COMPARISON OF PREMORTEM AND POSTMORTEM ESTIMATES OF PLUTONIUM IN THE SKELETON AND LIVER OF SIX INDIVIDUALS

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Assessment of organ burdens after internal exposures to radionuclides is often necessary to evaluate the health and regulatory implications of the exposure. The assessment of plutonium activity in skeleton and liver is usually estimated from measurements of plutonium excreted via urine. As part of the overall evaluation of internal dose assessment techniques, it is useful to compare the results of organ burden estimates made from evaluation of urinary excretion data with those made at death from tissue samples collected posthumously from the individual.

Estimates of plutonium in the skeleton and liver, based on postmortem analysis of tissue samples for six individuals, were obtained from the U.S. Transuranium Registry (USTR). Bioassay data and other radiation exposure information obtained from the individuals' files were used to estimate their skeleton and liver burdens at the times of their deaths, and these estimates were compared to those obtained through tissue analysis.

PREMORTEM ASSESSMENT OF INTERNAL ORGAN BURDENS

At the U.S. Department of Energy's Hanford Site, an empirically derived excretion model is used to estimate the uptake of plutonium to systemic circulation, and the metabolic assumptions in Publication 48 of the International Commission on Radiation Protection (ICRP) [1] are used to predict the resulting organ burdens at various times post uptake. The urinary excretion model uses the function recommended by Jones [2] to describe the expected daily excretion of plutonium via urine at times after an acute injection into the blood. However, in many cases, uptake by the blood is protracted rather than acute; i.e., at intake the plutonium is not immediately taken up by blood but is deposited at a presystemic site such as the lung or a wound. The transfer of plutonium from the presystemic deposition site into the systemic circulation is assumed to be governed by linear first-order kinetics and thus can be described in terms of a transfer rate constant, λ. Using Healy's method [3], Equation (1) describes the expected daily excretion of plutonium, E(t), after the deposition of Q(0) activity in the presystemic compartment.

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$$E(t) = Q(0)\lambda \int_{0}^{R} e^{-\lambda t} J(R-t)dt \qquad (1)$$

where J(R-t) is the value of the Jones excretion function at time R for plutonium entering the blood at time t post intake.

The excretion function is fit to the observed urinary excretion data by varying the transfer rate constant, λ, and the initial presystemic deposition quantity, Q(0). The λ and Q(0) values, providing the best fit to the excretion data, are then applied to a retention model to estimate the amount of plutonium in the skeleton and liver at times post intake. The retention model contains the presystemic compartment into which Q(0) is assumed to be deposited at the time of intake. Plutonium leaves the presystemic compartment enroute to the skeleton and liver according to the transfer rate constant, λ. Organ deposition fractions and retention half-times are based on recommendations in ICRP 48 [1].

This excretion model does not allow for the enhanced excretion that occurs during and after chelation therapy. Hanford experience has shown that the enhanced excretion rate after the administration of DTPA decreases with time post treatment and returns to levels predicted by the excretion model within 90 days of the end of treatment.

POSTMORTEM ASSESSMENT OF ORGAN DEPOSITION

The USTR accepts donations of organs and tissues from deceased plutonium workers for histopathological and biokinetic studies. At autopsy, donated tissues are removed and analyzed radiochemically. Tissue analysis procedures have been documented by Boyd et al. [4]. Tissue sample activities are scaled to either the known or Reference Man organ size [5]. The overall uncertainty in the organ burden estimates is not expected to exceed a factor of 2 [6].

EVALUATION OF EXPOSURE CASES

Assessments of skeleton and liver burdens at death were made for six individuals with well-defined exposure and bioassay histories. Premortem estimates were based on available urinalysis data and other information obtained from their files. Postmortem estimates were provided by the USTR. All six cases involved exposure to a mixture of plutonium isotopes consisting mainly of ^{239}Pu. In five of the six cases, exposure was via inhalation. In the sixth case (USTR 212) exposure was via a wound. The urine excretion function was fit using methods described previously. Only urine data representing 24-hour excretion periods was used. Sample results deviating from the excretion curve by a factor of 3 or greater were considered to represent either an erroneous measurement or an additional intake. In only one case did urine excretion data exceed the expected rate by this amount; because this result was not confirmed by follow-up samples it was determined to be erroneous. The initial selection of the presystemic

transfer rate constant, λ, used to fit the excretion model to the data was based on the solubility characteristics of the involved material. Final λ and Q(O) values for curve-fitting were obtained through regression analysis. Chelation therapy with DTPA had been applied in only one of the six cases (USTR 212). For this case, urinalysis results within 90 days following treatment were excluded.

Sample tissues of bone (vertebrae and rib) and liver were obtained at autopsy for all cases except USTR 212, for which the entire organs were donated for analysis. The entire liver and half of the skeleton were analyzed and thus the estimates of organ burdens for this case are expected to be the most accurate.

DISCUSSION OF RESULTS

Table 1 lists the premortem and postmortem estimates of the skeleton and liver burdens at death for the six cases. General consistency existed among the cases; typically, premortem estimates of skeletal burden were higher than postmortem estimates (five of six cases), while the converse was true for estimates of liver deposition. The premortem assessments averaged 1.6 and 0.6 times the postmortem estimates for skeleton burden and liver burden, respectively.

TABLE 1. Estimates of Plutonium in Skeleton and Liver, Bq

	USTR Case No.	Premortem Urinalysis	Postmortem Tissue Analysis	Ratio of Premortem-to-Postmortem Estimates
Skeleton	002	11	3.3	3.3
	006	1.8	0.89	2.0
	007	430	260	1.7
	010	130	96	1.4
	018	14	27	0.5
	212	130	100	1.3
				Mean=1.7±0.9

	USTR Case No.	Premortem Urinalysis	Postmortem Tissue Analysis	Ratio of Premortem-to-Postmortem Estimates
Liver	002	4.4	12	0.37
	006	0.85	0.56	1.5
	007	170	500	0.34
	010	57	270	0.21
	018	6.7	24	0.28
	212	56	87	0.64
				Mean=0.56±0.48

Skeleton-to-liver activity ratios at death (Table 2), were consistent for the premortem estimates averaging 2.3±0.2. Greater variability was observed among the postmortem data where skeleton-to-liver ratios averaged about one-third of the premortem ratio

average. In all cases, the postmortem estimates of skeleton-to-liver burden ratios were less than would be predicted using the distribution and retention recommendations in ICRP 48 [1].

TABLE 2. Skeleton-to-Liver Activity Ratios Based on Premortem Urinalysis and Postmortem Issue Analysis

USTR Case No.	Premortem Urinalysis	Postmortem Tissue Analysis	Age at Death	Years from Intake to Death
002	2.4	0.29	80	17
006	2.1	1.6	72	13
007	2.5	0.52	66	18
010	2.2	0.36	58	14
018	2.1	1.1	65	12
212	2.3	1.2	56	17
	Mean=2.3±0.2	Mean=0.85±0.53		

CONCLUSIONS

The assessment of organ burdens from evaluation of urine excretion measurements is roughly consistent with estimates based on postmortem tissue analysis. Individual estimates were within a factor of 3.2 for skeleton and a factor of 5 for liver with an overall average of about a factor of 2 for both skeleton and liver.

REFERENCES

1. International Commission on Radiation Protection (ICRP). 1986. The Metabolism of Plutonium and Related Elements. ICRP Publication 48, Pergamon Press, New York.
2. Jones, S. R. 1985. "Derivation and Validation of a Urinary Excretion Function for Plutonium Applicable Over Tens of Years Post Intake." Radiation Protection Dosimetry, Vol. 11, No. 1, pp. 19-27. Nuclear Technology Publishing, Ashford, England.
3. Healy, J. W. 1957. "Estimation of Plutonium Lung Burden by Urine Analysis." American Industrial Hygiene Association Quarterly 18(3):261-266.
4. Boyd, H. A., B. C. Eutsler, and J. F. McInroy. 1981. "Determination of Americium and Plutonium in Autopsy Tissue: Methods and Problems." Actinides in Man and Animals, ed. M. E. Wrenn, pp. 269-272. Salt Lake City Press, Salt Lake City.
5. International Commission on Radiation Protection (ICRP). 1974. Report of Task Group on Reference Man. ICRP Publication 23, Pergamon Press, New York.
6. Kathren, R. L., K. R. Heid, and M. J. Swint. 1987. "Comparison of Estimates of System Plutonium from Urinary Excretion with Estimates from Postmortem Tissue Analysis." Health Physics. 53:476-479.