ANL-6104

702288

Argonne National Laboratory

RADIOLOGICAL PHYSICS DIVISION

SEMIANNUAL REPORT

July through December, 1959

REPOSITORY Argonne Lab

COLLECTION

BOX No

FOLDER

PARTIAL DOCUMENT

0016930

TABLE OF CONTENTS

Page

An emission spectrum from radiation-damaged xylene.
I. B. Berlman 3

Nonradioactive energy-transfer measurements in an organic scintillation solution.
I. B. Berlman 5

Measurement of the amount of light emerging from a right cylinder cell containing a scintillating solution on varying the type of reflecting surface.
I. B. Berlman 6

Energy resolution of the "twin" scintillation fast neutron spectrometer.
R. Grismore, B. G. Oltman, and L. D. Marinelli 9

Drift velocity of electrons in nitrogen, helium, neon, argon, krypton, and xenon.
J. C. Bowe 11

Transport collision cross sections from electron drift-velocity data.
J. C. Bowe 12

Positive ion emission: Hydrogen effects.
H. A. Schultz 13

Late observations of the distribution of radium in the human skeleton.
R. E. Rowland 16

The radium distribution in the tooth of a dial painter.
R. E. Rowland 30

Retention and plasma clearance of the alkaline earth elements.

I. Introduction
R. E. Rowland 34

II. The retention and plasma clearance of barium in the beagle.
R. E. Rowland and C. H. Williams 34

III. Retention and plasma clearance of the alkaline earth elements in dogs.
R. E. Rowland 37

IV. The retention and plasma clearance of the alkaline earths by human beings.
R. E. Rowland 40

Autoradiographic dosimetry of mouse bones containing Ca^{45}, Sr^{90}, and Ra^{226}.
J. H. Marshall and M. P. Finkel 48

0016931

TABLE OF CONTENTS

Page

Some individual alpha-activity counts in mixtures.
J. Sadauskis 66

Gamma-ray studies on radioactive fallout.
P. F. Gustafson, S. S. Brar, and M. A. Kerrigan 69

The cesium-potassium trend in humans as a function of time.
C. E. Miller 78

Measurement of natural uranium in the lungs of a human.
C. E. Miller 80

Status of the radium dial project.
C. E. Miller 82

Retention of radium in humans from 21 to 29 years after intravenous administration.
C. E. Miller 85

Status report of study of long-term effects of radium in humans.
A. J. Finkel, C. E. Miller, and R. J. Hasterlik. 87

Radioactivity of commercial photomultiplier tubes.
H. A. May 89

Activity induced in meat by high-energy electron bombardment.
H. A. May 96

The Argonne meteorological model towing tank.
Paul Frenzen. 100

Errors in wind measurements associated with tower-mounted anemometers.
Harry Moses and H. G. Daubek 109

Atmospheric boundary layer simulation techniques for smoke diffusion experiments.
R. F. Weiss. 116

Publications 125

Papers to be published 126

0016932

LATE OBSERVATIONS OF THE DISTRIBUTION OF RADIUM IN THE HUMAN SKELETON*

R. E. Rowland

The deposition of the alkaline earth elements in bone is a subject which has changed from one of purely academic interest to one of widespread concern today. This concern is the result of the presence of one particular radioisotope in the biosphere, strontium-90. What effects will the radiations from this isotope have upon us after it is deposited within our bones?

In order to understand clearly the over-all problem of strontium-90 toxicity, there are many areas that need investigation. For example, we may start with the metabolism of the alkaline earth elements in bone: how well do they substitute, at trace concentrations, for calcium in the mineral of bone? Once a radioactive isotope is deposited within bone, it continually irradiates the surrounding tissues. What dose rates actually exist within bone, and what tissues actually receive this irradiation? What is the effect of this dose on these tissues? After an isotope is built into bone, how long does it remain? What natural processes work to remove it and at what rates? If these questions can be answered, do they lead us to a method of counteracting the deleterious effects of irradiation, or to a method of removing the radioactive isotope?

In an attempt to answer some of these questions, we have turned our attention to those human beings who have carried another radioactive alkaline earth, radium, in their bones for many years. Here, we feel, is information of extreme value in the assessment of the hazards of Sr^{90}, for although radium and strontium are not chemically identical, they do behave with remarkable similarity in bone. Furthermore, the information available describes the uptake and distribution of this element in human bone, and, after all, it is in the human being that our primary interest lies.

Most of us are familiar with the fact that many individuals acquired a burden of radium through their contact with the radium watch dial industry. However, in addition to these now famous dial painters, there were probably many times as many people who acquired a burden of this radioactive element through its use as a therapeutic agent in the 1920's. Through these two sources a very large number of people have been exposed to a bone-seeking radioisotope and have by this date carried it for 30 odd years. What has happened to them?

---

*Presented at Univ. Minn. Symposium on "Radioisotopes in the Biosphere," Oct. 19-23, 1959, and to be published in the Proceedings of the Symposium.

0016933

I have had the opportunity of examining bone samples from 19 individuals who have carried this element from a minimum of 10 years to a maximum of 40 years. Their body burdens ranged from a high of 20 μc down to about 1 μc of Ra^{226}. (For reference, the industrial maximum permissible burden is 0.1 μc.). Some of these individuals received relatively pure Ra^{226}, others received both Ra^{226} and Ra^{228}. The latter, mesothorium 1, is thought to be considerably more toxic than Ra^{226}.

These individuals, for the most part, received their radium as adults, although several of the women who painted watch dials started at age 15. The typical exposure period ranged from a few months to a few years; the routes of entry were both intravenous (for some medical cases), and oral (for dial painters and those who drank radium water).

When the bones of the dial painters were first examined by the autoradiographic technique, a spotty distribution of the activity was apparent. The term "hot spot" was coined to describe these radium concentrations. We now know that these concentrations exist in regions where new bone mineral was forming at the time the radium was acquired, and that in this mineral the original concentration of radium, expressed as the ratio of radium to calcium, was essentially the same as the radium to calcium ratio that existed in the blood plasma at the time the mineral was formed.(1)

When we examine the bone sections in greater detail a second type of distribution of radium becomes evident, the so-called diffuse distribution. By exposing an autoradiographic plate to a bone section for a considerably longer period of time than is needed to show the hot spots, this rather uniform distribution is made visible (Figs. 3 and 4).

Figure 3 is an autoradiograph produced by exposing a plate to a piece of cortical bone from the femur of a woman who died with a body burden of 2.7 μc Ra^{226}. This activity was obtained at age 20 through exposure as a radium dial painter for about one year. The autoradiograph shows the distribution of radium 33 years later, at age 53. The number of hot spots is unusually large.

Figure 4 is an autoradiograph of a piece of cortical bone from the tibia of a woman who died with a burden of 3.8 μc Ra^{226}. In this case the activity is reported to have been acquired during a two-month period at age 15 when the subject painted watch dials. Here we can see the diffuse distribution quite clearly, with a few superimposed hot spots. This bone sample obtained at death 32 years after the activity was acquired.

We believe that this diffuse distribution is the visible result of an exchange process which continually transfers calcium atoms from blood to bone and back again, and which is characterized by an unusually long time constant. In this process the alkaline earth elements can substitute

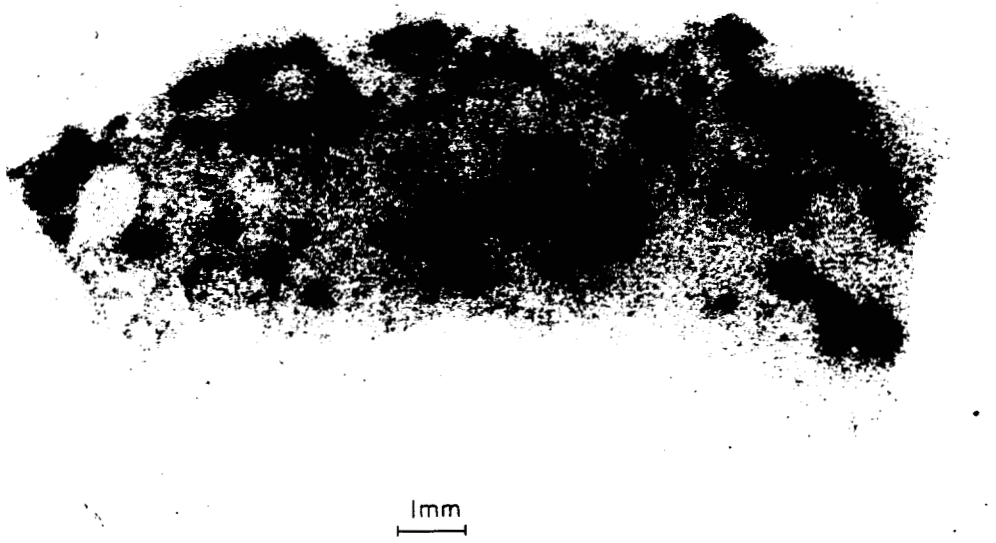

Fig. 3. An autoradiograph of a segment of cortical bone from the femur of case RB, exposed for 2 months on an Eastman Kodak No Screen autoradiographic plate. There are an unusual number of hot spots in this segment of bone.

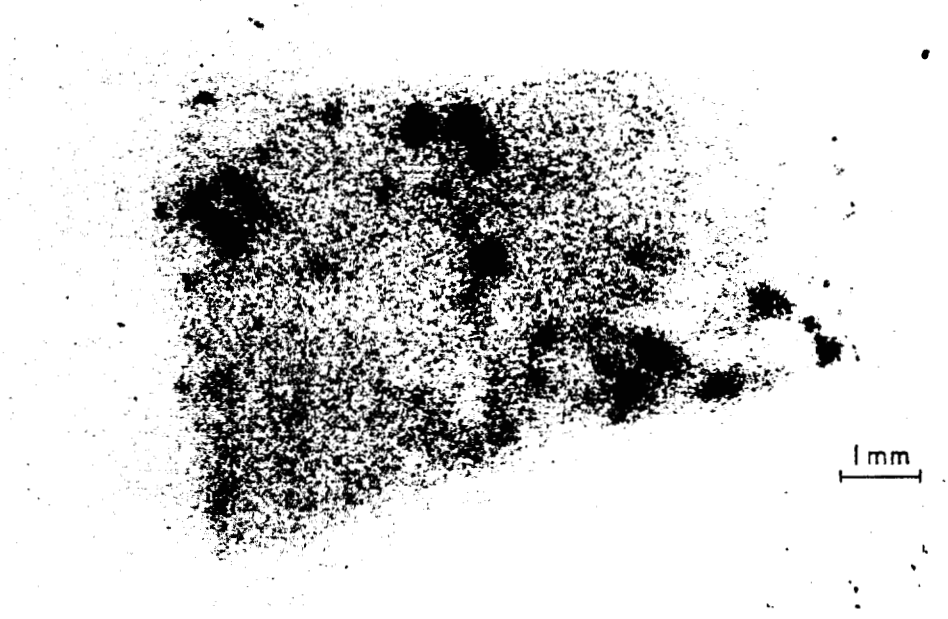

Fig. 4. An autoradiograph of a segment of cortical bone from the tibia of case 302, exposed one month on an Eastman Kodak No Screen[2] autoradiographic plate. Several hot spots are seen superimposed on the diffuse distribution.

0016935

remarkably well for calcium, at least at very low concentrations. Thus, the diffuse distribution we see today is the result of this exchange which labeled the bone mineral existing at the time these individuals were exposed to radium. This activity is not to be considered as permanently fixed within the bone mineral, however, for this same exchange process is slowly removing it from the bone.

The hot spots are not nearly as large in area as one would be led to believe from their appearance in these illustrations. When we employ a medium of considerably higher resolution, a thin emulsion which stays in contact with the bone section during development and fixation, such as illustrated in Figs. 5 and 6, we see that the hot spots in cortical bone are usually no larger than a single haversian system.

Figure 5 contains a microradiograph of a 100-micron thick bone section, and a stripping film autoradiograph of the area outlined in the microradiograph. The entire large haversian system in the center of the figure contains radium, but in order to show clearly the alpha tracks, we have greatly enlarged the autoradiograph. Note the scarcity of tracks over the adjacent bone and over the canal itself as compared to the number over the haversian system.

Figure 6 contains a similar microradiograph and autoradiograph pair; again the autoradiograph is shown at considerably higher magnification to make visible the individual alpha tracks. Both Figs. 5 and 6 illustrate hot spots found in the femur of a woman who, at age 32, received 41 weekly injections of 10 μc Ra^{226} each, and died 24 years later with a terminal burden of 3.6 μc. This type of repeated injection produced haversian systems completely labeled from outer cement line to the inner canal, for the blood contained this radioelement longer than the complete period (about three months) required for the formation of a human osteon.

An alpha-track autoradiograph, because of its property of resolving the short tracks of individual alpha particles, provides an excellent method, first suggested by Hoecker and Roofe,[2] of measuring the radium concentrations which exist in microscopic volumes of bone. A count of the number of alpha tracks per unit area in a suitable autoradiograph plate, exposed for a known time, can be employed to determine the concentration of radium per unit volume of bone if the range of the alpha particles in bone and the fraction of the gaseous daughter radon retained in bone are known.

The nineteen cases which have been analyzed thus far by this technique are listed in Table 3, and include data from 12 cases reported in a previous study.[3] They are arranged in three groups according to the length of time that the radium was carried before the bone sample was obtained.

0016936

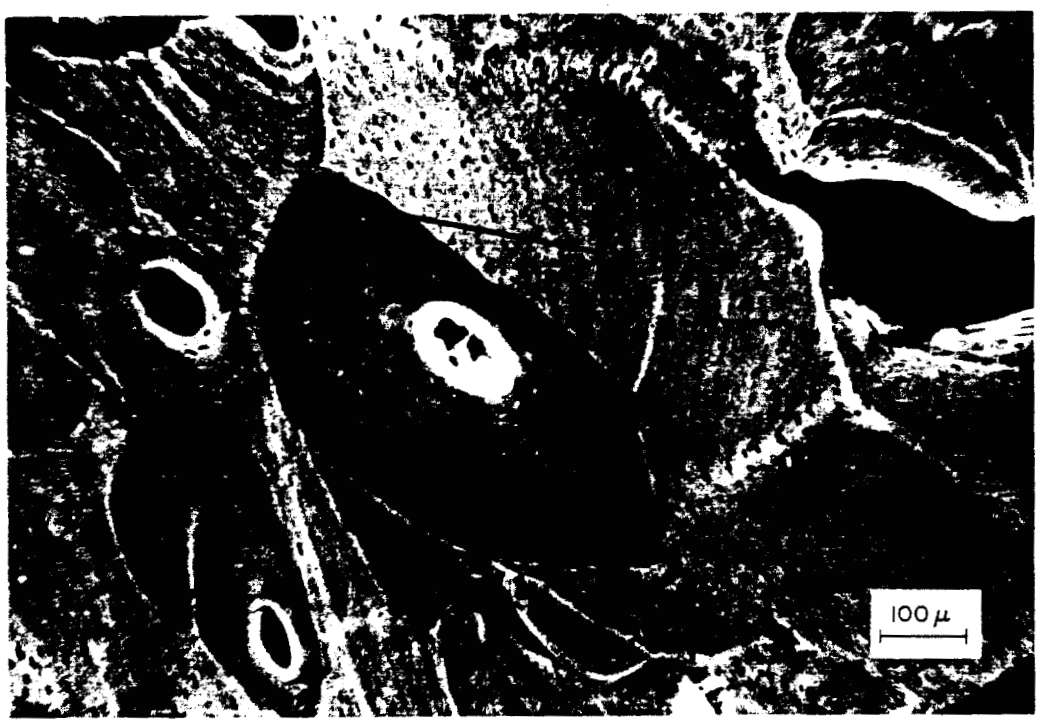

Fig. 5. A microradiograph and a stripping film autoradiograph of a 100-micron thick bone section from the femur of a woman who died with 3.6 μc Ra^{226} 24 years after receiving this isotope medically at age 32, (case R). The autoradiograph covers the outlined area of the microradiograph, and illustrates the intensity of the hot spot as compared to the adjacent diffuse radium distribution.

0016937

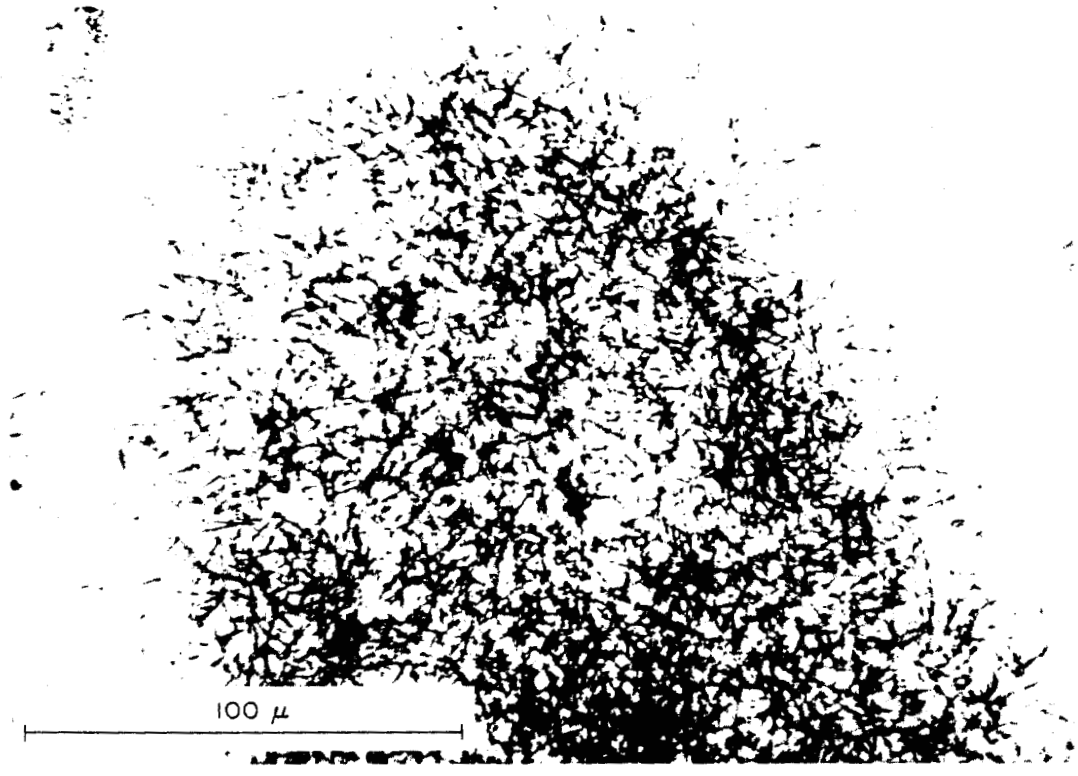

Fig. 6. A microradiograph and a stripping film autoradiograph of a 100-micron thick bone section from the femur of the same case illustrated in Fig. 5. The autoradiograph covers the outlined area of the microradiograph.

0016938

Table 3

Radium patients

Patient	Terminal radium burden, μc	Sex	Age radium acquired	Age at death	Years radium carried	Method of acquisition	Reference
EE	50.?	F	21-24	32	11	Dial painter	4
KS	19.?	F	15-20	31	16	Dial painter	4
IL	8.?	F	16-20	30	14	Dial painter	4
FR	7.	F	21-22	48	27	Dial painter	5
103	6.8	F	36	64	28	I. V. medically	6,7
R	3.6	F	32	56	24	I. V. medically	6,7
Q	1.2	M	33	59	26	I. V. medically	7
BM	1.2	M	21-23?	51	28-30?	I. V. medically	
112	1.2	F	25	48	23	Oral: medically	6,7
I	0.8	F	28	53	26	I. V. medically	7
118	10.5	F	48	84	36	Oral? medically	6,7
LS	8.	F	17	57	41	Dial painter	5
302	3.8	F	15	47	32	Dial painter	7
HG	3.	F	16-19	48	32	Dial painter	5
RB	2.7	F	20	53	33	Dial painter	
313	1.3	F	18-47	48	30	Dial painter	7
IJ	1.2	F	18-21		31	Dial painter	
03473	1.2	F	19-21		36	Dial painter	8
ML	~1.	F	16-17		39	Dial painter	

The three cases that carried radium between 10 and 20 years all acquired it from the painting of watch dials. Question marks are placed with the reported body burdens because these estimates were made many years ago (in the 1920's and 1930's). If these cases had contained Ra^{228}, as is highly probable, most of it would have decayed as a consequence of its 6.7-year half-life, leaving only the 1620-year Ra^{226} present today.

Of the second group, those surviving between 20 and 30 years, all but one happened to have acquired radium medically. Those acquiring this isotope medically generally received it at a more mature age than the dial painters, a good number of whom started painting in their late teens.

The third group contains those that carried radium 30 or more years; it consists almost entirely of former dial painters.

In Table 4 are listed the measured radium concentrations obtained by means of the alpha-track counts. For each case we have attempted to find the most intense hot spot and a representative average value of the over-all diffuse distribution. These values are expressed in terms of $\mu\mu c$ Ra^{226} per mg of bone. For comparative purposes there is included a calculated "uniform label," the body burden of radium divided by the bone

0016939

Table 4

Measured hot spot and diffuse concentrations

Patient	Terminal radium burden, μc	Maximum hot spot, μμc/mg	Average diffuse, μμc/mg	Calculated uniform label, μμc/mg	Ratio: hotspot to diffuse	Ratio: diffuse to uniform label
EE	50.?	19.	1.2		16	
KS	19.?		1.4			
IL	8.?	9.0	0.28		32	
FR	7.	30.	0.32	1.0	94	0.32
103	6.8	38.	0.30	1.2	127	0.25
R	3.6	16.	0.15	0.66	107	0.23
Q	1.2	12.	0.080	0.17	150	0.47
BM	1.2	6.0	0.043	0.17	140	0.25
112	1.2	1.4	0.075	0.20	19	0.38
I	0.8	13.	0.060	0.15	218	0.40
118	10.5	41.	0.50	2.0	82	0.25
LS	8.	16.	0.54	1.3	30	0.42
302	3.8	20.	0.54	0.67	37	0.81
HG	3.	9.3	0.39	0.50	24	0.78
RB	2.7	15.	0.38	0.49	40	0.78
313	1.3	2.8	0.15	0.30	19	0.50
IJ	1.2	4.7	0.046	0.20	102	0.23
03473	1.2	3.3	0.18	0.20	18	0.90
ML	~1.	6.0	0.10	0.17	60	0.59

mass. This represents the radium concentration per mass of bone that would exist if this radioelement were uniformly distributed throughout the skeleton. Bone mass was assumed to be 10% of body weight, while the body weight, if not known, was assumed to be 70 kg for males and 60 kg for females.

The data in this table can be employed in various ways to characterize the distribution of radium in human bone. The ratio of the specific activities of the hot spots to the adjacent diffuse distributions is a measure of the actual degree of nonuniformity existing in these cases. The average value of this ratio for 18 of these cases is 73. It will be noted that this ratio is usually higher in the bones of those who acquired their radium medically; this may reflect the fact that exposure to radium medically usually was for a shorter period than exposure via the dial industry.

When radium, or any alkaline earth radioisotope, is present in the blood for only a short time, the resulting hot spot to diffuse ratio is very high. With longer exposure to this radioisotope, the ratio will be lowered, for the diffuse deposition will continue to increase in magnitude, whereas the hot spots, formed at the specific activity of the blood, cannot increase in activity. This is illustrated by the Elgin State Hospital patients, R, Q,

0016940

and I, (Table 4) who received equal weekly injections of radium; R and Q received 41 and 45 injections, respectively, and we found hot spot to diffuse ratios of 107 and 150, while in case I, who received only 18 injections, we found a ratio of 218.

When we turn our attention to the diffuse distribution, a rather intriguing result is evident. The ratio of the measured diffuse concentration to the hypothetical uniform label ranges from a low of 0.23 to a high of 0.90, with an average value of 0.47. That is, for these 16 cases for which we can calculate a meaningful value for the uniform label, the average ratio of the measured diffuse to the uniform label is about one-half. Thus it is evident that this diffuse distribution is not an inconsequential fraction of the total body burden, but rather, a significant fraction of it.

The uniformity of this distribution is also quite remarkable. To be sure, variations do occur and are observed, and the value reported is the average value. However, the range of an average alpha particle in bone is 32 microns, so that, when we count the tracks over 1 mm^2 (the typical area surveyed for a single diffuse analysis), we are actually determining the bone radium content in a volume of 3×10^{-5} cm^3, containing 60 μg of bone. Yet, from this small volume we obtain values of the diffuse specific activity that vary by less than a factor of two from region to region.

Thus, it is convenient to think of the distribution of radium in the skeleton as occurring in two components. First of all, about half of the activity may be considered to be uniformly distributed throughout the skeleton. This, of course, is just the type of distribution of an isotope we would expect if it were continually present as a contaminant in our food throughout our lifetimes, such as may be the case with strontium-90. Our radium cases then have, superimposed on this uniform distribution, the intense hot spots. It would be most illuminating if we could determine which of these two types of distribution was the most likely to produce visible evidence of radiation-induced damage.

The data compiled in Table 4 can be employed in many ways. For example, if I may speculate for a moment, let us use these data to see if we can determine a bone turnover rate. Let us restrict the meaning of bone-turnover to new bone formation, such as the replacement of a resorption cavity within compact bone with a new osteon, or to the deposit of a layer of trabecular bone balanced by the removal of an equal volume elsewhere. That is, in the adult, let us consider a bone turnover occurring which does not increase the total volume of bone present.

Next, let us design a typical case in which the hot spot to diffuse ratio is 100, and the diffuse to uniform label is one half; further, let us specify that this is the situation 30 years after the exposure to radium, and that the exposure lasted for one year. Can we determine from these data the bone turnover rate?

0016941

From these figures it is apparent that, terminally, the hot spots must occupy 1% of the total bone volume (and contain 50% of the total body radium), whereas the diffuse label occupies the other 99% of the bone. If we make two assumptions, first, that bone resorption is not inhibited by radiation dose, and second, that bone turnover does not change with age, we can calculate a bone turnover rate. The calculations are shown in an appendix to this paper; the result shows that any turnover rate between 2 and 5 per cent would be expected to leave 1% of the bone labeled with hot spots after 30 years.* Note that a 5% rate would lead to a labeling of 5% of the skeleton after 1 year of exposure, while a 2% rate would yield a 2% label; however, after 30 years, only 22% of the original bone would be left if bone turnover were 5% per year, while at the 2% rate 55% of the original bone would still be left. These considerations tend to make the lower rate look more reasonable.** When we realize that radiation dose often does inhibit resorption, and that it seems reasonable to expect bone turnover to decrease with age in the normal human, then a yearly rate of 1% or 2% bone turnover might seem quite reasonable on the basis of these data.

We can go one step further in our analysis of the radium distribution data available from these human cases; we can compute the terminal dose rates that existed within the bone at the time of biopsy. For the calculation from bone radium concentrations to dose we follow the method of Spiers.[9] We have chosen to express the dose to a cell within bone, rather than to bone itself. For this cell we consider an osteocyte within a 10-micron spherical hole in bone, the lacuna. If, instead of this cell, we choose to consider the dose received by a 10-micron thick layer of endosteum, periosteum, or lining of the haversian canal, the value will be about one-half that listed for this lacuna in Table 5.

In this table we have listed the terminal dose rate to a lacuna existing in a hot spot and to one receiving radiation from the average diffuse radium distribution. The unit employed is rad per day, so that these data express the rate at which energy is delivered to the cell by the alpha particles. It can be seen from the table that rather sizable dose rates occur within the hot spots in some cases, and that even the least intense spots delivered over a rad per day to the osteocytes.

---

* We have been unable to report a meaningful value of the fraction of the bone volume occupied by hot spots because of the small fraction of the total skeleton that is available for study. Local variations in bone turnover may result in one sample having several times as many hot spots as an adjacent sample of bone.

** With a large volume of bone turned over, the diffuse distribution would be expected to appear quite spotty on an autoradiograph. The newly-formed mineral, while still containing radium, would contain the same radium to calcium ratio as existed in the blood plasma at the time of its formation. The blood plasma contains a lower radium to calcium ratio than the diffusely labeled bone a few months after the last exposure to radium, and this ratio continues to fall with time. Thus, the uniformity of the diffuse distribution seems to imply that the total bone turnover is not great.

Table 5

Terminal dose rates

Patient	Terminal body burden, μc	Terminal dose rate to a 10-μ lacuna		Minimum lifetime dose to a 10-μ lacuna	
		Hot spot, rads/day	Diffuse, rads/day	Hot spot, rads	Diffuse, rads
EE	50. ?	15.	0.95	60,000	3,800
KS	19. ?		1.1		6,400
IL	8. ?	7.2	0.22	37,000	1,100
FR	7.	24.	0.25	240,000	2,500
103	6.8	30.	0.24	310,000	2,500
R	3.6	13.	0.12	110,000	1,100
Q	1.2	9.5	0.064	90,000	610
BM	1.2	4.8	0.034	49,000	350
112	1.2	1.1	0.060	9,200	500
I	0.8	10.	0.048	95,000	460
118	10.5	33.	0.40	430,000	5,200
LS	8.	13.	0.43	190,000	6,400
302	3.8	16.	0.43	190,000	5,000
HG	3.	7.4	0.31	86,000	3,600
RB	2.7	12.	0.30	150,000	3,700
313	1.3	2.2	0.12	24,000	1,300
IJ	1.2	3.7	0.037	42,000	420
03473	1.2	2.6	0.14	34,000	1,800
ML	~1.	4.8	0.080	68,000	1,100

The terminal dose rates, multiplied by the number of days the activity was carried, have been listed here as the minimum lifetime doses. It is evident that tremendous doses have been received by these cells over a 20-, 30-, or 40-year period. Even in the diffuse distribution, these lifetime doses became quite respectable, and it must be recalled that almost every cell in bone receives at least this diffuse dose.

You will note the use of the term "minimum lifetime dose." Evidence is accumulating(3) that activity is slowly lost from both the diffuse distribution and the hot spots in bone by the same mechanism, which we term a "long-term" exchange process, that deposited the diffuse originally. Hence, earlier in the lifetimes of these individuals, greater radium concentrations may have existed in both the hot spots and the diffuse distributions, and hence, greater doses than we measure terminally may have been delivered. In addition, if any of these cases contained significant fractions of Ra^{228}, which by now has decayed considerably as a result of its 6.7-year half-life, this contribution to the total dose is also missing for our evaluation.

0016943

When we examine this list of 19 cases and their associated bone doses it is natural to ask, "What effect did this dose have on this individual ?" These cases, with one or two exceptions, were discovered to be radium cases as a result of their symptoms, so in this respect they are not representative of all radium cases. Only four of the list were without what may be considered to be radiation-induced tumors; these four are Q, I, 118, and 03473. It should be mentioned in this respect that in a current study at Argonne National Laboratory(8) some 180 former dial painters, now living, have been located, and their body burdens measured. Studies of this nature, covering radium-burdened subjects located on the basis of industrial exposure, in contrast to these who were located as a result of their symptoms, may give a clearer indication of the probability that a given dose and/or dose rate, will induce recognizable radiation damage to the human being.

In summary, the following facts have been observed from a study of these 19 individuals who carried radium for many years:

1. Two distinctly different isotope distributions exist in each of these cases who were exposed for, at most, only a few years: an intense hot spot distribution, and a remarkably uniform diffuse distribution.

2. The magnitude of the diffuse distribution is, on the average, about one-half as great as that of the uniform label, the distribution that would exist if all the activity in the bone were uniformly distributed.

3. The hot spots in these cases contain about 75 times as much activity per unit bone mass as the diffuse distribution; (the values actually range from a low of 16 to a high of 218).

4. The lifetime doses delivered to osteocytes in their lacuna reach tremendous levels in the hot spots, in some cases several hundreds of thousands of rads, while all the osteocytes in bone receive doses ranging from a few hundred to a few thousands rads. It is our hope that from these human data we can eventually pick out the significant factors and then employ them to evaluate the hazards of strontium-90 to mankind on a firm, realistic, basis.

I wish to acknowledge the support of Dr. R. J. Hasterlik of the Argonne Cancer Research Hospital and Dr. A. J. Finkel of the Argonne National Laboratory, who have contributed most of the specimens used in this study. This work has been undertaken at the suggestion of L. D. Marinelli; to him and Dr. J. H. Marshall I am indebted for continual advice and criticism.

0016944

References

1. Rowland, R. E., and J. H. Marshall. Microscopic Metabolism of Ra^{226} in Canine Bone. Argonne National Laboratory Radiological Physics Division Semiannual Report July through December 1958. ANL-5967, pp. 58-66.

2. Hoecker, F. E., and P. G. Roofe. Studies of Radium in Human Bone. Radiology 56 89-98 (1951).

3. Rowland, R. E., and J. H. Marshall. Radium in Human Bone: The Dose to Microscopic Volumes of Bone. Radiation Research 11 299-313 (1959).

4. Martland, H. S. Occupational Tumors: (6) Bones. In International Labour Office, Geneva, Occupation and Health. Supplement. October, 1959, Brochure13, pp. 1-23.

5. Aub, J. C., R. D. Evans, L. H. Hempelmann, and H. S. Martland. The Late Effects of Internally-Deposited Radioactive Materials in Man. Medicine 31 221-329 (1952).

6. Looney, W. B., R. J. Hasterlik, A. M. Brues, and E. Skirmont. A Clinical Investigation of the Chronic Effects of Radium Salts Administered Therapeutically. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 73 1006-1037 (1955).

7. Norris, W. P., T.W. Speckman, and P. F. Gustafson. Studies of the Metabolism of Radium in Man. Am. J. Roentgenol., Rad. Therapy & Nuclear Med. 73 785-802 (1955).

8. Miller, C. E., and A. J. Finkel. Unpublished information.

9. Spiers, F. W. Alpha-ray Dosage in Bone Containing Radium. Brit. J. Radiol. 26 296-301 (1953).

0016945

Appendix

Bone Turnover from Terminal Hot-Spot Data

Let us define the turnover of bone by an exponential function

$$N = xt_1 e^{-xt_2} .$$

Here N is the fraction of the total bone volume occupied by hot spots at the time of examination, t_2 years after exposure to radium; x is the yearly bone turnover rate; t_1 is the time, in years, of the exposure to radium, and $t_1 << t_2$, so xt_1% is the fraction of the labeled bone at the end of the exposure period.

The fraction of the original bone remaining after a given turnover rate has been operative for t_2 years is given by:

$$N_1 = e^{-xt_2} ,$$

From these two expressions we can calculate the fraction of the original bone remaining and the fraction of the total bone occupied by hot-spot deposits. The following table is based on an exposure (t_1) of one year and examination at the end of 30 years (t_2).

Table 6

Rate, % per year	Fraction (N) of bone that is hot spot after 30 years, %	Fraction (N_1) of original bone remaining after 30 years, %
10	0.5	5
5	1.1	22
4	1.2	30
3	1.2	40
2	1.1	55
1	0.74	74

0016946

THE RADIUM DISTRIBUTION IN THE TOOTH OF A DIAL PAINTER

R. E. Rowland

From a 55-year old dial painter (code 03473) who had been previously measured in the human body counter by C. E. Miller and assigned a body burden of 1.2μc Ra^{226}, we have obtained a single tooth.

This tooth was removed on January 26, 1959, shipped, air dried, to this laboratory and identified by the dentist as an impacted mandibular third molar (wisdom tooth). Since this woman painted dials for a two-year period, from age 19 to 21, there appeared to be a good chance that this tooth was growing during this period, and thus may have acquired considerable radium during its formation.

The radium content of this tooth was evaluated by gamma-ray analysis, using an 8" x 4" NaI(Tl) crystal in the steel room. The tooth was sealed in glass and the total gamma-ray count evaluated after the radon daughters had equilibrated with the parent Ra^{226}.

The total Ra^{226} content of this tooth was found to be 2.1×10^{-9}c, or about 0.2 per cent of the total body radium content. The calcium content of this tooth was not measured, but if we assume a value of 0.4 g (35 per cent of 1.2 g total weight), then the specific activity is about 5×10^{-9}c/g Ca. This is somewhat greater than the value for the average body specific activity, 1.2×10^{-9}c/g Ca.

Since the work of Mays et al.[1] had shown that the radon retention of beagle teeth was quite low (9 to 13 per cent), the radon retention of this tooth was measured to see if the retention in human teeth was also low. On February 6, 1959, the tooth was sealed in a glass vial and a gamma-ray spectrum obtained. Subsequently, 83 days later, after equilibrium had been attained, the spectrum was remeasured and the retention found to be 76 per cent. This value was considered to be too high, probably due to a radon leak, and the entire procedure repeated. The second evaluation, between May 6, 1959, and June 18, 1959, (a period of 43 days) yielded a value of 73 per cent.

It thus appears that the radon retention in this particular tooth, 36 years after the radium was deposited, is close to 75 per cent. Whether this is a typical value for human teeth or not, we cannot judge at the present time. It is, however, very great compared to the low retention (9 to 13 per cent) Mays measured in the beagle teeth.

In order to study the distribution of radium within this tooth, it was embedded in methyl methacrylate and sectioned longitudinally with a high-speed, water-cooled rotary saw into slabs 0.010 inches thick. These

0016947

sections were first microradiographed, and subsequently several types of autoradiographs were made from each. Satisfactory autoradiographs were obtained by using Eastman Kodak autoradiographic plates, type A, for periods from one to three months. Stripping film was also placed on some sections; a two-month exposure produced autoradiographs of very high resolution which served to localize the radium deposits. From NTA* plates on which sections had been placed for periods of three to twenty-six days, quantitative alpha-track counts were made to evaluate the radium concentrations.

A very intense line of radium is visible in the dentine, Fig. 7, and adjacent to this line is a broad area of rather uniform deposition. A low diffuse level of activity exists in the dentine between this intense line and the enamel. The enamel itself contains very little activity, yet study of the stripping film shows a thin line of alpha tracks immediately below the surface of the enamel. Such a deposition has been shown by Sognnaes[2] to be due to salivary secretion; whether such a process takes place in an impacted tooth we cannot judge.

As can be seen from the microradiograph some bone is adjacent to the tooth, but, as indicated by the autoradiograph, this bone contains very little radium. A sequestrum had been removed from this patient's left mandible during July 1958, and has been quantitatively analyzed for radium.[3] In Table 7 are listed the observed radium concentrations found in the tooth and bony sequestrum.

Table 7

Measured radium concentrations

Deposition	Bone	Tooth
Hot-spot	3.3 $\mu\mu c/mg$	
Diffuse	0.18 $\mu\mu c/mg$	
Dentine hot line		$21.1 \frac{\mu\mu c}{mg}$
Dentine diffuse		$0.088 - 0.15 \frac{\mu\mu c}{mg}$
Dentine uniform deposit		$5.6 \frac{\mu\mu c}{mg}$
Enamel diffuse		$5 \times 10^{-3} \frac{\mu\mu c}{mg}$
Enamel line		$0.3 \frac{\mu\mu c}{mg}$
Ratio: $\frac{\text{hot spot}}{\text{diffuse}}$	18	176
Ratio: $\frac{\text{diffuse}}{\text{uniform label}}$	0.9	0.6

*Eastman Kodak Co.

0016948

Fig. 7. A microradiograph (a) and an autoradiograph (b) of a 200-micron thick tooth section. Five locations where alpha-track counts have been made are indicated. These locations are identified in Table 7 as follows: 1. Dentine hot line. 2. Dentine uniform deposit. 3. Dentine diffuse. 4. Enamel diffuse. 5. Enamel line. Regions 4 and 5 are identified on the microradiograph because the low level of activity in these regions left no visible darkening on this reproduction of the original autoradiograph.

0016949

The radium concentrations in the tooth were calculated from the alpha-track counts assuming 75 per cent radon retention and an average alpha-particle range of 6.3 mg/cm^2 in both the dentine and enamel. In Table 7 are listed concentration values for five locations in the tooth; these locations are indicated in Fig. 7. The ratios of hot-spot to diffuse and diffuse to uniform label for the tooth were calculated using an average value of the observed dentine diffuse, 0.12 $\mu\mu c/mg$. The uniform label is defined as the concentration that would exist if all the radium in the body were uniformly distributed; in this case the value is 0.20 $\mu\mu c/mg$.

It is evident that the concentration found in the hot line in the tooth is considerably greater than that found in the bony sequestrum. However, it may well be that more intense radium deposits do exist in the remaining bone of this patient; the sample available for study was very small. Nevertheless, it appears that the concentration in the tooth is probably greater than any concentration in bone, for no dial painter in our previous survey had a hot-spot to diffuse ratio greater than 102,[3] the average value of this ratio for eleven dial painters being 43. (In contrast, the highest value for this ratio in patients who received radium intravenously was 218, the average value for five patients being 148.)

This high value is interpreted as follows: At the time of deposition, 36 years ago, radium substituted for calcium remarkably well, so that new mineral contained the same radium to calcium ratio as the interstital fluid with which it was in contact. Thus both in bone and teeth one initially might expect the same radium to calcium ratio. In bone, however, a slow exchange of calcium takes place between the interstital fluid and bone, which in time lowers the concentration of radium in both the hot spots and the diffuse distribution. It is this exchange, in fact, which is originally responsible for the diffuse distribution.

In the teeth, however, if this exchange took place at a very much lower rate, little loss of activity would be expected from the original concentrations. Thus, terminally, high concentrations should be found in the tooth and much lower concentrations in bone. Some exchange probably does take place within the dentine of the tooth since a diffuse distribution is apparent. If little loss has taken place from the dentine, then the diffuse distribution existing terminally is probably not greatly different in concentration from the original distribution.

References

1. Mays, C. W., M. A. Van Dilla, R. L. Floyd, and J. S. Arnold. Radon Retention in Radium-Injected Beagles. Radiation Research 8 480-489 (1958).

2. Sognnaes, R. F. Microstructure and Histochemical Characteristics of the Mineralized Tissues. Ann. N. Y. Acad. Sci. 60 545-579 (1955).

3. Rowland, R. E. Late Observations of the Distribution of Radium in the Human Skeleton. This report, p. 16.

0016950

RETENTION AND PLASMA CLEARANCE OF THE ALKALINE EARTH ELEMENTS

I. Introduction

R. E. Rowland

The retention, R, of either calcium, strontium, or radium at any time, t, after administration to a dog may be described by a power function of the form

$$R = a\,t^{-b}$$

where a and b are constants. It is significant that the exponent, b, has a value close to 0.2 for each of these elements when radioactive tracers are intravenously administered to dogs a year or so of age.

Directing our attention to the human being, we find the little information available seems to indicate that, although the retention of these elements may still be described by a power function, the value of the exponent, b, may vary with the element studied.

In order to summarize present knowledge of the retention of the alkaline earth elements, information available from rather extensive studies in dogs is reviewed and presented in Part III of this report. Data describing the plasma clearance rates of these tracers are included to show the relationship between the retention and the plasma clearance.

To overcome the lack of information found in regard to the retention and plasma clearance of barium in the dog, new data obtained from studies in this laboratory are presented in Part II; they are also included in the summary in Part III.

Finally, in Part IV, the available data describing retention and plasma clearance of these elements in the human being are discussed.

II. The Retention and Plasma Clearance of Barium in the Beagle

R. E. Rowland and C. H. Williams

In order to ascertain whether barium behaves in a manner similar to the other alkaline earth elements following intravenous injection into the dog, we measured the plasma clearance and retention of barium in two beagles. Ba^{133} was employed as the tracer. This isotope has a half-life of 7.2 years, decays by electron capture, and emits several gamma rays. Thus its

0016951

half-life is excellently suited for long retention studies, the radiation dose is minimal, for no beta particles are emitted, and the body burden is easily determined by means of scintillation counters. On the other hand, barium is a rather toxic material, and since Ba^{133} is not available carrier free, stable barium is injected with the tracer.

The injection material was in the form of $BaCl_2$ in 0.075 N HCl, at a concentration of 10μc/ml, with a stable barium level of 10 mg/ml of solution.

To test the toxicity of barium, a 4.75-kg mongrel puppy was injected with 5 mg of $BaCl_2$ in 0.1 N HCl, which was neutralized immediately before injection with 0.1 N NaOH. A total volume of 1 ml was injected into the external jugular vein over a period of 3 minutes, while the animal was anesthetized with Nembutal. This animal seemed to tolerate this level of barium quite nicely, and it appeared that we could safely inject quantities of stable barium of the order of 1 mg/kg body weight.

Two beagles were used in the study. The first, No. A22B, was 8 months old (245 days), and weighed 7.2 kg at time of injection. This dog received 6.1 μc Ba^{133}, as described above, neutralized with NaOH immediately before injection. The second dog, No. 576, weighed 10.1 kg and was of unknown age. This dog had been acquired $2\frac{1}{2}$ years earlier by the Laboratory, and was thought to be over a year old at that time, making him about 4 years old at the time of injection. This animal received 10μc Ba^{133} as previously described.

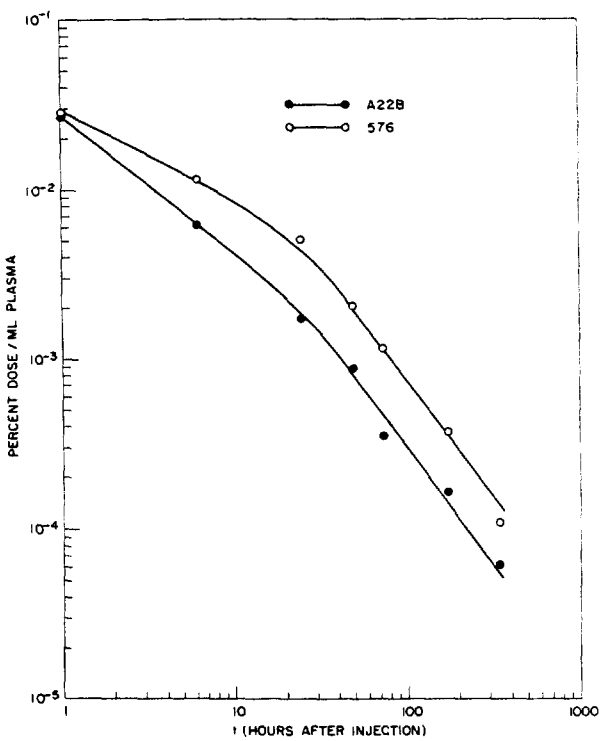

Fig. 8 Observed values of the concentration of Ba^{133} in the plasma of two beagles following intravenous injection of this isotope.

The plasma clearance studies were performed by measuring the Ba^{133} content of whole blood and assuming that the plasma content of the blood was constant. At each sampling of the blood, about 4 ml were obtained in a heparinized syringe from which 3 ml were removed, sealed in a glass vial and counted in a NaI(Tl) well counter. The observed values, plotted in Fig. 8, were calculated by comparison with two standards made from the injection solution.

The body burdens were measured by placing a 5" x 4" NaI(Tl) crystal, connected with a

256-channel analyzer in a reproducible position with respect to the dog in the steel room of the Division of Biology and Medicine. Immediately after the injection, each animal was counted, so that the original count included all of the injected activity. All subsequent counts were expressed as a fraction of the original count, and are so plotted in Fig. 9.

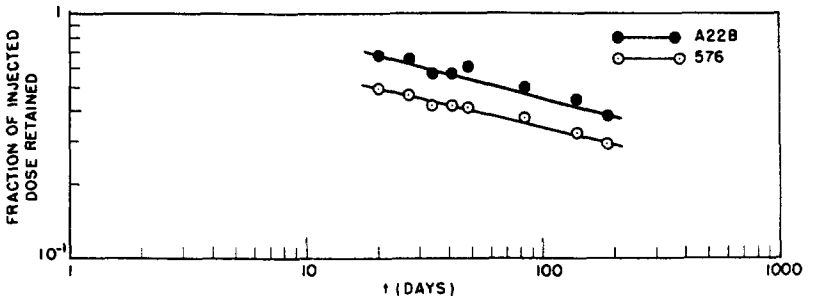

Fig. 9 Measured retention of Ba^{133} in two beagles following intravenous injection of this isotope.

Ba^{133} emits two strong gamma rays, one at 81 kev and one at 360 kev, as well as other less intense gamma rays. It was of interest to note that the shape of the spectrum, as recorded by this particular NaI(Tl) crystal, remained unchanged throughout the period of observation, namely minutes to months after the injection. This indicates that the effective absorption and scattering of the gamma radiation was essentially the same after the isotope was deposited within the bone as it was when the isotope was in the blood. Thus, in this case, the technique of recording an original burden measurement immediately after the injection, before any excretion has taken place, is valid as the 100% point, and the spectrum thus obtained may be compared directly to later spectra, even though the location of the isotope within the dog is not the same at later times.

Due to scheduling of the steel room, we were unable to count the dogs again until the 20th day after injection. After that time we were able to get weekly body burdens as long as it was necessary. This did mean, unfortunately, that we were unable to obtain the retention at one day, and thus obtain directly the value of the term, a, in the power function retention formula.

The measured values of the fractional retention are plotted for each dog in Fig. 9. It can be seen that the younger of the two animals retained more of the tracer than the elder, an observation in agreement with observations on strontium retention in dogs of various ages.(1)

The retention and the plasma clearance are expressed in Table 8 as power functions, where the time (t) is in days. The function for the retention, in terms of fractional retention, is based on the observations from 20 to 188 days. It will be noted from the value of the a term for the younger

0016953

dog, 1.36, that the data cannot be extended back to the first day as a straight line on the log-log plot. The function for plasma clearance expresses the concentration in per cent of injected dose per ml plasma after the first day. Actually the plasma data do not fit a power function well until after the second day; the value at t = 1 day was obtained by extending the straight line which fits the subsequent data back to this time.

Table 8

Retention and plasma clearance of Ba^{133} in two beagles

Dog	Age	Retention, fraction of injected dose	Plasma concentration, % of injected dose/ml plasma
A22B	245 days	$1.36\ t^{-0.24}$	$1.72 \times 10^{-3}\ t^{-1.27}$
576	~4 yr	$0.96\ t^{-0.23}$	$5.15 \times 10^{-3}\ t^{-1.28}$

The significance of these results will be discussed in Part III, where we compare the behavior of the other members of the alkaline earth family.

We wish to acknowledge the cooperation of P. F. Gustafson and S. Brar in the measurement of the body burdens of these animals. We are also extremely grateful for the assistance given by R. J. Flynn and D. D. Banister during the injections and subsequent care of the animals.

III. Retention and Plasma Clearance of the Alkaline Earth Elements in Dogs

R. E. Rowland

Excellent data on the behavior of radium and strontium in beagles are available from the studies conducted at the Radiological Laboratories at the University of Utah. In Tables 9 and 10 are listed the published power functions which describe the retention and plasma concentrations following intravenous injection into adult animals.

Table 9

Retention of the alkaline earth radioelements in dogs

Isotope	Breed	Age	Retention	Reference
Ca^{45}	Mixed	Adult	$0.76\ t^{-0.2}$	2
Sr^{90}	Beagles	17.7 mo	$0.68\ t^{-0.21}$	4
Ra^{226}	Beagles	Av = 1.3 yr	$0.787\ t^{-0.198}$	5
Ba^{133}	Beagle	245 days	$1.36\ t^{-0.24}$	This report
Ba^{133}	Beagle	~4 yr	$0.96\ t^{-0.23}$	This report

001694

Table 10

Plasma concentrations of the alkaline earths in dogs

Isotope	Breed	Age	Plasma concentration	Reference
Ca^{45}	Basenji and cocker	2 yr	$14.5 \times 10^{-3}\ t^{-1.24}$	3
Sr^{90}	Beagles	16-17 mo	$5.03 \times 10^{-3}\ t^{-1.25}$	7
Ra^{226}	Beagles	1.3 yr	$2.64 \times 10^{-3}\ t^{-1.24}$	5
Ba^{133}	Beagle	245 days	$1.72 \times 10^{-3}\ t^{-1.27}$	This report
Ba^{133}	Beagle	~4 yr	$5.15 \times 10^{-3}\ t^{-1.28}$	This report

The thesis of Maletskos[2] contains data describing the retention of Ca^{45} in dogs in which his results are described as sums of exponential functions from which is calculated a power function from the data for the retention between 20 and 100 days.

The plasma concentrations for Ca^{45} following intravenous injection into dogs were obtained from unpublished observations of Jowsey et al.[3]

As can be seen from Table 9 the retention of all of these alkaline earths may be described by power functions, and in each case the exponent is very close to 0.2. The only significant change is in the value of the a term; the variations are clearly shown in Fig. 10.

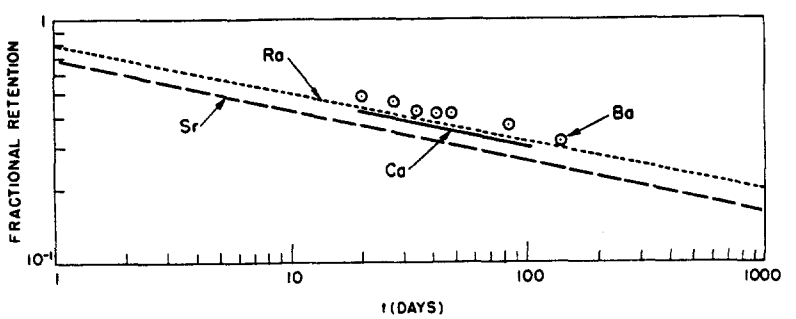

Fig. 10 Retention of four alkaline earth tracers in adult dogs. The strontium and radium curves are the published power functions of the Utah group (see text); the calcium curve is our power function fit to the data of Maletskos;[2] and the barium data are from the four-year-old beagle, No. 576.

0016955

The fact that this term is age-dependent has been previously mentioned;[1] in addition, Kornberg [6] has described an experiment with rats in which the value of this term, describing the retention of Sr^{90} after interperitoneal injection, was dependent upon the calcium content of the diet. Hence, these two variables, and perhaps others, can change the value of the constant term, a.

Kornberg also states that the retention of Sr^{90} by the rats may be described by a power function with exponent 0.2, and that this exponent was unaffected by the calcium content of the diet. This was not the case when the retention of Ca^{45} was studied, for the value of the exponent in the power function was found to be dependent on the calcium content of the diet, decreasing in magnitude with decreasing diet calcium. This is a significant difference in behavior between these two elements which has not been investigated in the dog.

When attention is given to the power function description of the plasma concentrations after the first day for these radioelements, another marked similarity is evident. In each case, as tabulated in Table 10, the plasma concentration may be described by a power function, and the exponents found for each alkaline earth isotope are very nearly equal. These data are presented in graphical form in Fig. 11 for adult dogs.

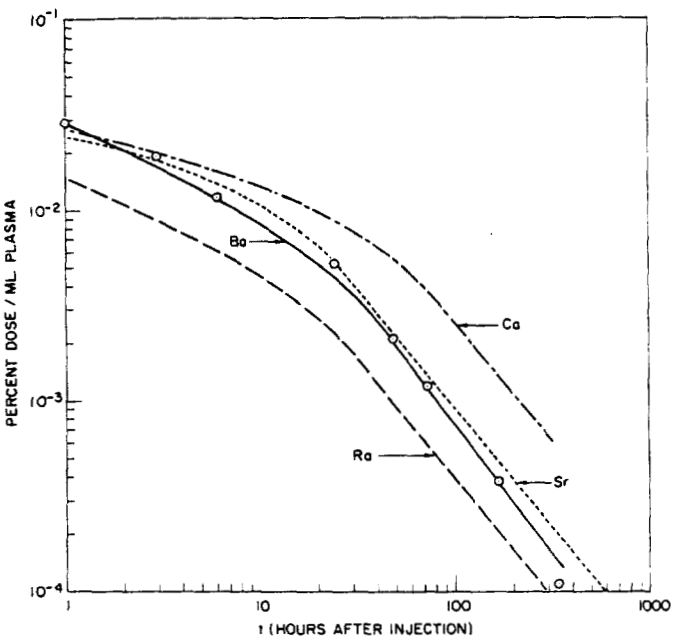

Fig. 11
Summary of the clearance of four alkaline earth tracers from the plasma of adult dogs following intravenous injection. Strontium and radium curves are those published by the Utah group (see text); the calcium curve is taken from unpublished data from our Laboratory;[3] and the barium data are from our four-year old beagle, No. 576.

Thus it is apparent that both the retention of these alkaline earth elements, when present in tracer quantities, and their clearance from the plasma, show little change from element to element. Even more impressive is the fact that the shape of the plasma clearance curve is predictable from the retention curve; that is, the value of the exponent in the power function

0016956

describing the plasma concentration is very nearly equal to the value of the exponent in the time derivative of the expression for the retention of these elements.

IV. The Retention and Plasma Clearance of the Alkaline Earths by Human Beings

R. E. Rowland

Having noted that the first derivatives of the equations describing the retention of alkaline earths in dogs are very closely related to the functions describing the plasma clearance of these elements, we inquire whether this relationship might also hold for the human being. The literature was searched for data describing the retention and plasma clearance in human beings of intravenously injected alkaline earth isotopes. These data are discussed below, grouped according to the element studied.

Calcium-45

Several authors have published data describing the removal of Ca^{45} from human plasma following intravenous injection.[8-11] These data are plotted in Fig. 12 expressed in units of per cent dose per mg Ca. The data of Bronner and Harris[11] were plotted in their paper transformed to a body weight of 35.6 kg. These have been transformed back to the original weight of the 21-year old male subject, 51.4 kg, by multiplying their data by the ratio of weights, 35.6/51.4. Also included in Fig. 12 are unpublished data from our Laboratory[13] describing the clearance of Ca^{45} from a 51-year old male radium patient, (Case BM).

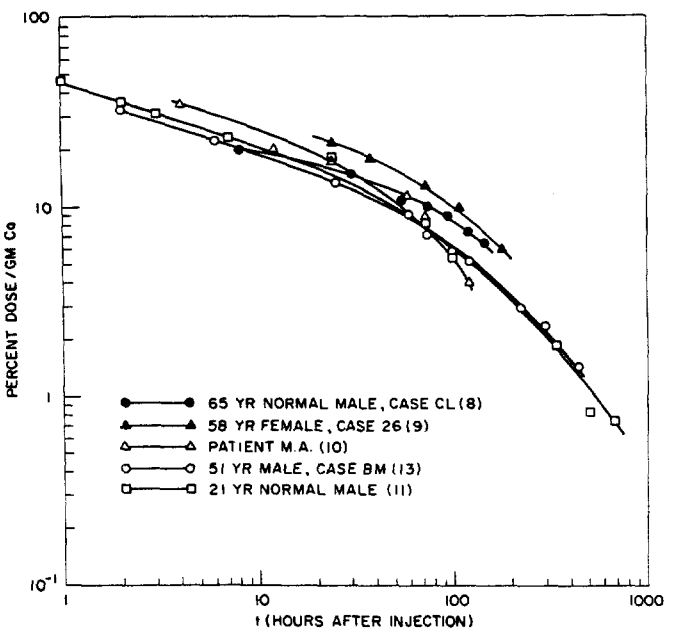

Fig. 12 A summary of the plasma clearance of Ca^{45} for five human cases, following intravenous injection of this isotope.

It will be noted from this figure that these plasma clearance curves do not become definite straight lines, indicative of a power function, during the time over which observations have been made. It appears as if plasma clearance would have to be

followed out to about 2000 hours (80 days) to prove definitely that such a behavior did or did not exist. However, if one defines the best straight line between 220 hours and 672 hours for the combined data from references 11 and 13, it appears to have a slope approximately equal to $t^{-1.2}$.

The best data found for the retention of Ca^{45} in a human subject are those of Bronner et al.,[12] who calculated the retention in a 21-year old male (same case as reference above) for 60 days from excreta studies. These are plotted in Fig. 13 and may be described by a power function

$$R = 0.96\ t^{-0.12}\ .$$

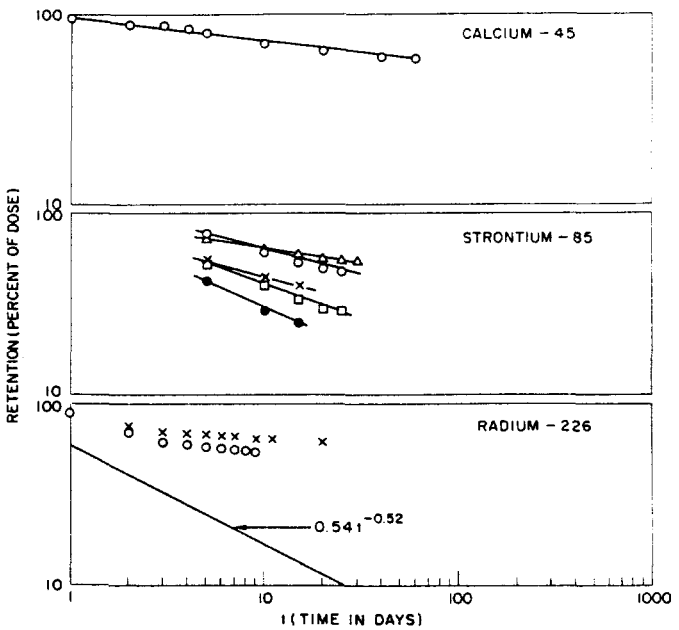

Fig. 13
The retention of calcium, strontium, and radium in human patients. The calcium data are from Bronner et al.;[12] the strontium data from Van Dilla et al.;[16] the two radium cases from Seil et al.[18] In all of these cases the retention was calculated from excreta measurements. Also plotted is the power function for the retention of radium from the observations of the Elgin State Hospital cases.[19]

From the derivative of this expression, one expects a plasma clearance described by $t^{-1.12}$, a value perhaps not greatly different from the value mentioned above, $t^{-1.2}$. While these seem to be in fair agreement, they certainly cannot be used to illustrate the equality of the first derivative of the retention equation to the slope of the plasma clearance equation.

Strontium

The removal of strontium from the plasma of human patients has been described by several authors. In Fig. 14 average values for these different groups given intravenous Sr^{85} are plotted. Two of these sets of data were kindly supplied by Dr. H. Spencer;[14,15] the third is from the work of Van Dilla et al.[16]

Also plotted in Fig. 14 is the disappearance of stable strontium from the plasma of a 40-year old, 85-kg male subject, following the injection of

100 mg Sr as SrCl. This study by Harrison et al.[17] indicates quite effectively that this larger quantity of stable strontium is cleared from the plasma at the same rate as the much smaller isotopic tracers.

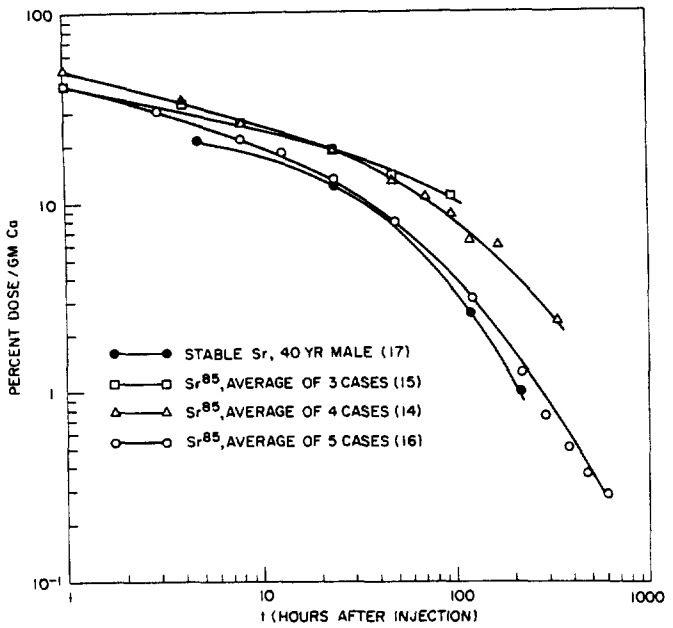

Fig. 14 Plasma concentrations following intravenous injection of strontium in human patients.

The data of Van Dilla et al.,[16] which extend out to 600 hours, seem to be approaching a straight line of slope $t^{-1.5}$, but data are needed for longer periods to verify this.

The retention of Sr^{85} in these five cases was measured during the period from 5 to 15 days, and in one case, 30 days after injection by measurement of total Sr^{85} excreted. In Fig. 13 the retention for each of these cases is plotted; each case seems to be described by a straight line over this interval, but the slopes differ from $t^{-0.16}$ to $t^{-0.44}$.

A study of the terminal distributions of Ca^{45} and Sr^{85}, as described by Schulert et al.[20] in a series of ten terminal patients who survived $\frac{1}{8}$ to 124 days after administration of the tracers, shows that a considerable fraction of the injected dose remains in the soft tissues many weeks after injection. Table 11, based on their published data, expresses the fraction of the retained dose found in the soft tissues of each patient.

Table 11

Percentage of retained calcium and strontium tracers in the soft tissues of terminal patients after intravenous administration

Patient	H.H.	S.K.	S.J.	C.C.	J.Z.	G.B.	S.G.	T.M.	A.W.	M.S.
Survival, days,	$\frac{1}{8}$	2	3	3	6	18	30	39	65	124
Ca^{45}	52	40	34	42	35	28	7.9	7.2	1.5	4.5
Sr^{85}	63	40	55	41	38	35	5.7	5.2	5	0.6

This high tissue fraction of the retained burden in man is in marked contrast to the situation in the dog. Glad et al.[1] described a double tracer

0016959

experiment with Sr^{85} and Ra^{226} in which a beagle was sacrificed 8 days after an injection of the two isotopes. At that time only 2.7% of the retained Sr^{85} and 7% of the retained Ra^{226} was in the soft tissues. This might account for some of the observed differences between the two species. Perhaps one should not look for power-law behavior in the plasma clearance rate until almost all of the body burden is deposited within the skeleton. If this were the case, then the expected relationship between the retention and plasma clearance rate would only be valid for a skeletally-bound isotope.

Thus it appears that the most interesting data describing the retention and plasma clearance of these isotopes will be found after the first 100 days. No such data are available for humans.

Radium

Radium is the isotope with which human beings have had the most experience, and it is on this experience that we base a good part of our knowledge of the effects of bone-seeking radioisotopes on man. Yet, nowhere in the literature are there any data describing the clearance of this element from human plasma.*

The retention of radium in human beings has been based on the measurements of the Elgin State Hospital patients;[19] from them has been obtained the well-known expression for their retention of radium,

$$R = 0.54\ t^{-0.52} \quad ,$$

which is plotted in Fig. 13.

Recently, Marinelli et al.[22] have described the retention and excretion of Ra^{226} from a young adult male who accidently inhaled $RaSO_4$. Their retention data, after the first 100 days, are described by a power function with $t^{-0.78}$, while the excretion is found to follow a power function with $t^{-1.78}$. These data, covering a period of 6.5 years, show definitely the relationship between the retention function and its differential, the excretion function, but only after the isotope had transferred from the lung to the skeleton.

---

* Aub et al.[21] measured the radium in the blood of a dial painter who was receiving medication in attempt to release radium from the skeleton. The woman had painted watch dials for a seven-year period, and at the time of treatment, seven years later, retained 18 μc of radium. If this had been a case of intravenous injections, the power function $R = 0.54\ t^{-0.52}$ would predict a retention of three quarters of one per cent of the injected dose ten years later. Assuming the mid-point of the exposure period as the equivalent time of injection, the injected dose would have been 2400 μc. If radium is cleared from the plasma in a manner similar to Sr^{90}, the plasma values will be described by the equation $P_t = 38\ t^{-1.5}$ per cent of dose/g Ca. Using this function the plasma activity is calculated to be 0.21×10^{-12} c/cc of blood ten years after injection. The measured values were about 1×10^{-12} c/cc blood, a factor of five greater than the predicted value. Since the medication was shown to increase the daily elimination of radium by factors of 3 to 6, this measured value may be interpreted as being remarkably close to the value predicted by a power-function behavior of the plasma concentration.

0016960

It should be noted that Marinelli et al.[23] in a description of the elimination of radium from several patients following accidental inhalation, pointed out that not all of their measured body burdens could be assigned to the skeleton or lung, so that a significant fraction of the measured radium might be in the soft tissues. This was based on the asumption that only skeletal radium released radon, and that this release was 70% of the total found. Later work of Mays et al.[24] has shown that shortly after acquisition, about 90% of canine skeletal radon is released. If this is also true for the human being, the increased radon release implies even more soft tissue radium than Marinelli had estimated and lends considerable weight to his suggestion.

One set of data is available in the literature describing the early retention of Ra^{226} following intravenous injection of this element. In 1915 Seil, Viol, and Gordon[18] described the retention of radium in a 23-year old male, following intravenous administration of 100 μc Ra^{226}. They measured the total excreta (and incidentally found a fecal to urinary ratio of about 10:1) and based their retention on this. They repeated this study on the same individual two moths later, and two sets of retention data are plotted in Fig. 13.

The curves plotted from their data can be seen to be similar in slope to that obtained for Ca^{45}; the data of Seil actually fit a power function with $t^{-0.11}$ in one case, and $t^{-0.16}$ in the other, while the Ca^{45} data are described by $t^{-0.12}$. These data contradict the Elgin patients' power function, as can be seen in Fig. 13, yet we must recall that this power function was essentially determined by the retention at 20 years and the known dose, but not on the basis of any data within the first few weeks.

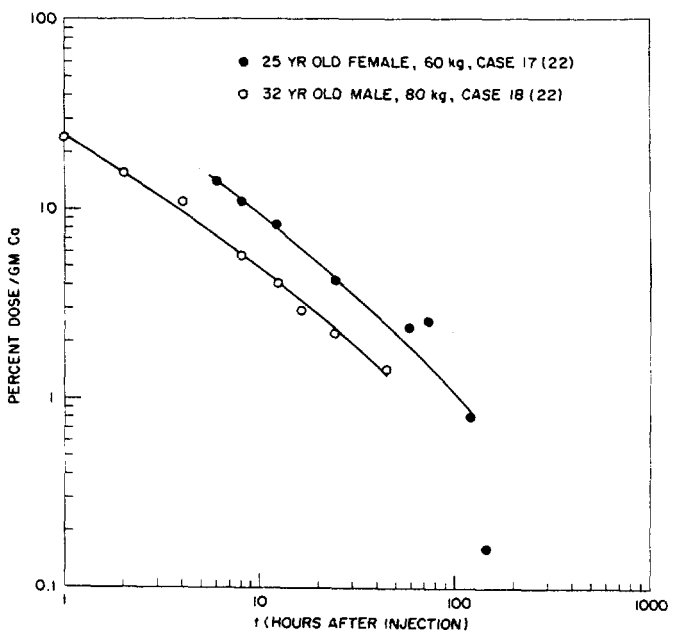

Fig. 15 Plasma concentrations following intravenous injection of Ba^{140} in human patients.

Barium

Here the only published study discovered is that of Bauer,[25] which describes the plasma clearance of Ba^{140} following an intravenous injection of $BaCl_2$ in a 25-year old woman. Bauer also kindly supplied the plasma values for a normal 32-year old male (Case 18 in the above reference). These are plotted in Fig. 15. It can be seen

0016961

that plasma measurements would have to be taken for a much longer time in order to determine whether or not a power law fits.

Summary

From this review of the retention and plasma clearance of intravenously injected tracers of the alkaline earth family, it becomes apparent that the power law formulation for the retention of these elements is valid for the dog, and that the differential of this expression has the same slope as the power law describing the plasma concentration of the tracer. In the human, however, the data seem to indicate that these relationships do not hold during the first few weeks following intravenous administration of an alkaline earth tracer. It is suggested that after the first three or four months a power law probably will describe the retention, and that its derivative, also a power law, will describe the plasma concentration or excretion function.

The lack of agreement at early times may, in part, be due to the fact that the body burden is not entirely a skeletal burden. A power law should probably be expected to describe only the loss of activity from the skeleton. Yet to be resolved is the basic question: can the retention of all of these alkaline earth elements in the human being be described by power functions with constant slope, (i.e., constant value of the exponent, b), such as is the case for the dog, or is b a function of the isotope employed?

References

1. Glad, B. W., C. W. Mays, and W. Fisher. Semiannual Progress Report, Radiobiological Laboratory, Coll. Med., Univ. Utah (Sept. 30, 1959) pp. 44-51.

2. Maletskos, C. J., A study of the dynamics of calcium metabolism in dogs. Ph.D. thesis, Massachusetts Institute of Technology (1954).

3. Jowsey, J., R. E. Rowland, J. H. Marshall, and F. C. McLean. Unpublished data.

4. Mays, C. W., D. H. Taysum, and W. Fisher. Annual Progress Report, Radiobiology Laboratory, Coll. Med., Univ. Utah (March 31, 1958) pp. 139-146.

5. Van Dilla, M. A., B. J. Stover, R. L. Floyd, D. R. Atherton, and D. H. Taysum. Radium (Ra^{226}) and Radon (Rn^{222}) metabolism in dogs. Radiation Research 8 417-437 (1958).

6. Kornberg, H. A. On the passage of pairs of elements through food chains. HW-60127 (May 1959).

7. Stover, B. J., and D. R. Atherton. Metabolism of Sr^{90} in adult beagle dogs. Proc. Soc. Exptl. Biol. Med. 99 201-205 (1958).

0016962

8. Heaney, R. P., and G. D. Whedon. Radiocalcium studies of bone formation rate in human metabolic bone disease. J. Clin. Endocrinol, and Metabolism 18 1246-67 (1958).

9. Bauer, G. C. H., A. Carlson and B. Lindquist. Bone salt metabolism in humans studied by means of radiocalcium. Act. Med. Scand. 158 143-150 (1957).

10. Bellin, J., and D. Laszlo. Metabolism and removal of Ca^{45} in man. Science 117 331 (1953).

11. Bronner, F., and R. S. Harris. Absorption and metabolism of calcium in human beings, studied with calcium-45. Ann. N.Y. Acad. Sci. 64 314-325 (1956).

12. Bronner, F., R. S. Harris, C. J. Maletskos, and C. E. Benda. Studies in calcium metabolism. The fate of intravenously injected radiocalcium in human beings. J. Clin. Invest. 35 78-88 (1956).

13. Marshall, J. H., R. E. Rowland and R. J. Hasterlik. Unpublished data.

14. Spencer, H., M. Brothers, E. Berger, H. E. Hart and D. Laszlo. Strontium-85 metabolism in man and effect of calcium on strontium excretion. Proc. Soc. Exptl. Biol. Med. 91 155-157 (1956).

15. Spencer, H., J. Samachson, B. Kabakow and D. Laszlo. Factors modifying radiostrontium excretion in man. J. Clin. Sci. 17 291-301 (1958).

16. Van Dilla, M. A., S. Wallach, and J. S. Arnold. Sr^{85} tracer studies in humans. Semiannual Progress Report, Radiobiological Laboratory, Coll. Med., Univ. Utah (Sept. 30, 1956) pp. 48-58.

17. Harrison, G. E., W. A. Raymond and H. C. Tretheway. The metabolism of strontium in man, paper No. 2. AERE-SPAR-2 (July 1955).

18. Seil, H. A., C. H. Viol and M. A. Gordon. The elimination of soluble radium salts taken intravenously and per os. Radium 5 40-44 (1915).

19. Norris, W. P., T. W. Speckman and P. F. Gustafson. Studies of the metabolism of radium in man. Am. J. Roentgenol., Rad. Therapy and Nuclear Med. 73 785-802 (1955).

20. Schulert, A. R., E. A. Peets, D. Laszlo, H. Spencer, M. Charles and J. Samachson. Comparative metabolism of strontium and calcium in man. Intern. J. Appl. Radiation and Isotopes 4 144-153 (1959).

0016963

21. Aub, J. C., R. D. Evans, D. M. Gallagher, and D. M. Tibbetts. Effects of treatment on radium and calcium metabolism in the human body. Ann. Intern. Med. 11 1443-1463 (1938).

22. Marinelli, L. D., H. F. Lucas, P. F. Gustafson and C. E. Miller. Excretion and retention of Ra^{226} in humans: A 2312-day follow-up of a single inhalation case. Argonne National Laboratory Radiological Physics Division Semiannual Report, July through December, 1958, ANL-5967, pp. 54-57.

23. Marinelli, L. D., W. P. Norris, P. F. Gustafson, and T. W. Speckman. Transport of radium sulfate from the lung and its elimination from the human body following single accidental exposures. Radiology 61 903-913 (1953).

24. Mays, C. W., M. A. Van Dilla, R. L. Floyd, and J. S. Arnold. Radon retention in radium-injected beagles. Radiation Research 8 480-489 (1958).

25. Bauer, G. C. H., A. Carlson and B. Lindquist. Metabolism of Ba^{140} in man. Acta Orth. Scand. 26 241-254 (1957).

0016964

THE CESIUM-POTASSIUM TREND IN HUMANS AS A FUNCTION OF TIME

C. E. Miller

The total-body gamma-ray spectra of 13 unexposed employees of the Laboratory chosen to be typical of the civilian population of the Chicago area have been measured periodically for Cs^{137} since March 1955.(1)

Their Cs^{137} body contents have been determined and are reported in units of $\mu\mu c$ Cs^{137} per gram of natural body potassium. The Cs/K ratios of eight subjects are presented in Table 17 for six dates during the past 18 months. It will be noted that the average value rose from 50 $\mu\mu c$ Cs^{137}/g of K in July 31, 1958 to a high of 64.4 $\mu\mu c$ Cs^{137}/g of K in June, 1959, and fell to 55 $\mu\mu c$ Cs^{137}/g K in December 1959. The data for the other five subjects are not included since they were not counted on one of the six dates. This omission does not alter the average ratio by more than 3 per cent.

Table 17

Cesium-137 Potassium-40 ratios in eight control subjects over a span of 18 months

Subject	7/31/58	11/20/58	3/19/59	6/17/59	9/14/59	12/8/59
C.L.	57	48.5	59	68.5	60	56.2
I.S.	51.5	52	59	54.6	54.5	47.4
H.M.	71.0	68.5	75.2	83.2	68.2	69.5
C.M.	43	58	76	81	64.2	62
B.O.	47	47.8	54.5	57.2	45.5	42.2
B.P.	43.5	46.2	53.5	59	54.7	53.5
R.R.	39	39.5	47	46	45.6	45.2
O.S.	48.4	51	61.8	65.5	64	63.1
Average	50	51.4	60.7	64.4	57.1	55

Mr. Ingvar Andersson, Atomic Energy Company, Stockholm, Sweden, measured 19 females during May and 27 males during June of 1959, finding a Cs^{137}/K ratio of 57 $\mu\mu c$ Cs^{137}/g K for the females and 73.5 $\mu\mu c$ Cs^{137}/g K for the males.(2) He also measured the author's content on June 1, 1959, and found a value in excellent agreement with the Argonne value. Thus, the results from these two laboratories can be compared directly.

Each of the above subjects was showered thoroughly before being counted and each wore special low-background coveralls during the measurements. A number of control subjects, measured while attired in their normal

street clothes, apparently contained from 5 to 10 per cent more Cs^{137}. Mr. Andersson likewise counted subjects while they were wearing first street clothes and then, special low-background clothing. He reported that subjects yielded a total counting rate 30 per cent higher when dressed in street clothing.

References

1. Miller, C. E., and L. D. Marinelli. In vivo Measurement of Cs^{137}. Argonne National Laboratory Radiological Physics Division Semiannual Report, January through June 1958. ANL-5919, pp 74-76.

2. Andersson, I. Gamma Radioactivity of Swedish People Measured During May and June 1959. FOA-2 Rapport, A-2051-2097, Stockholm (September 1959).

0016966

MEASUREMENT OF NATURAL URANIUM IN THE LUNGS OF A HUMAN

C. E. Miller

A sample of natural uranium was measured in the lung-equivalent phantom to determine the feasibility of routinely monitoring employees for the presence of accumulated uranium in their lungs. The physical details of the lung-equivalent phantom, and the reliability of the data obtained therewith, have been published elsewhere.(1,2)

An 8" x 4" NaI(Tl) crystal was placed 1 cm from the surface of the lung-equivalent phantom and the gamma-ray spectra obtained of background and of 2 g normal uranium in the phantom. A spectrum was also obtained with this crystal 1 cm from the surface of an uncontaminated subject's chest. The net spectra of the uncontaminated human, of background, and of 0.02 g of natural uranium are given in Fig. 41.

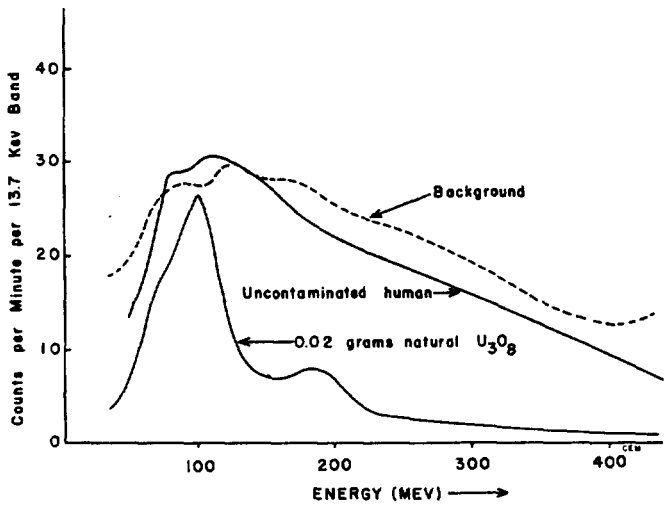

Fig. 41

The data necessary to determine the counting time needed to realize a desired accuracy, namely, the counting rates of background, of the typical human, and of 0.02 g uranium in two energy bands are given in Table 18. In calculating the standard deviations, the assumption was made that background and the unexposed human were counted for 50 minutes each. The standard deviations that would result if the subject under study were counted for 10 minutes, 50 minutes and 100 minutes were calculated from the data given in the third column. From these standard deviations and the data of the fourth column, the uncertainties of the measurements - expressed in terms of grams of natural uranium - are given in the last three columns.

A ten-minute measurement with one 8" x 4" NaI(Tl) crystal against the chest would give an uncertainty of 0.0015 g or 10 percent of maximum permissible level (MPL). Either the uncertainty could be reduced 30 percent, or the counting time could be reduced to five minutes if a second crystal were used simultaneously against the subject's back.

0016967

Table 18

Energy band	Background, c/m	Net unexposed human, c/m	Total, c/m	0.02 g U_3O_8, c/m	U_3O_8, g		
					Counting Period		
					10 min	50 min	100 min
73 kev to 127 kev	110.8	118.9	229.7	81	0.0015	0.0008	0.0007
155 kev to 195 kev	82.4	68.7	151.1	22.8	0.004	0.0022	0.0019

If the gamma-ray background of the steel room is absolutely reproducible day after day, then the subject's gross spectrum can be compared to his pre-employment gross spectrum. If the backgrounds do vary slightly, the background would have to be run each day and the subject's net spectrum compared to his pre-employment net spectrum.

The counting time necessary to determine the lung content within 10 percent of MPL is not so unreasonably long as to exclude the use of chest measurements on a semiroutine basis in feed material plants. Such measurements would be valuable, particularly in those instances where an employee has submitted a contaminated bioassay specimen. The largest expenditure of time will undoubtedly be involved in showering (decontaminating) the subject before the measurement.

References

1. Miller, C. E., H. A. May and L. D. Marinelli. The Use of Low Level Spectroscopy in the Evaluation of Radioactive Contamination of the Human Body. AECU-4156 (1959); also "Symposium on Technical Methods in Health Physics," Riso, Denmark, May 25-28, 1959, AEC Report, TID-7577, pp. 1-25.

2. Miller, C. E., and L. D. Marinelli. Low-Intensity Spectrometry of the Gamma Radiation Emitted by Human Beings. Proceedings of the Second United Nations International Conference on the Peaceful Uses of Atomic Energy. Geneva; United Nations, 1958. Vol. 23, pp. 113-123; also Progress in Nuclear Energy, Series VII, Medical Sciences, London: Pergamon Press, 1959. Vol. 2, pp. 87-104.

0016968

STATUS OF THE RADIUM DIAL PROJECT

C. E. Miller

The majority of the former radium dial painters that have been studied at Argonne National Laboratory have been employees of one of the "Radium Art Studios," which were owned by the Radium Chemical Company of Pittsburgh, Pa. This organization operated art studios in several towns in the Middle West. In order to protect the anonymity of the subjects but still permit a discussion of the status of this study, the towns where these studios were located will be designated by letters.

A "Radium Art Studio" was established in Town A in 1917 or 1918. Radium dials for watches and other instruments were painted in the A studios until late in 1921 at which time the studio moved to Town B. The studio moved from Town B to Town C in September, 1922 where it remained until 1935 at which time it was moved to New York City. The Radium Dial Company simultaneously operated another studio for about eight months during 1925 in a town which will be designated as Town D. Although the company may have owned other studios, these are the only ones pertinent to our discussion.

No employment records or lists of employees who painted radium dials have ever been available and furthermore, probably do not exist for this period of interest (1918-1930). In the past the names of former dial painters have been obtained from other former dial painters who were subjects for the ANL study. The memories of these persons were aided by group photographs taken at the studios or at social gatherings in the 1920's and which have recently come into our possession.

In June 1959, sets of city directories were finally located for three of the towns (B, C, and D) in which studios were located. Since the city directories gave the occupations of the persons listed, employment lists have been reconstructed for the period during which the canvasses for the directories were made for Towns B and C. Unfortunately, city directories were only compiled on even-numbered years; nevertheless, it is felt that the lists are very complete for a particular date during the <u>even</u> year. Evidently the canvassers obtained the employment lists directly from the studios since individuals are listed in the directory who worked at the studio but lived in an outlying town.

Town B

A total of 48 individuals were listed in the B City Directory of 1922 as being employees of the Radium Art Studio. Of these, 23 have been studied, 13 are deceased, 2 are waiting to be scheduled, 6 have not been cooperative, and 4 have not been contacted. The 23 studied subjects have supplied the

0016969

names of 6 additional individuals who painted for a short period of time but were not listed in the directory.

It is of interest to note that although the current body contents of all individuals thus far counted vary over a wide range, (0.005 μc to 1.61 μc), most of the subjects who worked at studio B have a body content of from 0.1 to 0.2 μc.

Town C

The occupation of each person listed in the 1924, 1926, 1928, and 1930 City Directories for Town C was checked and lists of the employees of the Radium Art Studio in each of these years compiled. These names obtained from the city directories, as well as the names obtained by identification of individuals in group pictures that had been taken at the studio at known times, have been integrated into an alphabetical master list of 191 different names. Of these 191 individuals, 87 have been measured, 40 are deceased, 38 have been contacted but are unwilling to cooperate, 10 are waiting to be scheduled, 10 have been located but not contacted, and the whereabouts of 8 are unknown.

This compilation has become valuable as a guide in selecting additional patients. The dates of employment that the subjects gave when interviewed at ANL, as well as the years in which their names appeared in the directories have been included in the master list. The subject's body content of radium also has been recorded. It was observed that those employees who did not work before 1926 did not have an appreciable body content of radium. As a general rule, an individual who started working after July 1925 contains at the present time less than 0.05 if not less than 0.01 microcurie of radium.

Not all individuals who worked during the period from 1922 through 1924 contain appreciable quantities of radium. However, all of those employees of Studio C who do contain from 0.1 μc to 2.4 μc did work some time during the 1922 to 1925 period. Furthermore, every subject from this studio who contains over one microcurie, as well as the majority of those who are deceased, worked during the year 1924. Unfortunately, most of the uncooperative ones worked during 1924 so a major effort will be made to obtain their assistance since they may be expected to contain at least 0.1 μc.

No list or picture has been found which can be used to identify those individuals who worked at Studio C between September 1922 (when the studio opened) until the first city directory canvass in April 1924. The five measured individuals who worked during this period contain from 0.1 μc to 0.6 μc. An effort will be made to determine whether there are other employees of this period who have not been located.

0016970

Town D

A "Radium Art Studio" was located in Town D for about eight months during 1925. Since the directories were compiled on even years, the employees were not listed in either the 1924 or 1926 directories. These employees are being located through the cooperation of the ones that have been to the Laboratory. Most of the subjects who worked in Town D and who did not transfer to Town C, when Studio D closed down, have a current body content that is less than 0.01 μc.

Town A

Recently the names of fourteen individuals who painted watches in Studio A have been obtained. Although information has been obtained relating to the home towns and relatives of some of these painters, no effort has been made to trace these subjects to date. Information that is available would indicate that individuals from this group would probably contain from 0.1 μc to 2 μc.

Conclusion

When the radium body content of the subjects is correlated with the period of employment, it is found that, as a general rule, those individuals who worked after July 1925 contain less than 10^{-8} c while those employed before this date contain 0.1 μc or more. Consequently, only those women who painted watches before July 1925 are being traced and asked to cooperate.

There are about sixteen former dial painters from Studio B and about forty from Studio C who, if possible, will be persuaded to participate. It is the goal of the Argonne group to study these 56 subjects before July 1, 1960 and thus to complete this phase of the project.

0016971

RETENTION OF RADIUM IN HUMANS FROM 21 TO 29 YEARS AFTER INTRAVENOUS ADMINISTRATION

C. E. Miller

The most reliable data on Ra^{226} excretion at long intervals following I. V. excretion are those of Norris, Speckman and Gustafson.(1) They were obtained from mental patients injected in 1931 at the rate of 10 $\mu\mu$c per week, measured first 1 to 7 months after the last injection and 6, 233, and 258 months thereafter. Although the rates of excretion, as calculated by the retention curve as of 1951-1953, were in agreement with actual measurements of fecal excretion, there have been some doubts cast on the validity of the "power law of retention" based on some shorter-term Sr^{90} studies on primates and accidentally exposed men.(2,3)

Because of the importance of the issues involved and the unique opportunity of repeating the measurements (in vivo on these patients) six years later, nine of them were measured again for Ra(B + C) with the low-level crystal spectrometer.

Owing to difficulties involved in the management of these mental cases, their measurements may not yet be precise. They are of sufficient accuracy to be compared as shown in Table 19. In the last column the 1959 Ra(B + C) estimate is computed as percent of the average of the May 1951 and July 1953 Ra values.

Table 19

Patient	May 1951		July 1953		July 1959	
	RaB + RaC μc	Radon μc	RaB + RaC μc	Radon μc	RaB + RaC μc	% Retained
A	0.57	1.03	0.6	1.15	0.49	84
J	0.32	0.66	0.24	0.66	0.22	79
K	0.22	0.70	0.22	0.70	0.36	(163)
N	0.57	1.15	0.5	1.20	0.37	69
O	0.39	0.55	0.34	0.68	0.23	62
S	0.19	0.35	0.2	0.42	0.322	(165)
T	0.27	0.71	0.32	0.77	0.29	100
U	0.19	0.39	0.22	0.36	0.17	81
Paul N	0.077	0.39	0.1	0.42	0.156	(175)
Total	2.8		2.74		2.61	94% (78%)

It is worthy of note that the average content has diminished to only 94% if all patients are included. Three of them - K, S and Paul N, reveal, however, abominably high values, well off the estimated combined error of 25%

0016972

in the 1951-1953 values and 10% or better in the 1959 estimates. If these patients are excluded - and there are good reasons to conclude that movements during measurement produced serious errors - then average decrease for the group is 78%, well within the experimental error of the value of 84% expected by the law

$$\text{Retention} = A\,t^{-b}$$

where $b \simeq 0.52$.

A final conclusion awaits exhaled radon measurements and remeasurement of the γ-ray emission from the whole body.

References

1. Norris, W. P., T. W. Speckman and P. F. Gustafson. Studies of the Metabolism of Radium in Man. Am. J. Roentgenol., Ra Therapy & Nuclear Med. 73 785-802 (May 1955).

2. Durbin, P., and H. Jones. Proceedings of Second United Nations International Conference on the Peaceful Uses of Atomic Energy. Geneva: United Nations, 1958. Vol. 23, pp. 140-141.

3. Stewart, C. G., E. Vogt, A. J. W. Hitchman and N. Jupe. Proceedings of Second United Nations International Conference on the Peaceful Uses of. Atomic Energy. Geneva: United Nations, 1958. Vol. 23, pp. 123-132.

0016973