylor, D. M. 1962. Some aspects of the comparative metabolism of plutonium and americium in rats. *Health Physics* 8:pp. 673-677.
- Taylor, D. M. 1969. The metabolism of plutonium in adult rabbits. *British Journal of Radiology* 42:44.
- Taylor, D. M. 1972. Cellular deposition and retention of ^{239}Pu in relation to the induction of neoplasms, *In Radiobiology of Plutonium*. Stover, B. J. and W. S. S. Jee (Eds.). J. W. Press, University of Utah, Salt Lake City.
- Taylor, D. M. and J. P. M. Bensted. Long-term biological damage from plutonium-239 and americium-241 in rats.
- Thomas, R. G. 1968. Transport of relatively insoluble materials from lung to lymph nodes. *Health Physics* 14:111-117.
- Thompson, R. C. 1967. Biological factors, *In Plutonium Handbook* (Vol. II) O. J. Wick (Ed.), Gordon and Breach, New York, pp. 785-831.
- Thompson, R. C., J. F. Park, W. J. Bair. 1972. Some speculative extensions to man of animal risk data on plutonium, *In Radiobiology of Plutonium*, B. J. Stover and W. S. S. Jee (Eds.), J. W. Press, University of Utah, Salt Lake City.
- Tremmel, E. B. 1968. The Nuclear Industry. USAEC Division of Industrial Participation. Washington, D. C.
- Turner, G. A. 1967. Ph.D. Thesis. University of London.

- Turner, G. A. and D. M. Taylor. 1968. The binding of plutonium to serum proteins in vitro. *Radiation Research* 36:pp. 22-30.
- Tyree, W. H. and R. W. Bistline. 1970. A feasibility study of detecting ^{239}Pu in vivo with a Ge(Li) detector array. AEC Report RFP-
- Weast, R. C. (Ed.). 1964. Handbook of Chemistry and Physics, 45th edition. The Chemical Rubber Co., pp. B99-B100, B127-B128.
- Weeks, M. H., W. D. Oakley and R. C. Thompson. 1955. Influence of plutonium concentration on effectiveness of therapeutic agents. *Radiation Research* 2(3).
- Wilson, R. A. 1967. Controlling and evaluating plutonium deposition in humans, In Plutonium Handbook (Vol. II), O. J. Wick (Ed.). Gordon and Breach, New York, pp. 833-844.
- Yoffey, J. M. and F. C. Courtice. 1970. Development, structure and organization of the lymphatic system, In Lymphatics, Lymph and the Lymphomyeloid Complex. Academic Press, London, New York.

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