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NEPTUNIUM METABOLISM
A BIBLIOGRAPHY AND SUMMARY
OF PERTINENT DATA

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NEPTUNIUM METABOLISM

A Bibliography and Summary
of Pertinent Data^(a)

by

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May, 1968

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PREFACE

- (a) This paper is based on work performed under United States Atomic Energy Commission Contract AT(45-1)-1830.
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NEPTUNIUM METABOLISM

A. INTRODUCTION

Studies reported in the literature on the metabolism of neptunium are relatively rare when compared to information available on the metabolism of other elements of the actinide series such as uranium or plutonium. The early work on neptunium metabolism was done at the University of California Radiation Laboratory, while the most recent studies have been reported by the Russians. The bulk of available data, however, has been generated at Hanford by members of the Biology Department of Battelle-Northwest (formerly Hanford Laboratories, General Electric Company).

The rat has been the subject animal for most neptunium metabolism studies. A few investigators have used the sheep, but no information is available on the metabolism of neptunium in man.

Neptunium-237 has been the isotope of choice for most studies. However, because of its low specific activity (one μCi of ^{237}Np weighs about 1.5 mg), a considerable quantity is necessary for measurable activity levels. The chemical toxicity of ^{237}Np , therefore, plays an important role in metabolism studies and many of the reports cited herein deal with the histopathological, morphological and physiological changes produced following administration of large doses of ^{237}Np . In a few cases, ^{239}Np was the isotope of neptunium used. Because of its relatively short half-life, much smaller quantities can be administered to obtain reliable data on initial uptake, but long-term retention studies are impossible.

This report summarizes available information on the metabolism of neptunium. Results are grouped according to the method of isotope introduction into the experimental animal. Differences in metabolism due to chemical form, valence state, experimental animal, etc. are discussed under each major section where appropriate.

B. INJECTION

In a series of experiments with rats, Ballou et al.^(1,2) found that following intravenous injection of approximately 0.7 μCi ^{237}Np citrate, the concentration of ^{237}Np was highest, initially, in the liver. After 3 days, the concentration in bone equals that in the liver, and bone concentration remained highest throughout the remainder of the experiment (21 days). Approximately 43% of the dose remained in the animals after 21 days. During this period, 36% of the dose was recovered in the excreta, about evenly divided between urine and feces. A summary of their results is presented in Table I.

Mahlum et al.⁽³⁾ followed the long-term retention of ^{237}Np following intravenous injection of 1.7 μCi ^{237}Np citrate. The level of ^{237}Np

TABLE I⁽¹⁾

Retention of Neptunium Administered Intravenously
(Dose 0.71 μ C--Two Rats Per Group)

Tissue	1 Day		3 Days		7 Days		21 Days	
	% Dose	% Dose/g	% Dose	% Dose/g	% Dose	% Dose/g	% Dose	% Dose/g
Liver	16	1.8	12	1.5	10	1.0	6.6	0.66
Femur	0.96	1.3	1.1	1.5	0.92	1.5	1.0	1.3
Kidney	2.0	1.2	1.3	0.81	1.0	0.59	0.95	0.48
Spleen	---	---	0.6	1.0	0.51	0.98	0.51	0.93
Lymph nodes	0.095	0.35	0.16	0.40	0.14	0.23	0.11	0.27
Residual carcass	33	0.22	34	0.24	28	0.20	24	0.14
Muscle	---	0.06	---	0.06	---	0.05	---	0.04
Total rat	70	0.26	60	0.23	52	0.20	43	0.14
Urine	7.5		9.1		10		19	
Feces	2.5	8.1			13		16	
Total recovery	80	77			75		79	

deposited in bone (~1.5% of dose/g bone) and the adrenal gland (~0.8% of dose/g adrenal) remained fairly constant over a 207 day retention period. Liver deposition decreased steadily throughout this period with two apparent half-lives of ~10 and ~70 days.

Ballou^(4,5) showed that ^{237}Np citrate deposits in the adrenal and the deposition is characterized by two bands of radioactivity; the one sub-capsular in the area of the zona glomerulosa, and the other bordering the medulla, associated with cells in the zona reticularis. Ballou points out that this concentration in the zones of the gland has important consequences in the dose sustained by tissue since the radioactivity is concentrated in one-fifth of the total gland.

Mahlum and Clark⁽⁶⁾, Mahlum^(7,8,9,10,11) and Berlin and Mahlum⁽¹²⁾ found that hepatic and renal damage was sustained in rats at dosages equal to or greater than 6 mg $^{237}\text{Np}/\text{Kg}$ as the citrate. Hepatic damage consisted of morphological changes--cloudy swelling, fatty degeneration and lobular necrosis, and biochemical changes--fat accumulation, elevated Ca^{2+} and reduced K^+ concentrations. Renal tubular damage was similar to that observed in uranium poisoning. Both hepatic and renal damage appeared earlier and were more severe in female than in male rats.

A recent Russian paper⁽¹³⁾ gives the results of an experiment in which rats were administered ^{237}Np nitrate intravenously. The authors found that the ^{237}Np left the blood stream rapidly and that maximum accumulation occurred in the skeleton (34.7% of injected dose), liver (10%), and kidney (6.5%). After one month, the elimination of ^{237}Np from the skeleton occurred with an effective half-life of 82.5 days. Liver elimination exhibited two effective half-lives--4.6 days (54.3%) and 46.6 days (45.7%). After 3 days, the isotope was eliminated from the kidneys with a T_{eff} of approximately 82.5 days. The main route of elimination was via the urine, especially during the first hours. The authors point out that their results do not always agree with previous published data (especially in relation to rapid clearance of ^{237}Np from the blood, low concentration in the adrenals, relatively high rate of elimination from bone, and primary importance of the kidneys in elimination) because of differences in chemical form and valence state.

The early work on neptunium metabolism was done by means of intramuscular injection of a neptunium compound in the rat. For the most part, the chemical form was not reported. Hamilton^(14,15,16) found that as high as 60% of the absorbed dose was found in the skeleton and 5% was found in the liver. The effective half-life was > 50 days for elimination from the skeleton and about 12 days for the liver.

A University of California report⁽¹⁷⁾ indicates that the skeleton retains 27.5% of the absorbed dose at 64 days following intramuscular injection of NpO_2^{++} . The liver and kidney retained 2.8% and 2.0% respectively. High

neptunium concentrations were also noted in the heart and spleen. Urinary excretion of neptunium was about two times higher than fecal excretion.

The other experimental animal used for neptunium metabolism studies has been the sheep. In general, the sheep results agree with the rat data. In studies^(18,19) in which sheep were administered graded doses of from 0.75-12 mg ^{237}Np citrate/Kg body weight, the liver and kidney accumulated the highest concentration of ^{237}Np . No data was reported on bone uptake. The liver appeared to be the most vulnerable organ. Liver function was impaired in animals which received doses as low as 1.5 mg (1.0 μCi) per Kg of body weight. While some kidney damage was produced, the damage produced in the liver was far more severe. The most severe liver function impairment was usually observed on the fourth day post-injection.^(20,21)

C. INGESTION

In 1947, Hamilton⁽¹⁴⁾ found that $< 0.05\%$ of the administered dose of ^{239}Np in an unspecified chemical form was absorbed from the GI tract in the rat. Ballou et al.⁽¹⁾ have shown that absorption from the GI tract varies from about 0.001% to about 2% of the administered dose. Absorption appears to be influenced by the valence state of the ingested material, absorption decreasing in the order $\text{Np}^{6+} > \text{Np}^{5+} > \text{Np}^{4+}$, and by the chemical form, the absorption of neptunium citrate being about two times greater than the absorption of neptunium nitrate. This level of absorption is more than ten times greater than the figures published by the ICRP for calculation of MPC. The authors, however, point out that these studies involved the administration of milligram quantities of neptunium and state that limited studies with the short-lived ^{239}Np suggest that the absorption of trace quantities of neptunium may be ten times lower. This suggestion was verified in subsequent studies.⁽³⁾

D. INHALATION

Studies on the inhalation of neptunium as a contaminant of an industrial material processed by an AEC contractor have been reported by Bair and Case^(22,23), Bair et al.⁽²⁴⁾ and Ballou et al.⁽¹⁾ Following inhalation of about 10 mg of dust, there was a maximum retention in the lung of 5% of the initially deposited material. Of that absorbed from the lung, a major fraction was deposited in bone. This, however, amounted to a maximum of not more than 2% of the neptunium initially deposited in the lung. Total absorption from the lung, including the ^{237}Np in all internal organs and that excreted in the urine, did not exceed 4% of the initially deposited dose. More than 90% of the initial dose was excreted in the feces.

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