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AUGUST, SEPTEMBER, AND OCTOBER 1951

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DIVISION OF BIOLOGICAL AND MEDICAL RESEARCH QUARTERLY REPORT, AUGUST, SEPTEMBER, OCTOBER, 1951

Editor

Austin M. Brues, Director, Division of Biological and Medical Research

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Administration

Austin M. Brues, Director
Hermann Lisco, Associate Director
Leonidas D. Marinelli, Associate Director
E. Lawrence Powers, Associate Director
Rosson L. Cardwell, Assistant to the Director

PERSONNEL CHANGES

During this quarter three junior scientists have resigned from the division: Mrs. Betty G. Redfield, who joined Dr. Barron's group in 1944; Miss Ella B. Tyree, a member of Dr. Patt's Physiology Group for five years; and Miss Margaret Sanderson, who has assisted Dr. J. Garrott Allen for six and one-half years.

Dr. B. Vincent Hall, a senior zoologist who for the past two years has carried on research under a half-time appointment, has resumed his full-time teaching schedule at the University of Illinois. He will remain on the laboratory staff as a consultant and will continue his studies on tumor radiosensitivity.

Three associate scientists have been added to the staff. A former National Cancer Institute Research Fellow at the University of Wisconsin, Dr. Robert W. Swick, will collaborate with Dr. Donald L. Buchanan's Physiological Chemistry Group on radiotoxicity studies. Dr. Herbert Kubitschek, who has a Ph.D. in physics, will advise the staff generally in physical technique and experimental design, collaborate in the neutron program, and carry on research in radiation microbiology. Mr. Clyde P. Stroud, who will shortly complete his doctorate in zoology at The University of Chicago, has joined the Neutron Radiobiology Group and will assist Dr. Howard Vogel.

BUILDING PROGRESS

The outside brickwork on the new building is essentially complete. Window frames have been installed but still require glazing and window sills. The roof fill is finished and ready for surfacing. Progress has been made on the interior with regard to flooring, wiring, piping, and air ducts. Trial painting on the ceiling of some of the laboratories has already been done.

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Radium Toxicity Program

Robert J. Hasterlik
Leonidas D. Marinelli
Austin M. Brues
William B. Looney
William P. Norris
Andrew H. Stehney
Charles E. Miller

PROGRESS REPORT: RADIUM TOXICITY PROGRAM

L. D. Marinelli, P. F. Gustafson, R. E. Rowland, and C. E. Miller

In connection with the Radium Toxicity Program, this group has undertaken extensive study on the measurement of the γ activity in human beings which is due to the nonemanating fraction of the radium present in the body. After preliminary studies on γ-ray activity originating in the surroundings (background), it became apparent that in order to investigate individuals containing less than one μ g of Ra within reasonable time, it would be necessary to rely on NaI scintillation counters. Experiments were performed to utilize the spectrometric potentialities of this counter to a) increase the ratio of the patient signal to the background activity noise, and b) to ascertain whether our estimates on any single individual would prove independent of the pulse size band selected for measurement.

A survey of different rooms at this laboratory and at the Institute of Radiobiology of The University of Chicago showed conclusively that the signal (one μg Ra at one meter) to noise (background) ratio could be substantially improved in a lead-lined room (1/8 to 1/2-inch thickness) by utilizing pulses corresponding to γ rays of energy lower than 370 kev. Selection of this energy range did not decrease materially the total net counting rate available.

Studies of the response of the counter to radium imbedded in presdwood or water phantoms indicated that, on account of scattering, the counting rate depended in a complex manner on the "depth"* at which the Ra was located, and to a much lesser extent, on the total thickness of the phantom. When the counting rate is expressed as function of depth (keeping the back of phantom to counter distance equal to one meter) a relationship results possessing striking similarity to "depth dose" curves obtained with therapeutic X rays in presdwood or water phantoms. The curve cannot be

*Hereinafter depth denotes the distance between the radium source and the face of the phantom nearest to the detector.

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expressed in terms of a function of the form

$$N_4 \quad \frac{e^{-\mu d}}{x^2}$$

where

μ = coefficient of absorption per cm of presdwood or water (broad beam)

d = depth in phantom in cm

x = source to counter distance in meters

N_4 = reading of the Ra source at one meter.

The ratios of the experimental counting curve to the $N_4 e^{-\mu d}/x^2$ curve vary with the depth of the radium and with the pulse band selected for counting. In Figure 19, A shows these ratios for pulses of γ-ray energy less than 370 kev and Figure 19 B shows the same function where pulses of energy higher than 370 kev are counted. The figure refers to phantoms of 30 x 30 cm cross section and depth of 20 and 28.7 cm, respectively. These findings are consistent with the theory of the Compton effect and point out that smaller corrections, and hence more accurate results, are obtained if only the hard radiation is counted.

In practice, however, pulses of energy greater than 370 kev represent only a rather small fraction ($\sim$1/5) of the total available for counting. Moreover, owing to the small thickness of lead that can be economically applied to a counting room, the signal to background ratio is uncomfortably small whenever radium contents are lower than one μg. These two factors contribute to large statistical errors if counting times are limited to suit the patient's comfort.

It has been possible, nevertheless, to obtain satisfactory precision with both methods by counting repeatedly four patients on different days and by selecting patients with high Ra content.

In order to estimate the radium burden it has been necessary to make some assumptions. They are:

1) The average absorption in the human body is equal to that obtained with a presdwood or water phantom. This is justified on the basis of extensive work reported in the radiological literature.

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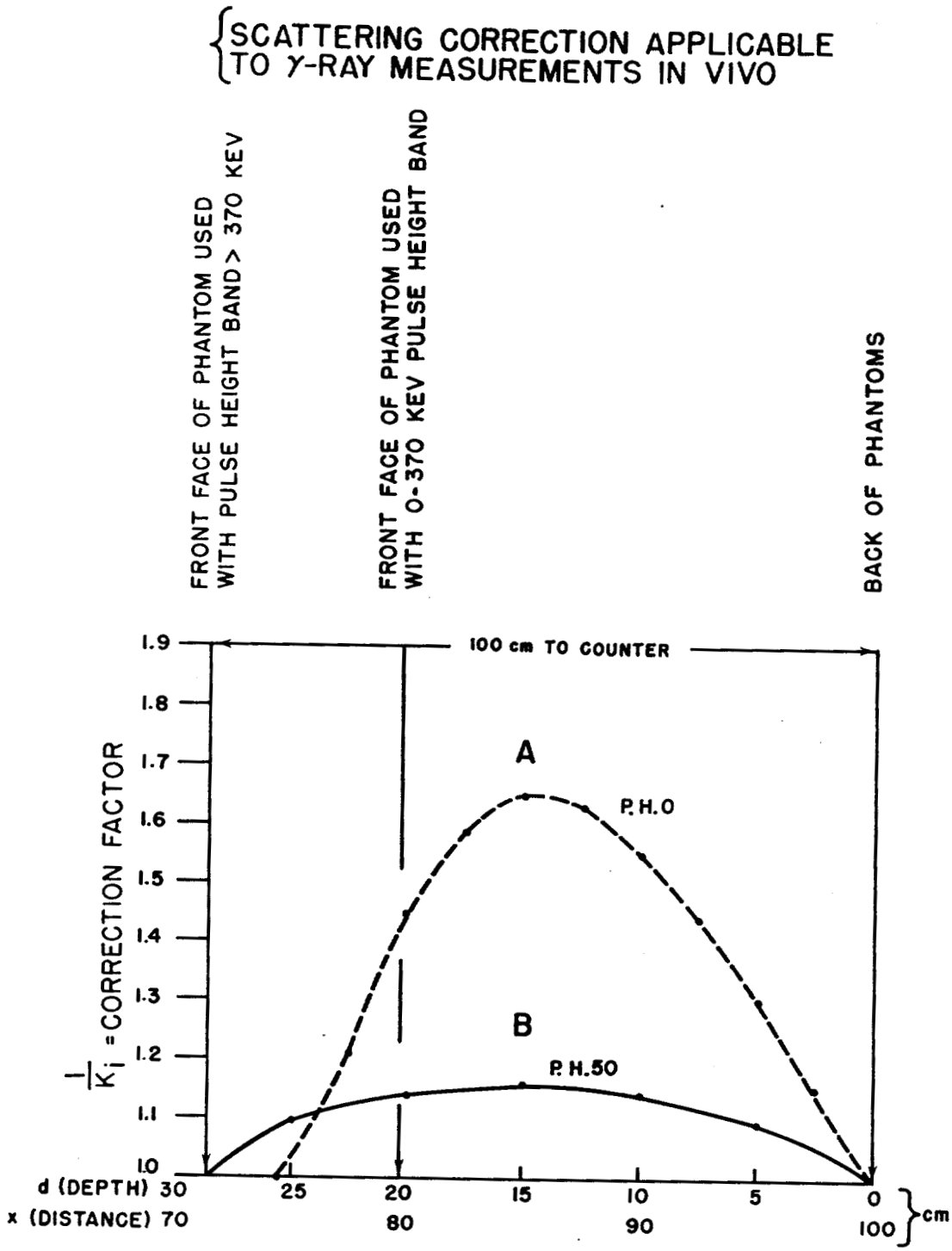

Figure 19. Correction factor K_i to be applied to formula (1) in the form $K = \sqrt{K_i K_{i'}}$ in order to account for effect of body scatter in measurements of γ-ray activity in vivo. The ordinates represent typical ratios of experimental counting rates obtained by moving a Ra source within a presdwood phantom to the value of $N_4 x^{-2} e^{-\mu d}$ which holds only for radiation originating directly from the Ra source.

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2) The average depth of radium in the body is five cm from the surface. This assumption is consistent with our knowledge of Ra localization in chronic cases and does not alter our measurements to any practical extent even if it were in considerable error.

Following Evans[1], the radium content can be written as

$$\mu g = K(1 - \frac{d}{x}) \ (N_1 N_2 / N_4^2 e^{-\mu d})^{1/2} \qquad (1)$$

where:

$K \simeq 0.7$ (scattering factor for counting below 370 kev)

$K \simeq 0.93$ (scattering factor for counting above 370 kev)

both of these values obtained as the square root of product the values obtained from graphs such as shown in Figure 19 (interpolated for phantom thicknesses equal to the average thickness of the patient) and taken at five cm from either end of the phantom.

d = average thickness of patient in meters.

x = standard distance from back of patient to detector; i.e., one meter.

N_1 = reading of patient facing counter and placed on arc of circle one meter in diameter with center at the counter.

N_2 = same as N_1 but with patient facing away from counter.

N_4 = counting rate of one μg of Ra at one meter from counter.

In a group of six patients measured with the two pulse bands the following results were obtained:

Patient	Equivalent γ-ray activity (μg)		Ratio of A/B
	Pulses <370 kev (A)	Pulses >370 kev (B)	
C.S.	.54	.61	.88
D.A	2.07	2.22	.93
A.M.	.54	.57	.95
C.L.	1.20	1.34	.90
A.D.	5.12	4.80	1.07
D.D.	2.44	2.19	1.11
AVERAGE			0.97

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These experiments have given us a certain confidence in the correctness (±15%) of our method which, in addition, has yielded results consistent also with the estimates of Rn in the breath exhaled by these patients.*

Estimates of γ-ray activity to date have been extended to 34 patients, 28 of which, however, have been tested either at one meter (pulse band 0 to 370 kev) or in a standard sitting position. With both pulse bands in the latter case the significance of the readings was established by comparison with the six patients whose Ra burden was established by the absolute method.

In addition, special measurements on Ra localization have been made on five human beings who had inhaled radium as a result of a single accident. The measurements consisted of readings in a lead-lined room with a scintillation counter at 10 cm distance from the back of the patient seated on a "standard" chair. Two sets of readings were taken with the crystal at 64 cm and 59 cm from the floor. The former corresponded to the 12th lumbar vertebra and the latter to the height used in preliminary tests at the site of the accident. Two patients were measured on the cot at 100-cm distance by the absolute technique, in order to establish the significance of the chair readings for this particular localization. On the basis of this, the estimated (±15%) nonemanating and emanating fraction of the radium burden is as follows:

Patient	γ ray (μg)	Emanating Ra* (μg)	Rn fraction (% of total)	Remarks
Ras	.15	.05	25	Absolute technique
Car	.19	.024	11	Absolute technique
Cha	.11	.013	10	Chair technique
Sch	.09	.015	14.0	Chair technique
Kue	.07	.025	26.0	Chair technique

It should be noted that the Rn fraction for this group is radically different from the value of 0.69 obtained in the chronic series.* Scanning of the patients with our setup, built in record time** for the occasion and covering on the average a 15 cm diameter field, revealed that essentially all

*To be reported by Dr. W. P. Norris.

*The splendid assistance of J. Kotora is hereby acknowledged.

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γ-ray activity was confined to a cube 20 cm x 20 cm x 20 cm located axially in the body, in approximate anterior-posterior symmetry and with center located at 40 cm from the top of the cranium.

It is planned to keep these individuals under observation for some time in order to study the transport of Ra from the lung.

LITERATURE CITED

1. Evans, R. D. 1937. Radium poisoning. II. The quantitative determination of the radium content in the radium elimination rate for living persons. Am. J. Roentgenol. Radium Therapy, 37:368-378.

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PROGRESS REPORT: MEDICAL ASPECTS OF THE RADIUM TOXICITY PROGRAM

W. B. Looney

Up to the present clinical studies have been made on 36 patients. One 68-year-old male given radium chloride intramuscularly 25 years ago has an estimated total-body radium of 13.9 μg. This is the largest amount of radium found in any patient studied thus far; complete roentgenographs, however, indicated only minimal skeletal changes.

Two radium dial workers in a nearby town have been studied. According to the plant manager radium has been the only alpha emitter used in the manufacture of luminous dials since the founding of the company. In one patient, 44 years old, who worked from ages 16 to 27 and has an estimated total-body radium of 0.68 μg, small areas of decreased density were observed in the skull and minimal streaked areas of decreased density in the left radius and fibulae.

The other radium dial worker is 45 years of age and has worked continuously since 1924. She has an estimated total-body radium of 1.7 μg. This patient broke her left femur in 1948, and it was refractured four months later as the result of a fall on crutches. It was one year before she was able to return to her normal duties. Roentgenographs (October 10, 1951) revealed areas of decreased density in the bones of the skull, radii, ulnae, left tibia, and fibulae, and left metatarsals. There was mottling of the head of the left femur and a healed fracture of the shaft.

The patient with a fibrosarcoma of the left foot described in earlier reports (estimated total-body radium content 1.3 μg) died August 15, 1951 with generalized metastatic disease.[1]

LITERATURE CITED

1. Looney, W. B. 1951. Radium toxicity: Clinical studies on 24 patients. ANL-4625. P. 55

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Radiochemistry

William P. Norris
Walter E. Kisieleski
Richard Sato
Lois A. Woodruff
Blanche J. Lawrence

PROGRESS REPORT: RADIOCHEMISTRY

W. P. Norris

Radium toxicity and metabolism (T. W. Speckman and M. Myrick). The continued work in radium toxicity and metabolism during this quarter has included observations of both human and animal material. Determinations of exhaled radon have been used to estimate the equivalent emanating radium in cases of radium poisoning in humans. These measurements, coupled with determinations by γ-ray measurement of the nonemanating fraction (by L. D. Marinelli and P. F. Gustafson of this laboratory), indicate the total-body radium content and likewise show the emanating fraction to be approximately 70 per cent, substantially higher than the value of 45 per cent reported by Evans.[1] Of interest in this regard were the observations of personnel exposed to radium sulfate dust in a recent industrial mishap. As long as a month after the exposure the percentage of total-body radium appearing as exhaled radon was 25 per cent or less in all the individuals tested. These findings, are further confirmed by those of Marinelli which show unusually high γ activity in the lung region, indicate the effective low solubility of radium sulfate in the lung and the consequent retention of radon.

Some autopsy material has become available and is being used in various ways to study the distribution of radium. Also a number of analyses have been done to determine the radium content of blood and excreta. Alpha counting leaves much to be desired in this work, and alternative methods of measurement are being investigated.

Essentially all observations on human beings are being paralleled by experiments with animals in order to observe the early period.

Separation of ions by electromigration and/or chromatography (R. Sato and W. E. Kisieleski). The separation of trace amounts of inorganic ions either by electromigration in a moist filter paper cell or by combination of electromigration with chromatography which results in differentiation in two directions has been carried to the point where clean, quantitative separations may be achieved in the majority of cases.[2] Dr. H. Strain of the Chemistry Division, Argonne National Laboratory, collaborated in this work.

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The use of electromigration in the separation of complex ions and proteins has given promising results. It would appear that the equipment will require some modification before optimum results are achieved.

Determinations of Ca^{40} and Ca^{45} (Blanche J. Lawrence). Techniques for the analysis of Ca^{45} associated with either macro or micro quantities of Ca^{40} have been developed to a point of high precision and accuracy. Calcium is precipitated as the oxalate and filtered onto the sintered plate of a modified Gooch crucible where it is counted to determine Ca^{45}. The precipitate is then dissolved in $HClO_4$ and titrated with cerate to determine total calcium. The method is presently being prepared for publication.

LITERATURE CITED

1. Evans, R. D. 1937. Radium poisoning. II. The quantitative determination of the radium content in the radium elimination rate for living persons. Am. J. Roentgenol. Radium Therapy, 37:368-378.

2. Sato, T. R., W. P. Norris, and H. H. Strain. 1951. Apparatus for continuous electrochromatography. Ind. Eng. Chem. Submitted for publication.

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