Health Physics Pergamon Press 1962. Vol 8, pp. 753–760. Printed in Northern Ireland

(4)

729064

THE LOS ALAMOS SCIENTIFIC LABORATORY'S EXPERIENCE WITH PLUTONIUM IN MAN*

W. H. LANGHAM, J. N. P. LAWRENCE, JEAN McCLELLAND and L. H. HEMPELMANN†

Los Alamos Scientific Laboratory University of California Los Alamos, New Mexico

(*Presented by* J. N. P. Lawrence)

Abstract—The present paper presents an historical account of the Los Alamos Scientific Laboratory's industrial medical experience with exposure of personnel to Pu^{239}. Observations cover the period from the beginning of the Manhattan Project through 1960. In the early days, exposures were of an acute or semiacute nature. Improved industrial hygiene and engineering methods have changed the problem to one of chronic low-level exposure, largely via inhalation. Consideration of the Laboratory's experience during the past 17 years suggests that the present problem areas are: (1) the diagnosis of body burden under chronic exposure conditions and with little or no specific index of exposure other than a persistent low-level urinary excretion rate, and (2) the choice of the critical organ when exposure is largely via chronic low-level inhalation.

INTRODUCTION

A comprehensive discussion of the Los Alamos scientific Laboratory's industrial medical experience with Pu^{239} would be a history of the nuclear weapons program. During the latter part of 1943 and the first part of 1944, the Laboratory's plutonium operations consisted of research activities involving milligram amounts of material. During the latter part of 1944, gram amounts were processed in research activities directed principally toward production of pure plutonium metal and studies of its physical and nuclear properties. By mid-1945, kilogram amounts of plutonium were processed from which nuclear components of the Alamagordo and Nagasaki weapons were fabricated. Plutonium processing has remained at the kilogram level, although major operations no longer consist of production and fabrication of weapon components. The specific purpose of this report, however, is not historical documentation of the Laboratory's activities in the nuclear weapons field, but rather emphasis, in a chronologic manner, of some experiences and observations that may be helpful in present and future industrial medical control of this important fissionable material.

* This report is based on work performed under the auspices of the U.S. Atomic Energy Commission.

† Present address: Strong Memorial Hospital, University of Rochester, Rochester, New York.

THE PLUTONIUM MAXIMUM PERMISSIBLE BODY BURDEN

Historical development

Although no satisfactory method of diagnosing personnel exposure to plutonium was in operation during 1943 and the first nine months of 1944, a maximum body burden of 4–5 μg was assumed to be acceptable as an operational guide. This value was derived on the basis of bone as the critical organ and direct comparison of energy deposition from the 0.1 μg maximum permissible body burden of fixed radium, assuming a 50 per cent exhalation of radon:

$$(MPC)_{Pu} = 0.1 \times \frac{24{,}500}{1600}\left[\frac{4.8}{5.15} + \frac{0.5(5.5)}{5.15} + \frac{0.5(6.0)}{5.15} + \frac{0.5(7.7)}{5.15}\right] = 4.3\ \mu g.$$

In the spring of 1945, a representative (Colonel Hymer Friedell) of the Medical Director's Office of the Manhattan District convened a meeting at Los Alamos to discuss the Laboratory's maximum permissible body burden

8008897

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 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

	Dose per tissue* (%)	
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 $Pu(NO_3)_4$.

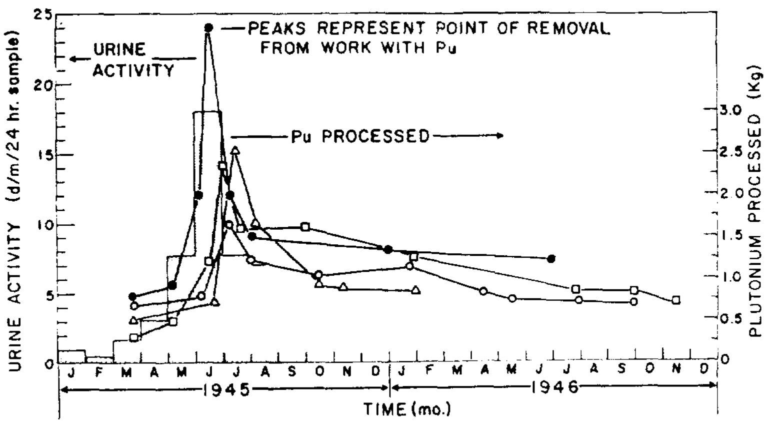

FIG. 1. Urinary excretion curves indicating relatively acute exposure of four plutonium recovery process operators.

Although respiratory protection was provided, the route of exposure undoubtedly was via inhalation, as indicated by a strong correlation between high urine counts and frequency of contamination of the nasal vestibule.[16] Figure 1 shows urine assay curves for four of the plutonium recovery process operators and the monthly amount of material put through the recovery process. The shape of the assay curves and their apparent relation to the amounts of plutonium processed show the exposures were of a relatively acute nature. Although it was not possible to estimate the amount of plutonium in the respiratory lymph nodes and lungs of these cases, the insoluble nature of Pu(IV) at tissue pH would lead to the supposition that the concentrations in these tissues might have been considerably greater than in the skeleton.

Follow-up examinations of Manhattan Project exposure cases

Twenty-four of the 27 Laboratory employees who had accumulated measurable body burdens of plutonium prior to January of 1947 were carefully examined in 1952, 1955 and again in 1960. Examinations consisted of medical history, complete physical check-up, laboratory studies, and roentgenograms. Laboratory studies included white blood cell, red blood cell, and differential blood counts, and urinalyses. At the recommendation of Dr. William Christensen (who made radiographic studies of the beagles at the University of Utah plutonium toxicity project), the roentgenograms taken were of the chest, pelvis, single projection film of right femur, right distal femur showing metaphyseal detail, and detailed dental films showing interalveolar crests.*

One member of the group died in 1959 from coronary thrombosis. His body burden of plutonium was estimated as 0.2 μg. All other subjects were in good health and actively employed in 1960. At no time have any of the subjects showed symptoms or signs of radiation injury. Laboratory examinations and roentgenograms in 1960 were within the normal limits, and their medical histories revealed no unusual incidence of medical complaints. After 15 yr there were no subjective or objective indications that they had small body burdens of plutonium.

In 1958 (12–13 years after their original exposures), 24-hr urine samples were collected from all follow-up cases and analyzed for plutonium by the current nuclear track-counting technique. Re-estimation of their body burdens showed that three of the group originally thought to have burdens of 0.1–0.3 μg were negative. The majority of the others showed burdens of from 1 to 3 times their original estimates. This is not surprising, considering the possible error in extrapolation of the urinary excretion curve to 12–13 years. A 10 per cent error in the exponent of t would produce an error of at least a

* Credit is due Dr. CHRISTENSEN also for interpretation of the roentgenograms.

factor of two in the body burden, when the excretion curve is extrapolated to 10 years. Recalculation of the urinary excretion function, using a weighted least squares analysis programmed for the IBM 7090 computer, suggests the possibility of at least a 10 per cent error in the exponent of *t*.

CHRONIC INDUSTRIAL EXPOSURES

Diagnosis of body burden

Because of vastly improved industrial hygiene and engineering measures, relatively acute exposures like those experienced during the Manhattan Project have not been encountered. A very important current problem, therefore, is diagnosis of body burden under conditions of very low-level chronic exposure. In many instances, there may be little or no specific indication (high air counts, contamination accidents, etc.) of any positive exposure, but rather a gradual increase in urine assays with increasing length of employment. In this case, there is no known time of exposure on which to base an estimation of body burden from the urinary excretion equation given previously. LAWRENCE[17] and SNYDER[18] have developed computer programs, based on the original urinary excretion equation, that attempt to estimate chronically accumulated body burden from a series of urine assay values. Applicability of these methods to the estimation of body burden under presently prevailing conditions of exposure has not been established unequivocally.

LAWRENCE has applied his computer method to all urinary data accumulated at the Los Alamos Scientific Laboratory, including the data collected from the original 27 exposure cases that occurred during the Manhattan Project. His estimates[17] of the body burdens of the latter group average approximately 50 per cent higher than the original estimates made in 1945–1946.[16] This agreement is surprisingly good. However, the accuracy of either of the estimates is not known, and both are subject to the inherent uncertainties in the basic urinary excretion function and in the analytical errors of the urinary assay procedure.

Summary of plutonium exposures from 1945–1960

With full appreciation of the uncertainties inherent in estimating plutonium body burden under conditions of chronic exposure, LAWRENCE[19] applied his computer method to the plutonium urinary excretion data collected on all Los Alamos employees from 1945 to 1960. Data were available on 4215 employees. Many had terminated; others had transferred to jobs not involving further potential exposure; and 1639 were on the active employment list as of December 31, 1960. No attempt is made here to look for correlations of body burden with length of employment, specific job assignment, air counts, operational procedures, frequency of contamination accidents, etc. A search for such correlations could be the subject of a future paper. Table 2 merely shows a breakdown of the number of employees as a function of the fraction of the maximum permissible body burden derived from the urine assay data by the computer method.

Table 2. *Summary of Los Alamos plutonium exposures* (1945–1960) *grouped according to the fraction of the maximum permissible body burden*

Fraction of maximum permissible body burden	No. of employees
0.0–0.1	3884
0.1–0.2	164
0.2–0.3	61
0.3–0.4	25
0.4–0.5	13
0.5–0.6	13
0.6–0.7	13
0.7–0.8	8
0.8–0.9	3
0.9–1.0	8
1.0–2.0	14
2.0–3.0	5
3.0–4.0	4
Total	4215

Assuming 0.1 of the maximum permissible body burden as the lower limit of positive detection, the data suggest that about 8 per cent of the employees examined during 15 years of operation showed positive plutonium exposure. Sixty-eight (1.6 per cent) had 0.5 of the maximum permissible body burden or greater, and 23 (0.5 per cent) had exposures equal to or greater than the maximum permissible level.

TREATMENT OF PLUTONIUM EXPOSURE CASES

While at Los Alamos, FOREMAN[20] reported treatment of two cases of positive plutonium exposure with the sodium calcium salt of ethylenediaminetetraacetic acid ($CaNa_2EDTA$). In the first case, twice daily treatment with 2.5 g of $CaNa_2EDTA$, begun 5 days after exposure and continued for 15 days, resulted in approximately a 24 per cent decrease in the subject's body burden. Treatment of the second case was much less effective because of complications created by the presence of a considerable amount of plutonium in a contaminated wound and very little in the systemic circulation. Treatment was effective largely in indicating presence of contamination in the wound site, which was surgically removed.

CONTAMINATED WOUNDS

LISCO[21] observed that as little as 1 μg of plutonium injected subcutaneously into mice resulted in formation of a malignant fibrosarcoma in the region of injection. Management of potentially contaminated wounds has been a troublesome problem which, until the recent development of a low energy X-ray crystal spectrometer for wound monitoring,[22] was handled on an intuitive basis. HEMPELMANN recognized the problem in 1944 and introduced the practice of washing and excising wounds inflicted in a potentially contaminated environment or with a potentially contaminated object. Seventy-eight wounds were excised during 1944–1945 and the excised tissues analyzed for plutonium (Table 3). Only 3 of the 78 tissues excised by HEMPLEMANN contained significant amounts of plutonium, and the practice was discontinued because no method of determining the extent of contamination was available and the practice discouraged employees from reporting minor injuries. Unsuccessful attempts were made at that time to develop a wound-monitoring device. The nature of the wound and the chemical form of the plutonium strongly influence local deposition in the wound site and rate of absorption into the systemic circulation.

Table 3. Plutonium analyses of tissues excised from potentially contaminated wounds at Los Alamos

No. of excisions	Average plutonium content (dis/min)
72	12*
3	94
1	1950
1	2600
1	3280
1† (First excision)	850,000
(Second excision)	30,000

* Lower limit of detection.

† Reported by FOREMAN.[20]

TRUJILLO and LANGHAM[23] studied entrapment and absorption of PuO_2 from contaminated abrasions in the skin of rabbits. Deep skin lesions were produced with sandpaper, after which the abraded area was contaminated with fine particles of PuO_2. Some lesions were washed almost immediately and excised for analysis. Others were excised at various intervals and the excised tissues analyzed and studied autoradiographically. About 50 per cent of the PuO_2 was removed by ordinary surgical cleaning of the wound. The autoradiograph shown in Fig. 2 indicates that the remainder of the plutonium was incorporated into the eschar and lost when the wound healed and the eschar detached. Analyses of the carcasses of several animals failed to show absorption of detectable amounts of plutonium into the systemic circulation, even though several hundred μg had been applied to the wound.

Deep cuts and puncture wounds, however, pose a more serious problem. LUSHBAUGH and LANGHAM[24] recently reported a microscopic and autoradiographic study of a dermal lesion from implanted plutonium. Approximately 4 years after a contaminated puncture wound, a machinist noticed the appearance of a small nodule in the general location of the original wound. The nodule was removed after a γ-ray spectrometer measurement indicated the presence of about 0.1 μg of plutonium. Figure 3 shows an autoradiograph and a photomicrograph of a section through the nodule. The autoradiograph showed precise confinement of α-tracks to the area where the photomicrograph revealed epithelial changes typical of radiation damage. The pathologist's conclusion was that the lesion, although minute in size, showed severe changes quite similar to those observed in known precancerous conditions.

FIG. 2. Autoradiograph of a perpendicular section through a PuO_2-contaminated abrasion-type wound in the skin of a rabbit.

FIG. 3. Autoradiograph (top) and photomicrograph (bottom) of a perpendicular section through a dermal lesion appearing 4 years after a plutonium-contaminated puncture wound in the palmar surface.[24]

Table 4. Plutonium analyses of autopsy samples

Case no.	Body burden (μc)*	Tissue and plutonium concentration (dis/min per g) Respiratory lymph nodes	Lungs	Liver	Vertebrae
A-318	0.02	125	4.8	9.9	2.1
A-344	—	0.12	0.042	—	—
A-404	0.000	0.01	0.006	0.002	—
A-426	0.000	0.002	0.11	0.02	—
A-428	0.02	46	7.4	2.2	—
A-438	0.000	0.003	0.03	0.006	—
A-451	0.008	25.4	6.3	2.7	0.5
A-459	0.000	0.44	0.06	0.02	0.001
A-387	0.003	0.14	0.03	0.02	—

* Estimated from urinary excretion.

TISSUE DEPOSITION FROM CHRONIC OCCUPATIONAL EXPOSURE

In December 1958, a plutonium process operator, who had been exposed to plutonium largely via chronic low-level inhalation for about 6 years, received a lethal dose of radiation in a criticality accident. Analyses of samples of his tissues and organs showed the highest plutonium concentration in pulmonary lymph nodes, followed in decreasing order by liver, lungs and bone.(10) Concentration in lymph nodes was about 60 times that in the vertebrae. His body burden, estimated from urinary assays, was approximately 0.02 μc (50 per cent of the maximum permissible body burden). As a result of this observation, attempts have been made to obtain occasional autopsy samples of lymph nodes, lungs, liver, kidney and vertebrae from Los Alamos employees dying from natural causes. Results of plutonium analyses of all samples to date are summarized in Table 4. Obviously, the data are too few to support any quantitative conclusions. It is of qualitative interest, however, that the order of plutonium concentration was usually respiratory lymph nodes > lungs > liver > bone. Undoubtedly, the exposure, if any, received by these people was via chronic low-level inhalation. Analyses of both lymph nodes and bone were available in only two cases for which urinary assays definitely indicated a positive exposure. In both cases, the plutonium concentration in the lymph nodes was of the order of 50 times that in bone.

Acknowledgments—It is not possible to acknowledge all who have contributed to the industrial medical control of plutonium at Los Alamos during the past 17 years. The authors, however, are especially grateful to Dean D. Meyer and William D. Moss, who are responsible for collection of most of the data referred to in this report.

REFERENCES

1. Recommendations of the National Committee on Radiation Protection and Measurements, *Maximum Permissible Amounts of Radioisotopes in the Human Body and Maximum Permissible Concentrations in Air and Water*, National Bureau of Standards Handbook 52, U.S. Government Printing Office, Washington, D.C. (1953).
2. Recommendations of the International Commission on Radiological Protection, *Brit. J. Radiol.* Suppl. 6 (1955).
3. Recommendations of the National Committee on Radiation Protection and Measurements, *Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water for Occupational Exposure*, National Bureau of Standards Handbook 69, U.S. Government Printing Office, Washington, D.C. (1959).
4. Report of ICRP Committee II on Permissible Dose for Internal Radiation (1959), *Health Phys.* **3**, 1 (1960).
5. J. C. Aub, R. D. Evans, L. H. Hempelmann and H. S. Martland, *Medicine* **31**, 221 (1952).
6. W. B. Looney, *Science* **127**, 630 (1958).
7. L. A. Temple, D. H. Willard, V. H. Smith and R. W. Wagner, Hanford Atomic Products Operation, HW-47500, 165 (1957); and HW-53500, 154 (1958).

8. W. J. Bair, Hanford Atomic Products Operation, HW-56636 (1958).
9. J. N. Stannard, *Progress in Nuclear Energy*, Series VII, p. 90. Pergamon Press, New York (1959).
10. H. Foreman, W. Moss and W. Langham, *Health Phys.* **2,** 326 (1960).
11. W. H. Langham, S. H. Bassett, P. S. Harris and R. E. Carter, Los Alamos Scientific Laboratory Report, LA-1151 (1960).
12. W. H. Langham, *Brit. J. Radiol. Suppl.* **7,** 95 (1957).
13. W. H. Langham, *Amer. Ind. Hyg. Assoc. Quart.* **17,** 305 (1956).
14. W. H. Langham, *Health Phys.* **2,** 172 (1959).
15. B. J. Stover, D. R. Atherton and N. Keller, *Rad. Res.* **10,** 130 (1959).
16. L. H. Hemplemann and W. H. Langham, Los Alamos Scientific Laboratory and Univ. of Rochester School of Medicine, AECU-2633 (1953).
17. J. N. P. Lawrence, *Health Phys.* **8,** 61 (1962).
18. W. S. Snyder, *Health Phys.* **8,** 767 (1962).
19. J. N. P. Lawrence, unpublished data, Los Alamos Scientific Laboratory (1962).
20. H. Foreman, *Metal-Binding in Medicine* (Edited by J. M. Seven and L. A. Johnson) p. 160. J. B. Lippincott, Philadelphia (1960).
21. H. Lisco, M. P. Finkel and A. M. Brues, *Radiology* **49,** 361 (1957).
22. E. A. Putzier, J. R. Mann and V. P. Johnson, *Amer. Ind. Hyg. Assoc. Quart.* **19,** 384 (1958).
23. T. T. Trujillo and J. Langham, unpublished data, Los Alamos Scientific Laboratory (1960).
24. C. C. Lushbaugh and J. M. Langham, *A.M.A. Arch. Dermatol.* in press (1962).