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of plutonium. By this time, a method of estimating body burden from urinary analyses had been worked out and nine Laboratory personnel were believed to have burdens approaching 1 μg. Because of apparent differences in the bone deposition patterns of radium and plutonium in rats, the decision was made to introduce a safety factor of approximately 5 and lower the maximum permissible body burden to 1 μg. This value remained in effect until the Tripartite Permissible Dose Conference at Chalk River, Canada, on September 29–30, 1949. At this meeting, Dr. Austin Brues presented results of comparative chronic toxicity experiments in rats and mice which indicated Pu^{239} was 15 times as damaging as Ra^{226} when the two were injected in equivalent microcurie amounts. The Conference recommended, therefore, that the maximum permissible body burden be lowered to 0.1 μg, as follows:

$$(MPC)_{Pu} = 0.1 \times \frac{24{,}000}{1600} \times \frac{1}{15} = 0.1\ \mu g.$$

The stringent maximum permissible air concentrations imposed by such a conservative body burden would produce serious delays in the Laboratory's plutonium operations; hence the Chalk River Conference recommendations were re-examined by the AEC's Division of Biology and Medicine prior to official adoption. Re-examination consisted of a wave of intense correspondence (principal participants—Drs. SHIELDS WARREN, AUSTIN BRUES, R. D. EVANS, K. Z. MORGAN and W. H. LANGHAM) that culminated in a meeting in the office of the Division of Biology and Medicine on January 24, 1950. At that time, Dr. BRUES pointed out that two factors mitigated the assumption that 0.1 μc of fixed Pu^{239} was equivalent to 0.1 μc of fixed Ra^{226} for the derivation of a human tolerance level. First, the Pu:Ra toxicity ratio of 15:1 was based on injected amounts in small animals and, since plutonium was ~75 per cent retained in rodents and radium about 25 per cent, the ratio on the basis of retained dose could be lowered by a factor of 3. Second, since radon was approximately 50 per cent retained in man and only 15–20 per cent retained in rodents, the toxicity ratio on the basis of relative energy deposited could be lowered by at least another factor of 2. Strictly on biological grounds, therefore, a fixed plutonium body burden for man could be derived from the animal experiments, as follows:

$$(MPC)_{Pu} = 0.1 \times \frac{24{,}000}{1600} \times \frac{1}{15} \times \frac{3}{1} \times \frac{2}{1} = 0.6\ \mu g\ (0.04\ \mu c).$$

As a result of this meeting, Dr. SHIELDS WARREN of the Division of Biology and Medicine authorized 0.5 μg (0.033 μc) of Pu^{239} as the AEC's official operating maximum permissible body burden. In 1951, the International Committee on Radiological Protection at a meeting in London recommended 0.04 μc. This value was endorsed at the Tripartite Conference on Permissible Dose at Harriman, New York, in March of 1953, and in the fall of 1953 both the National Committee on Radiation Protection and Measurements[1] and the International Commission on Radiological Protection[2] recommended in their official publications a Pu^{239} maximum permissible body burden of 0.04 μc. Both organizations have held to the 0.04 μc value in their most recent recommendations.[3,4]

Although derivation of the presently accepted value differs somewhat from that proposed by BRUES in 1950, it is still based on a comparison with 0.1 μc of Ra^{226}, assuming the skeleton as the critical organ. Two difficult questions still prevent unanimous acceptance of the recommended value. The first question involves adequacy of the maximum permissible body burden of Ra^{226} itself,[5,6] and the second involves the choice of the skeleton as the critical organ for Pu^{239} under conditions of chronic inhalation exposure.[7–9] In the latter case, plutonium concentrations in the pulmonary lymph nodes, lung tissue, and liver appear to be considerably higher than in bone.[10] The question, therefore, becomes one of relative sensitivity of these tissues to damage under conditions of chronic α-radiation exposure.

Experimentation in support of the estimation of body burden

During the early days of the Manhattan Project, the excretion and retention data on which to base a method of diagnosing Pu^{239} body burden were largely from experiments on rats. It seemed imperative, therefore, to determine

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COLLECTION CHR/Plutonium DOCS
BOX No. 2 of 2
FOLDER REPRINTS Pu
0001387

retention and excretion of plutonium in a limited number of terminal human patients. Sixteen cases were studied, the first beginning in April of 1945.[11] Life expectancy of the individual and relative freedom from kidney disease were the principal criteria for case selection. As a rule, individuals were chosen who were past 45 yr of age and who were suffering from well-established disorders that made survival for 10 more yr highly improbable. Adherence to this rule avoided the possibility of development of late radiation effects from plutonium.

Plutonium^{239} was administered via intravenous injection, usually as the Pu(IV)-citrate. Doses ranged from 4.6 to 6.5 μg. Although no acute toxic effects were expected from such small doses, clinical laboratory observations were carried out, especially with regard to hematological changes and liver and kidney functions. No acute subjective or objective clinical effects were observed. Urine and fecal samples were collected daily for plutonium analyses. The results of these studies have been reported previously.[11–14] The data showed that plutonium excretion in man was expressed most conveniently by power functions. Over a period of 138 days after injection, urinary excretion (Y_u) was represented by the expression,

$$Y_u = 0.23t^{-0.77},$$

in which Y_u was the per cent of the injected dose excreted per day, and t (>1) was the number of days between injection and sample collection. The empirical fit to the fecal excretion data (Y_f) was:

$$Y_f = 0.63t^{-1.09},$$

and to urinary plus fecal excretion (Y_{u+f}) was:

$$Y_{u+f} = 0.79t^{-0.94}.$$

It is not possible to state specifically the limits of accuracy of these expressions for the representation of plutonium excretion by normal healthy men. First, the cases were not normal; second, many of them died within 30 days (only three lived the full 138-day observation period), which seriously limited the period of observation; and third, methods of plutonium analysis in 1944–1946 were crude and inaccurate compared to present methods. The primary virtue of the expressions is that they are based on the only human data available.

Autopsy material for plutonium tissue distribution studies was obtained from seven of the 16 cases. Although tissue sampling was extremely poor, it was possible to make a crude estimate of plutonium in the major organs and tissues. Table 1 shows a comparison of these data with more extensive and accurate observations on beagles.[15] The agreement between plutonium distribution in the beagle and in man was quite good and perhaps fortuitous, considering the inadequacy of human samples. The primary value of the human data lies in the fact that it adds confidence to the use of animal data as a basis for deriving a maximum permissible plutonium body burden for man.

Table 1. Distribution of intravenously administered plutonium in major tissues of the beagle and man

Tissue	Dose per tissue* (%) Beagle	Man
Skeleton	60	66
Liver	21	23
Spleen	0.2	0.4
Kidneys	0.2	0.4

* Approximately 5 months after injection.

PLUTONIUM EXPOSURES DURING THE MANHATTAN PROJECT

Number and nature of early exposures

Before the AEC assumed responsibility from the Manhattan District (January 1, 1947), 27 Los Alamos Scientific Laboratory personnel had accumulated plutonium body burdens of from 0.1 to 1.3 μg (0.007–0.09 μc). Twelve of the 27 cases had body burdens of 0.5 μg or greater. Nine of the 12 cases occurred in the same operation—recovery of plutonium from waste materials. This operation consisted of dissolving the waste materials and plutonium in strong acids, pH adjustment of the solution, precipitation of the plutonium as the peroxide, resolution of the peroxide, and final precipitation of the plutonium as the oxalate. The entire operation was conducive to the formation of a fine aerosol of plutonium salts, perhaps largely $Pu(NO_3)_4$.

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